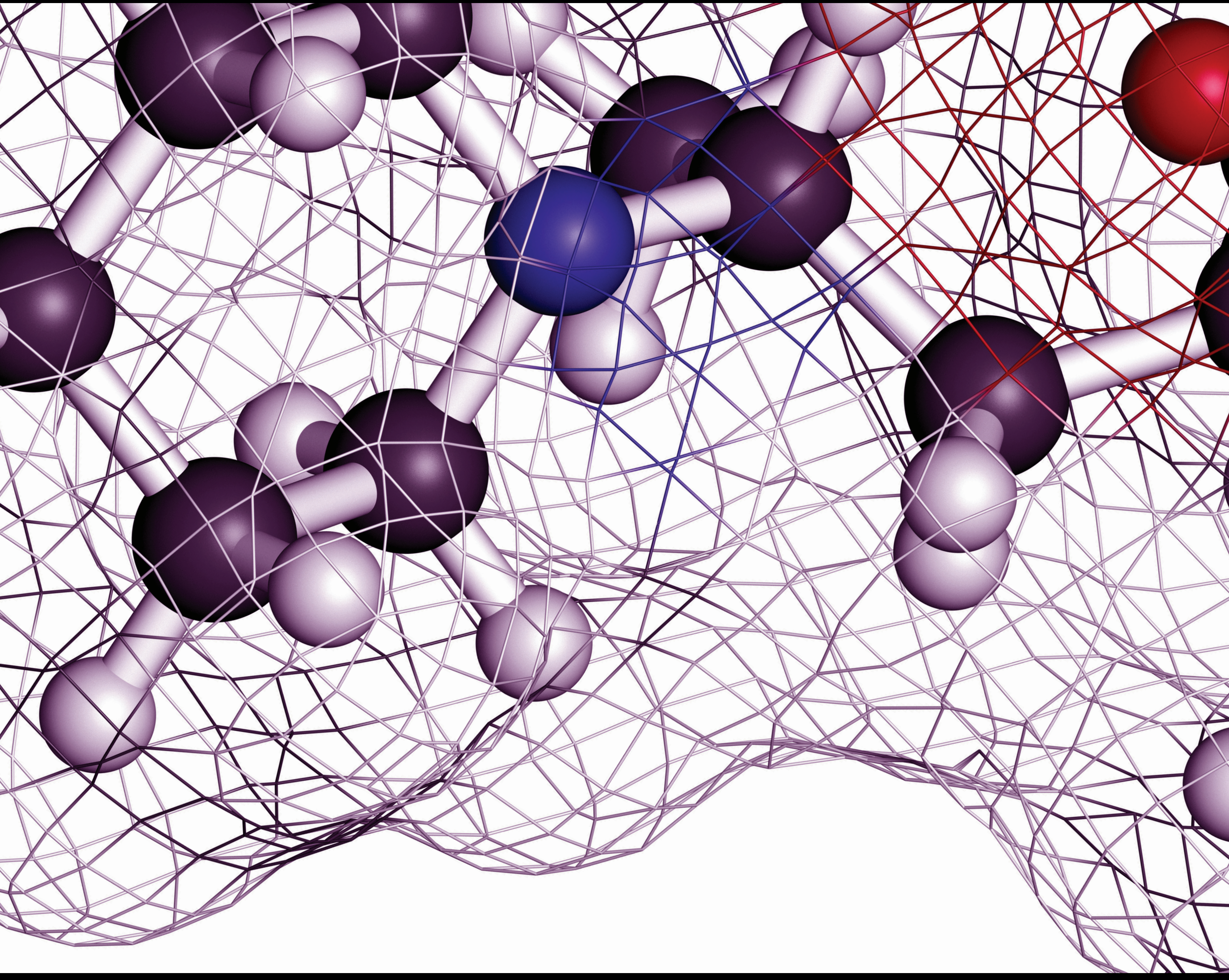
Pain Research and Management

Pain of Temporomandibular Disorders: From Etiology to Management

Lead Guest Editor: Mieszko Wieckiewicz
Guest Editors: Shiau Yuh-Yuan and Klaus Boening



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Editorial Board

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Editorial

Pain of Temporomandibular Disorders: From Etiology to Management

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Temporomandibular disorders (TMD) are musculoskeletal disorders with primary symptoms of pain localized to the face and temple and limitation of jaw function [1]. TMD is the second most common musculoskeletal disorder after chronic low-back pain causing pain and disability of the body [2]. TMD is not a disease entity but rather a broad term comprising many disease entities. In recent years, there has been a very intensive and varied development of research on etiology, epidemiology, symptomatology, and management of TMD-related pain. According to the widely used definition introduced by the International Association for the Study of Pain, pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [3].

The symptoms of TMD can include pain or tenderness of temporomandibular joints (TMJs) area, clicking, popping, or crepitus in the TMJs, limited jaw movements, masticatory muscle pain, headache, tinnitus, impaired hearing, and earache. It had been proved that TMD are related to multiple causes and biopsychosocial model which is a broad view that attributes disease outcome to the intricate, variable interaction of biological factors, psychological factors, and social factors [4].

The understanding and management of TMD pain usually require a multidisciplinary approach and that is the main target of this special issue. Interdisciplinary therapeutic possibilities should concern TMJs and neuromuscular structures of the masticatory system and supportive tissues at head and neck areas. Moreover, the involvement of psychological and social factors makes physical approaches insufficient. Based on this understanding, the editors of this special issue have invited researchers with wide scope of knowledge and study on pain of TMD.

Original and review articles related to the pain of TMD associated with basic and clinical studies on multiple branches of medicine and novelty in management have been welcome. The published papers introduce the multidisciplinary problem to the reader. The aim of this issue was also to show the novelties in management of TMD pain. A group of articles describe the etiology of the disorders, as well as its epidemiology, accurate diagnostics, and management methods. The special issue aims at collecting a multidisciplinary approach on the pain of temporomandibular disorders in basic and clinical aspects. Current views included in this issue will hopefully allow us to assess a perspective of the TMD-related pain and to develop and familiarize with new research related to the most recent multidisciplinary view points.

Mieszko Wieckiewicz
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Klaus Boening

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Clinical Study

Comparison between Collagen and Lidocaine Intramuscular Injections in Terms of Their Efficiency in Decreasing Myofascial Pain within Masseter Muscles: A Randomized, Single-Blind Controlled Trial

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Background and Objective. A novel option for myofascial pain (MFP) management and muscle regeneration is intramuscular collagen injections. The aim of the study was to evaluate the efficiency of intramuscular injections of collagen and lidocaine in decreasing MFP within masseter muscles. *Methods*. Myofascial pain within masseter muscles was diagnosed on the basis of the Diagnostic Criteria for Temporomandibular Disorders (II.1.A. 2 and 3). A total of 43 patients with diagnosed MFP within masseter muscles were enrolled to the study (17 male and 26 female, 40 ± 3.8 years old) and randomly divided into three groups. The first group received injections using 2 ml of collagen MD Muscle (Guna), the second group received 2 ml of 2% lidocaine without a vasoconstrictor, and the third group 2 ml of saline as a control (0.9% NaCl). All patients received repeated injections at one-week intervals (days 0 and 7). The visual analogue scale was used to determine pain intensity changes during each follow-up visit (days 0, 7, and 14) in each group. The masseter muscle activity was measured on each visit (days 0, 7, and 14) with surface electromyography (sEMG) (Neurobit Optima 4, Neurobit Systems). *Results*. We found that sEMG masseter muscle activity was significantly decreased in Group I (59.2%), less in Group II (39.3%), and least in Group III (14%). Pain intensity reduction was 53.75% in Group I, 25% in Group II, and 20.1% in Group III. *Conclusions*. The study confirmed that intramuscular injection of collagen is a more efficient method for reducing myofascial pain within masseter muscles than intramuscular injection of lidocaine.

1. Introduction

Myofascial pain within masticatory muscles is a popular muscle disorder among patients attending dental practitioners [1–3]. Mental status and bruxism may lead to excessive muscle effort and development of muscle pain [4–7]. The main syndrome of myofascial pain is a trigger point, which is a hard, palpable, localized nodule, painful on compression [8]. Myofascial pain is a symptom of muscle damage. Muscle regeneration is similar to muscle embryonic cell development.

Muscle injury can occur as a result of disease (dystrophy), contact with miotoxins, trauma, contusion, ischemia, temperature, and excessive muscle contraction [9]. Eccentric muscle contraction results in muscle damage and inflammation, resulting in muscle collagen accumulation, and occurs during the repair process of exercise-induced muscle injury [10]. Mechanical stress and cryolesions also induce collagen accumulation and production. During mechanical damage to muscles, sarcomere myofilaments are disrupted, the sarcolemma is damaged and fibers disintegrate [9]. After the muscle damage, interleukin-6 is released, and it induces fibroblasts to produce collagen [11, 12]. During muscle regeneration, stem cells proliferate and undergo differentiation into myoblast cells [13]. Simons' integrated hypothesis postulates energy crisis as the reason for the initial sarcomere contracture, which leads to increased metabolism and decreased capillary blood circulation [14]. The result is local hypoxia, muscle damage, and inflammatory mediators releasing, for example, catecholamines, neuropeptides, and cytokines. Then, muscle inflammation, persistent pain, and myofascial tenderness begin. Contraction knots are formed, as an effect of local injury, ischemia, and fiber lock. The blood flow around and within the trigger point is diminished. High-resistance and retrograde diastolic blood flow in the trigger point have been observed [14]. Vascular resistance is caused by musculature contracture and vessel compression. The effect is pain, tenderness, and nodularity of muscle tissue. Järvholm et al. have found that intramuscular pressure in trigger points decreased local blood flow and caused local ischemia [15]. Many trigger points localized together form myogelosis, where the level of oxygen is extremely low. In this mechanism, the level of ATP (adenosine triphosphate) is decreased. ATP is necessary for breaking the bonds between muscle myofilaments after muscle contracture. A low level of oxygen is a potent factor for bradykinin release [14]. Current approaches for trigger point management are needling, injections, and deep massage.

Lengthening contractions or endurance training may cause skeletal muscle damage, especially to the extracellular matrix (ECM) and muscle fibers. Collagen synthesis in muscle tissue, after damage, is elevated for 3 days [16]. Procollagen is synthesized in the endoplasmic reticulum and is extruded into the ECM. Premature collagen (tropocollagen) is then altered into the matured collagen protein. ECM is essential in muscle cell development and regeneration, and it is an important cell surrounding, which coordinates cell behavior and communication [17]. Interactions between muscle cells and ECM build a very important network in tissues undergoing mechanical stress. The lack of collagen in ECM is a reason for inappropriate muscle regeneration and muscle dystrophies. The lower the number of newly formed microfibers, the fewer the cross-sectional connections and the lower the produced muscle mass [18]. Collagen is strictly needed for proper muscle regeneration. Collagen decreases apoptosis and increases myoblast proliferation [18]. The extracellular matrix is also necessary for growth factors (PDGF and TGFβs) which regulate the process of stem cell proliferation and differentiation. During healing after injury, ECM is remodeled. Undesired substitutions occur, when fibrotic, connective tissue substitutes for muscle cells. Excessive production of fibrillar collagen can produce a scar, instead of newly formed muscle tissue. In the beginning of the regeneration process, a thick collagen network is formed to locate myogenic cells [18]. Collagen extrusion is mainly performed by interstitial fibroblasts.

Muscle elastic modulus ($E = 12\,\text{kPa}$) may increase ($E > 18\,\text{kPa}$) after the muscle injury, during the regeneration phase, because of the higher muscle stiffness and collagen network organization [18]. In chronic temporomandibular disorders, we can observe a reorganization of muscle activity resulting in poor muscle function [19].

Muscle regeneration is performed by stem cells. Myogenic cells are located under the basal lamina surrounding myofibers. Muscle-specific stem cells—satellite cells—precursors of mature myofibers, are responsible for skeletal muscle regeneration after repeated injuries [20]. Stem cells are regulated by collagen VI: biochemical signals, promoting proliferation, and differentiation of newly formed muscle cells.

Collagen is a molecule in ECM that plays an important role in building the base membrane of the myofiber endomysium in skeletal muscles [21]. Collagen is a major protein in ECM of skeletal muscles that builds networks and also present in the nervous system (in endo, peri, and epineurium of Schwann cells) and maintains proper nerve myelination [22, 23]. Collagen is provided to the muscles by interstitial fibroblast cells. Fibroblasts synthetize collagen I and collagen III at different ratios during muscle regeneration. Cultured fibroblasts secrete and deposit collagen VI with beneficial effects on muscle stiffness. Fibroblasts are the main source of collagen and could become an attractive option for medical therapy in the future. Collagen also provides biochemical signals for satellite cells to proliferate into myocells [18]. It is the main component of ECM, needed for muscle regeneration. Excess collagen production can result in cicatrization [24]. Lehto et al. analyzed collagen synthesis in gastrocnemius muscle in rats [25]. 14C-labeled proline was administered intraperitoneally to animal calves. The radioactivity of muscle probes was measured by liquid scintillation spectrophotometry. The uptake of labeled collagen and glycosaminoglycans showed the exact regeneration period: between 10 and 14 days after an injury. The uptake decreased after 21 days post injury. A collagen matrix is injected to guide muscle cell regeneration and differentiation.

There are three phases of muscle regeneration: myofiber breakdown and inflammation; stem cell activation and proliferation; and differentiation into new myofibers [26]. Muscle regeneration can form either a functionally efficient muscle contractile system or a scar [27, 28]. First, necrosis takes place and myofibers are disrupted; the blood level of muscle protein is increased (creatine kinase and troponin). The first inflammatory cells in injured muscle are neutrophils, as soon as 1–6 h after the muscle damage [29, 30]. The next group of inflammatory cells is macrophages that appear in injured tissue after 48 h. The necessary condition for muscle regeneration is blood supply with a bloodstream. Revascularization is modulated by many endocrine factors, for example, the fibroblast growth factor (FGF), which has angiogenic properties. Transforming growth factor-beta (TGFβs) stimulates collagen production, proteoglycans, fibronectin, and ECM protein production and angiogenesis [25]. The platelet-derived growth factor (PDGF) also influences angiogenesis *in vivo*.

Lidocainum hydrochloricum 2% is used as a popular analgesic drug in dentistry and cardiology as an antiarrhythmic drug. The mechanism of action is one where sodium channels are blocked causing a decrease in the heart rhythm rate. Neurons cannot send signals to the central nervous system. This was discovered in 1946, and since then, it has been one of the most popular and essential drugs in medicine. It is used for infiltration, blocks, and surface tissue anesthesia. Lidocaine has a very fast onset of action: approximately 1.5 min. It is often used in combination with adrenaline to prolong the effect of anesthesia. In trigger point therapy, it is used without vasoconstrictor agents, because of the risk of ischemic necrosis. The length of analgesia duration is about 30 min to 3 hours. Lidocaine can also be used as an inhalation drug to prevent coughing, especially during intubation. Some patients can be unresponsive to lidocaine, for example, those with Ehlers–Danlos syndrome [31].

The aim of the study was to evaluate the efficiency of intramuscular injections of collagen and lidocaine in reducing MFP within masseter muscles.

2. Materials and Methods

2.1. Study Participants. Within a group of 102 Caucasian patients who had been referred to the Department of Temporomandibular Disorders at the Medical University of Silesia in Katowice, Poland, the principal investigator (ANB) found 50 with MFP within masseter muscles who were eligible and included in this trial.

The inclusion criteria were the following:

(1) Age ≥18 and ≤80

(2) Presence of myofascial pain and myofascial pain with referral within masseter muscles according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) (II.1.A. 2 and 3) [32]

(3) Presence of trigger points within masseter muscles under palpation (latent or active)

(4) Patients' agreement for taking part into the research study.

The exclusion criteria were the following:

(1) Patients undergoing orthodontic treatment

(2) Patients being treated with or addicted to analgesic drugs and/or drugs that affect muscle function

(3) Patients after traumas to the head and neck region in the previous 2 years

(4) Edentulous patients and patients with unsupported occlusal contacts in the lateral region of the occlusal arches

(5) Patients being treated by neurologist for neurological disorders and/or neuropathic pain and/or headache

(6) Patients after radiotherapy

(7) Pain of dental origin

(8) Pregnancy or lactation

(9) Presence of malignancy

(10) Presence of severe mental disorders

(11) Drug and/or alcohol addiction

(12) Presence of contraindications for injection therapy

(13) Patients with needle phobia

(14) Presence of hypersensitivity to substances to be used in the study.

This study was approved by the Bioethical Committee of the Medical University of Silesia in Katowice, Poland (KNW/0022/KB1/61/I/15), and retrospectively registered at ClinicalTrials.gov NCT03323567 (27 October 2017). The study was performed in accordance with the Declaration of Helsinki as well as the International Conference on Harmonisation: Guidelines for Good Clinical Practice. All included patients gave their consent to participate in the study and received verbal and written information describing the trial.

2.2. Study Protocol. This randomized, controlled, single-blind, three-arm trial followed the consolidated standards of reporting trials (CONSORT) statement [33] and was performed between 10 January 2016 and 12 December 2017 in the Department of Temporomandibular Disorders at the Medical University of Silesia in Katowice, Poland. The patients were divided randomly into three groups: Collagen (Group I, $n = 18$), Lidocaine (Group II, $n = 15$), and Saline (Group III, $n = 17$). The randomization was carried out by a researcher who was not involved in the qualification of patients, conduct of interventions, or collection of data (MW). After allocation, 7 patients declined to participate. Consequently, the groups were structured as follows: Group I, $n = 15$, 5 males, 10 females, mean age 37.2 ± 4.97; Group II, $n = 13$, 5 males, 8 females, mean age 42.8 ± 0.98; and Group III, $n = 15$, 7 males, 8 females, mean age 40.3 ± 1.18. Patients were not informed what substance they would be injected. The injections were performed by a principal investigator (ANB) who knew what substance she was administering.

The trial consisted of four visits: (1) screening for study participation and inclusion, (2) first injection of study substances (baseline), (3) 1st follow-up and second injection of study substances, and (4) 2nd follow-up. The period between visits 2, 3, and 4 was one week (0, 7, and 14 days) (Figure 1).

The activities undertaken by the investigators during the trial are presented in Table 1.

2.3. Treatment. Group I was injected into the masseter trigger points using 2 ml of Collagen MD Muscle (Guna, Italy), Group II 2 ml of 2% Lidocaine (Lignocainum hydrochloricum WZF, Polfa Warsaw, Poland) without vasoconstrictor, and Group III 2 ml of saline as a control (0.9% NaCl) at 2nd and 3rd visits. In all groups, disposable syringes (2 ml) and needles (0.4×19 mm) were used for injections. During the intervention, trigger points within masseter muscles were identified with palpation of the masseter muscle, and each group was injected with the same amount

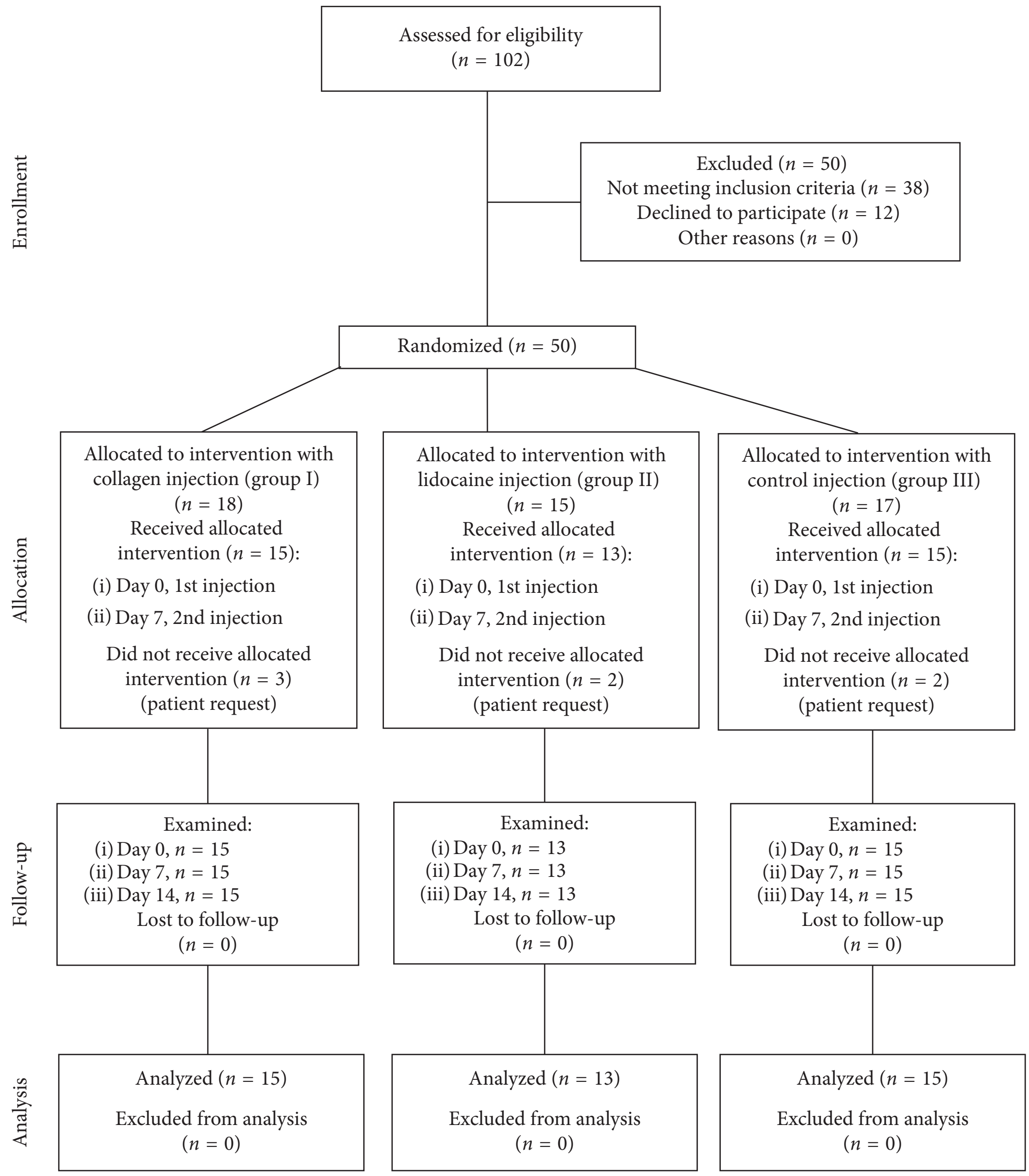

Figure 1: CONSORT three-arm diagram showing the flow of participants through each stage of the presented randomized controlled trial.

Table 1: Activities of investigators during the trial.

Visit	1 (screening and inclusion)	2 (baseline)	3 (1st follow-up)	4 (2nd follow-up)
Day of the study	–	Day 0	Day 7	Day 14
Injection	–	+	+	–
Measure EMG	–	EMG.I.1. EMG.II.1. EMG.III.1. EMG.I.1.NP EMG.II.1.NP EMG.III.1.NP	EMG.I.2. EMG.II.2. EMG.III.2. EMG.I.2.NP EMG.II.2.NP EMG.III.2.NP	EMG.I.3. EMG.II.3. EMG.II.3. EMG.I.3.NP EMG.II.3.NP EMG.II.3.NP
Measure VAS	–	VAS.I.1. VAS.II.1. VAS.III.1.	VAS.I.2. VAS.II.2. VAS.III.2.	VAS.I.3. VAS.II.3. VAS.III.3.

EMG.I.1. = EMG, Group I first measurement; NP = no pain.

of the appropriate substance (2 ml) into the trigger point structure. Injections were deposited approximately 1–1.5 cm under the skin surface. In 40 patients, the injections were unilateral and in 3 patients, bilateral in two masseter muscles with the same substance (2 subjects in Group I and 1 subject in Group II).

2.4. Treatment Outcome Measures. To measure treatment outcome, a surface electromyography (sEMG) and visual analogue scale (VAS) were used at the 2nd, 3rd, and 4th visits with one week breaks between visits (0, 7, and 14 days). For the assessment of masseter muscle activity, a surface electromyography was performed with a Neurobit Optima device (Neurobit Systems, Poland). The rest values for masseter muscle were measured for both sides. Muscle activity in the form of surface electromyography data was measured with 5 electrodes positioned bilaterally: in the origin region on the zygomatic arch and maxillary process of the zygomatic bone and in the insertion region on the angle and lateral surface of the mandible ramus. Two electrodes were positioned at each side of the patients head and one, a reference electrode, on the patient's neck. The patient remained seated on a dental chair, keeping his or her mandible in a resting, comfortable, and relaxed position, without tooth contact. The electromyographic evaluation was performed after cleaning the skin surface with cotton pads and an alcohol solution (Octenisept, Schulke, Germany). Electrodes were fixed on the skin covering the masseter muscle and on the patient's neck with a self-adhesive gel. The patient was asked to perform an isometric contraction of the masseter muscles to find the best place for electrode fixation. A 0–10 visual analogue scale with the endpoints marked "no pain" (0) and "worst experienced pain" (10) was used to evaluate the effectiveness in pain reduction of the substances studied. Pain evaluation using VAS and surface electromyography was performed by two investigators (JBK and KWD) and muscle injections were performed by the other investigator (ANB).

2.5. Sample Size Estimation. Normal distribution of VAS values was assumed. With the division into three groups, the analysis of variance for repeated measurements was planned, with equal sized groups. The power to achieve was 0.9 with the significance level set to 0.05.

Additional assumptions were the following:

(1) Expected VAS values in individual research groups and subsequent measurements (Table 2).

(2) Standard deviation for all measurements was SD = 1.5.

(3) For the correlation matrix, the LEAR (linear exponent AR (1)) model was adopted, with base correlation set to 0.85 and correlation decay rate equal to 1.

The total number of subjects needed was 36, given the above assumptions; thus, the minimum number of subjects per group was 12. Sample size estimation was performed by using SAS, version 9.4 (SAS Institute Inc., Cary, NC).

Table 2: Expected VAS values and measurements.

Observation	Group	Baseline	1st follow-up	2nd follow-up
1	VAS.I	8	5	3
2	VAS.II	8	6	5
3	VAS.III	8	7	6

2.6. Randomization and Blinding. Patients who met the inclusion criteria were randomized by computer-generated simple randomization into one of the following groups: Collagen (Group I, $n = 18$), Lidocaine (Group II, $n = 15$), and Saline (Group III, $n = 17$). MW conducted the randomization and prepared the list of interventions by enrolment numbers. ANB administered the injections, according to the list. Patients and members of the study group (ANB, JBK, and KWD, who performed and collected pain intensity using VAS and muscle activity using surface EMG) were blinded for allocation and treatment.

2.7. Statistical Analysis. A one-way repeated measures analysis of variance was carried out. To verify the assumptions of the method in all groups, the analysis of the normality of the distribution was performed with Shapiro–Wilk test. The homogeneity of variance was analyzed by Hartley's test, Cochran–Cox test, and Bartlett's chi-square test. Mauchley's sphericity test was also performed. From the analysis of variance, it follows that the assumptions of a one-way repeated measures analysis of variance are met in the analyzed groups. In order to verify statistical hypotheses, the level of significance of alpha = 0.05 was assumed. The calculations were carried out in Statistica 12.0 (StatSoft, Poland).

3. Results

3.1. Demographics and Statistics. The present study included 43 Caucasian patients (17 males and 26 females). The mean age was 39.97 ± 3.78 years. Demographic characteristics of the patients are summarized in Table 3. There were no differences in age or gender between the groups ($p > 0.05$).

Data collected using sEMG and VAS were analyzed using descriptive statistics and briefly presented in Table 4.

Collected values for sEMG masseter muscle activity and pain intensity were normally distributed. The statistical analysis showed that the decreases in the mean values of EMG and VAS over time are statistically significant ($p < 0.001$). The mean values and 95% confidence intervals are shown in the Figures 2 and 3.

3.2. Primary Treatment Outcome

3.2.1. Evaluation of Masseter Muscle Pain Intensity. Masseter muscle pain intensity was assessed and compared before injection of collagen (VAS.I.1.), lidocaine (VAS.II.1.), and saline (VAS.III.1.) after 7 days (VAS.I.2., VAS. II.2., and VAS. III.2.) and 14 days (VAS.I.3., VAS. II.3., and VAS. III.3.) during baseline and follow-up visits.

Table 3: Baseline characteristics of 43 patients with MFP within masseter muscles included in the study.

	Group I	Group II	Group III
Male/female, n	5/10	5/8	7/8
Age (years)	37.2 ± 4.97	42.8 ± 0.98	40.3 ± 1.18
Duration of myofascial pain (weeks), mean (SD)	30.2 ± 31.48	34.3 ± 29.26	38.3 ± 26.47
Bilateral involvement of myofascial pain (number of patients)	2	1	0

Table 4: Descriptive statistics of sEMG and VAS values.

	N	Average	Minimum	Maximum	Stand. dev.	One-way repeated measures ANOVA
EMG.I.1. (μV)	15	56.67	47	65	5.95	
EMG.I.2. (μV)	15	32.67	28	41	3.85	$p < 0.001$
EMG.I.3. (μV)	15	23.73	20	29	2.81	
EMG.I.1.NP (μV)	15	34.3	27	45	5.17	
EMG.I.2.NP (μV)	15	34.6	27	42	4.35	$p = 0.344$
EMG.I.3.NP (μV)	15	35.2	25	44	5.47	
VAS.I.1.	15	8.07	5	10	1.58	
VAS.I.2.	15	4.67	2	8	1.54	$p < 0.001$
VAS.I.3.	15	3.73	1	7	1.94	
EMG.II.1. (μV)	13	59.07	49	70	4.79	
EMG.II.2. (μV)	13	41.20	37	49	3.36	$p < 0.001$
EMG.II.3. (μV)	13	35.07	29	45	4.40	
EMG.II.1.NP (μV)	13	38.7	29	60	7.3	
EMG.II.2.NP (μV)	13	39.2	31	55	6.8	$p = 0.353$
EMG.II.3.NP (μV)	13	37.7	29	52	6.4	
VAS.II.1.	13	8.33	6	10	1.23	
VAS.II.2.	13	7.40	5	9	1.12	$p < 0.001$
VAS.II.3.	13	6.07	4	9	1.58	
EMG.III.1. (μV)	15	64.13	56	72	5.34	
EMG.III.2. (μV)	15	60.20	54	69	4.41	$p < 0.001$
EMG.III.3. (μV)	15	55.27	50	64	4.83	
EMG.III.1.NP (μV)	15	36.6	26	43	8.3	
EMG.III.2.NP (μV)	15	34	29	41	4.5	$p = 0.138$
EMG.III.3.NP (μV)	15	36.5	29	42	4.3	
VAS.III.1.	15	8.13	6	10	1.19	
VAS.III.2.	15	6.80	4	9	1.57	$p < 0.001$
VAS.III.3.	15	6.53	3	9	2.03	

Pain intensity reduction was observed in all groups: in Group I, the average pain intensity reduction in VAS scale was 4.3 = 53.75%; in Group II, the average decrease in pain intensity was 2 = 25%; and in Group III, the average value of pain elimination was 1.63 = 20.1% as well (Table 5, Figure 2). Comparing data between measurements performed on days 7 and 14, the authors observed statistically significant pain reduction in all cases, between baseline, 1st follow-up visit, and 2nd follow-up visit (Table 5).

3.3. Secondary Treatment Outcome

3.3.1. Evaluation of the Surface Electromyography. Masseter muscle activity was assessed and compared before injection of collagen (EMG.I.1.), lidocaine (EMG.II.1.), and saline (EMG.III.1.) after 7 days (EMG.I.2., EMG. II.2., and EMG. III.2.) and 14 days (EMG.I.3., EMG. II.3., and EMG. III.3.) during follow-up visits. Only rest muscle electromyographic activity was measured in trigger point region on the painful side.

EMG activity of masseter muscles was measured in each group for three times, during baseline and follow-up visits (Figure 3). Mean values for all collected sEMG results are presented in Figure 2. The most significant reduction of sEMG values was observed in Group I (32.9 μV, 59.2%). In Group II, a 23.5 μV (39.3%) reduction was observed. The lowest reduction of sEMG values was noticed in Group III (8.9 μV, 14%) (Table 6). In each group, a statistically significant reduction was observed ($p < 0.001$).

3.3.2. Evaluation of the Surface Electromyography on the Side without Myofascial Pain. Masseter muscle activity was also assessed and compared on the asymptomatic side before injections of collagen (EMG.I.1. NP), lidocaine (EMG.II.1.

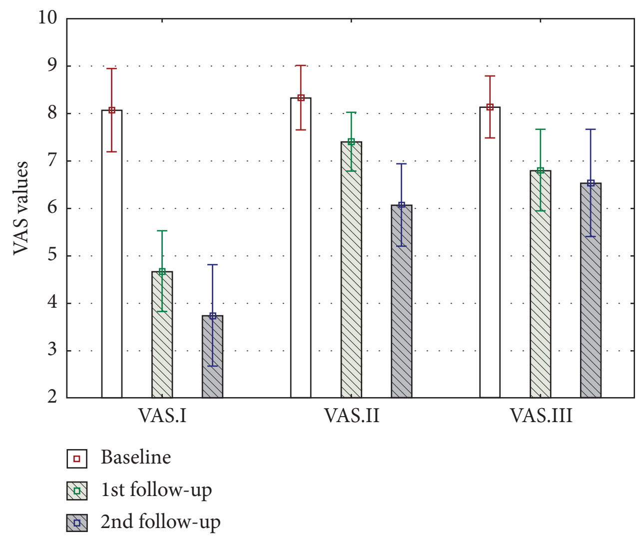

Figure 2: VAS mean value changes in Group I, Group II, and Group III during the trial (days 0, 7, and 14).

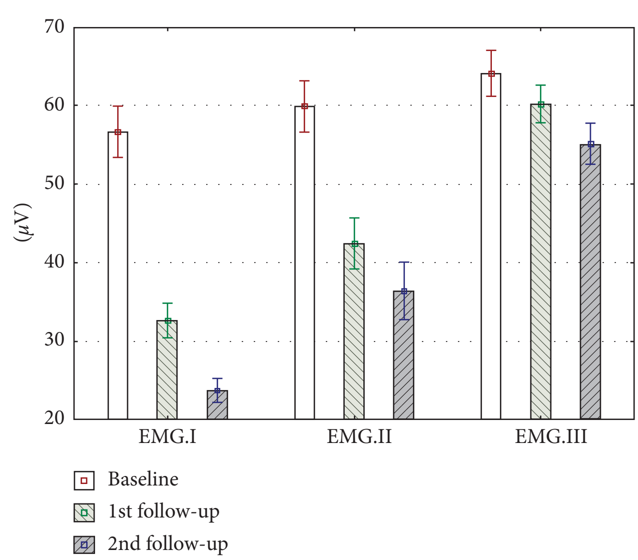

Figure 3: Changes in mean values of superficial electromyographic activity of masseter muscles in Group I, Group II, and Group III during the trial (days 0, 7, and 14).

NP), and saline (EMG.III.1. NP) after 7 days (EMG.I.2. NP, EMG. II.2. NP, and EMG. III.2. NP) and 14 days (EMG.I.3. NP, EMG. II.3. NP, and EMG. III.3. NP) during follow-up visits (Table 6). In 3 subjects, pain was observed bilaterally. In each group, no statistically significant changes of sEMG were observed ($p > 0.001$).

3.4. Adverse Effects. Approximately 30 minutes after the injection of collagen into the masseter muscle, patients described pain during movement, edema, and muscle stiffness. After approximately 1 hour, pain symptoms were gone. In a few patients (9 subjects), bruises appeared after the injection, directly at the needle insertion points. These adverse effects were temporary and completely reversible. There were no serious adverse effects during the trial.

Table 5: Changes in VAS mean values in Group I, Group II, and Group III after 14 days.

Visit	Group I	Group II	Group III
Baseline	8	8.3	8.13
1st follow-up visit	4.6	7.4	6.8
2nd follow-up visit	3.7	6	6.5
VAS changes	**−4.3**	**−2**	**−1.63**
Percentage VAS changes	**−53.75%**	**−25%**	**−20.1%**

Table 6: Changes in EMG mean values in Group I, Group II, and Group III after 14 days.

Visit	Group I (μV)	Group II (μV)	Group III (μV)
Pain side			
Baseline	56.6	59.9	64.1
1st follow-up visit	32.6	42.4	60.2
2nd follow-up visit	23.7	36.4	55.2
EMG changes	**−32.9**	**−23.5**	**−8.9**
Percentage EMG changes	**−59.2%**	**−39.3%**	**−14%**
No pain side			
Baseline	34.3	38.7	36.6
1st follow-up visit	34.6	39.2	34
2nd follow-up visit	35.2	37.7	36.5
EMG changes	**+0.9**	**−1**	**−0.1**
Percentage EMG changes	**+2.6%**	**−2.5%**	**−0.3%**

4. Discussion

Intramuscular injections of collagen, lidocaine, and saline into the trigger points of masseter muscles in the treatment of myofascial pain reduction within masseter muscles varied across study groups in terms of their level of success. The best results were achieved in Group I: maximal reduction of sEMG activity (32.9 μV; 59.2%) and best antinociceptive results (reduction, 4.3; 53.75% on the VAS scale). There are not many research studies analyzing collagen intramuscular injections, besides Milani [34], Yu et al. [35], and Alfieri [36]. These authors stated in their research studies a positive muscle reaction to intramuscular collagen injections, but these studies were not related to orofacial muscle pain.

However, despite the fact that the result is satisfactory, we would like to emphasize that the trial had limitations. The main limitation was the short period of observation of the reduction of pain intensity and the single-blind nature of the trial. Both these limitations resulted in our restricted funding and possibilities of carrying out the trial.

According to the current literature, biomaterial guided regeneration is a new approach for myofascial pain syndrome. This is confirmed by Kuraitis et al. who injected a collagen matrix enhanced with sialyl LewisX (sLeX) to guide skeletal muscle differentiation and regeneration [26]. Muscle tissue damaged by an injected substance has the ability to perform myogenesis and revascularization. We found that satellite cells are active in muscle cell regeneration and collagen VI participates in the activation of satellite cells [17]. The extracellular matrix is a special collagen supply for new myocytes formed in the process of muscle regeneration. The composition of ECM is extremely important for the proper regeneration process to avoid substitution by fibrotic connective tissue, that is, scar production. It is probable that the collagen molecules that were provided by intramuscular injections help to produce an extracellular network that keeps myocytes in their proper positions. The presence of satellite cells in an extracellular matrix is called "a pool" of pluripotential cells for myocyte formation. In this study, the authors noticed better muscle tissue properties and less pathological symptoms after extracellular collagen delivery.

In the clinical trial, we noticed muscle function advancement after collagen intramuscular injections, but Kato et al. found that muscle collagen protein synthesis is not regulated by elevated nutritional or intravenous levels of collagen, but just by mechanical stress [37]. Some authors have observed a better muscle tissue condition and muscle activity decreasing after intramuscular collagen injections. Lawrence and De Luca found a positive correlation between muscle myoelectric signals and the muscle force of the maximal voluntary contraction [38, 39].

In Group II, intramuscular lidocaine injections were performed to decrease pain and to eliminate trigger points. McMillan et al. performed a comparative research between dry needling and procaine injection into the trigger points of masseter muscles in patients with temporomandibular disorders [40]. They concluded that therapy with dry needling and procaine is questionable, because they did not notice any difference in the end point of his study between experimental groups. We found similar results in our study, but in comparison with Group I, lidocaine and dry needling were far less effective.

Antinociceptive results were also observed, but not as successful as in Group I. We can also find some articles about myofascial pain therapy with prolotherapy, which involves the injection of an irritant solution of lidocaine and dextrose into the joint, ligament or painful muscle [41, 42]. Sung et al. identified the correlation between lidocaine concentration and exposure time and tissue cell death [43]. In the future, it would be important to compare anesthetics that are less toxic, for example, ropivacaine. We observed in our research study some effectiveness of injections, with different solutions. We found that we have achieved the best regenerative results with collagen injections, but lidocaine and saline injections also produced pain level decreases as well as sEMG activity decreases. Blasco-Bonora performed a dry-needling technique in masseter muscle trigger points and also achieved an improvement in muscle pain reduction and jaw opening in patients with sleep bruxism [44]. Kalichman and Vulfsons stated in their study that deep dry needling is more effective than superficial dry needling in the therapy of musculoskeletal pain [45]. Masseter muscle lies just underneath the skin, so injections were not very deep (approximately 1.5 cm), but we can call it deep wet needling. Injecting collagen into the trigger point in our opinion may be favorable, not only because of the specific mechanism of action in regenerating muscle tissue, or as a buffer collagen supply, but also as a therapeutic injection. Dry needling and injections into the trigger points have some common points with acupuncture methods [46–49].

It should be noted that a significant effect in terms of reducing sEMG muscle activity and pain intensity was obtained after two injections and the study intervention did not pose a risk of significant adverse effects and high interoperative risk.

5. Conclusions

The study confirmed that intramuscular injection of collagen is a more efficient method to reduce myofascial pain within masseter muscles than intramuscular injection of lidocaine. Due to the short observation time, further long-term trials should be conducted.

Data Availability

The datasets supporting the conclusions of this article are included within the article. Access to other data will be considered by the corresponding author upon request.

Disclosure

The research study was performed as a part of the employment in the Medical University of Silesia in Katowice, Poland, and Wroclaw Medical University, Poland.

Conflicts of Interest

The authors declared no conflicts of interest.

Authors' Contributions

Aleksandra Nitecka-Buchta created trial concept, performed intramuscular injections of collagen, lidocaine, and saline, analyzed the data, and wrote and edited the manuscript. Jolanta Batko-Kapustecka and Karolina Walczynska-Dragon performed and collected pain intensity using VAS and muscle activity using surface electromyography. Mieszko Wieckiewicz conducted the randomization, analyzed data, wrote and edited the manuscript, and finally revised it before submission. All authors read and approved the final manuscript.

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Review Article

Temporomandibular Disorders: "Occlusion" Matters!

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By analogy with the journal's title Pain Research and Management, this review describes TMD Research and Management. More specific are the (1) research aspects of "occlusion," still one of the most controversial topics in TMD, and (2) as much as possible evidence-based management aspects of "TMD" for the dental practitioner. *Research*. The disorders temporomandibular dysfunction and the synonymous craniomandibular dysfunction are still being discussed intensely in the literature. Traditionally, attention is mostly devoted to occlusion and its relationship with these disorders. The conclusions reached are often contradictory. Considering the definitions of temporomandibular and craniomandibular dysfunctions/disorders and "occlusion," a possible explanation for this controversy can be found in the subsequent methodological problems of the studies. Based on a Medline search of these terms over the past 40 years related to contemporary terms such as "Evidence Based Dentistry" and "Pyramid of Evidence," these methodological aspects are examined, resulting in recommendations for future research and TMD-occlusal therapy. *Management*. To assist the dental practitioner in his/her daily routine to meet the modern standards of best practice, 7 guidelines are formulated that are explained and accompanied with clinical examples for an evidence-based treatment of patients with this disorder in general dental practices.

1. Introduction: Research Section

To date, over 22,000 papers are published concerning the disorders temporomandibular dysfunction and the synonymous craniomandibular dysfunction. In this paper, the term "Temporomandibular Disorders," henceforth "TMD," is used to present a collection of the 4 studied terms and its abbreviations: temporomandibular disorders, temporomandibular dysfunction (TMD) and craniomandibular disorders, and craniomandibular dysfunction (CMD).

Recently, a paradigm shift regarding "TMD" has occurred from the biomedical model, more specifically from occlusion, to a biopsychosocial model of disease. The biopsychosocial model was introduced in medicine in 1977 and published in 1978 by Engel [1, 2]. The model was based on general systems and intended to provide a total framework in which all the levels of organization pertinent to health and disease could be conceptualized. One of the levels of organization in the musculoskeletal pain condition "TMD" is the entity "occlusion." This paper addresses "occlusion" because the interaction between occlusion and "TMD" still has not been unambiguously clarified, leading to controversial research conclusions. This review paper aims to clarify the existing controversy with a scientific approach of the literature in order to provide (1) recommendations for future research and (2) up-to-date evidence-based tools for "TMD" management in the general dental practice.

2. Materials and Methods

In this study, a two-track scientific approach was followed. Literature searches were executed focusing on (1) randomized controlled trials, the highest level in the pyramid of evidence, and all trials and (2) the search terms "evidence based dentistry," "biopsychosocial model," and "occlusion." Web of Science searches in the Medline database were executed over, respectively, a 67-year period for the data in Tables 1 and 3 (1950–2017) and a 40-year period for the data in Table 2 and Figures 1 and 2 (1977–2017). All searches were executed in December 2017.

Search terms and topics were Craniomandibular Disorders, Craniomandibular Dysfunction, Temporomandibular Disorders, Temporomandibular Dysfunction, CMD, TMD,

Table 1: Web of Science search in the Medline database showing the number of papers of functional disturbances of the stomatognathic system: “TMD” over the period 1950–2017, which is focused on the biopsychosocial model (BPSM) and “occlusion” specified for different types of trials: clinical trial (CT), controlled clinical trial (CCT), randomized controlled trial (RCT), all trials, and evidence-based dentistry (EBD).

Term/topic of the search	All papers	BPSM	Occlusion					
		Papers	Papers	CT	CCT	RCT	All trials	EBD
Craniomandibular disorders	826	2	174	13	3	11	15	2
Craniomandibular dysfunction	448	1	113	8	2	6	8	1
Temporomandibular disorders	14316	31	1533	47	11	37	63	20
Temporomandibular dysfunction	6686	11	1256	40	9	26	45	5
CMD	1848	1	50	3	1	2	3	0
TMD	4802	22	399	13	3	18	25	5
All 6 search terms: “TMD”	21686	35*	2419	69	16	52*	86	21*

*Studies that detailed the subject of this review.

Table 2: Web of science search in the Medline database for RCTs in the period 1977–2016 with the keyword “TMD” + “Occlusion” by the first author, characteristics of the trial number of citations, and abstracted summary of the result or effect of the trial.

Author	Year	Characteristics of the trial	Citation	Effect/result	Reference number
Leal de Godoy et al.	2015	Laser therapy–TMD diagnostic criteria	0	No	[26]
Costa et al.	2015	Occlusal appliance–headache	0	No	[6]
Cioffi et al.	2015*	Occlusal interference–EMG muscular activity	0	“Little”	[4]
Rampello et al.	2013*	Universal occlusal appliance–TMD diagnostic criteria	2	“Favorable”	[40]
Yu et al.	2013	Full denture lingualized occlusion–“TMD”	0	“Remission”	[53]
Jakhar et al.	2013	Surgical procedure TMJ–CT evaluation	3	“Improvement”	[18]
Michelotti et al.	2012*	Education/occlusal appliance–musc. pain and mouth op.	32	“Education slightly better”	[36]
Ap Biasotto-Gonzalez et al.	2010	Food texture–EMG activity	1	“Less variation”	[54]
Ueda et al.	2009	Jaw excercises–OSA	11	“Help relieve”	[48]
Hamata et al.	2009*	2 types of occlusal splints–TMD clinical and EMG	10	“Remarkable reduction”	[17]
Diernberger et al.	2008	Prefered chewing side–epidemiologic study	37	Several “associations”	[12]
Monaco et al.	2008	Osteopathic manipulative treatment–kinesiographics	12	“Induce changes”	[37]
Toro et al.	2007	Surgical procedures analgesics–jaw movements	6	“A valid aid”	[44]
Conti et al.	2006	2 types of occlusal appliances–TMJ pain	34	“No differences”	[5]
Le Bell et al.	2006*	Occlusal interferences–subjective sign of TMD	29	“Stronger symptoms”	[25]
Wolfart et al.	2005	Prosthetic appliance–SDA and molar occlusion	37	No	[52]
Ueki et al.	2005	Surgical procedures–skeletal stability	32	No/“similar”	[49]
Michelotti et al.	2005*	Occlusal interference–TMD signs and symptoms	47	No/“adapted fairly well”	[35]
Magnusson et al.	2004*	2 types of occlusal appliances–TMD signs and symptoms	28	“Some or significant”	[31]
Fayed et al.	2004*	2 types of occlusal appliances–magnetic resonance	11	“Effective, one superior”	[13]
Turp and Schindler	2003	Refer to the trial of Le Bell 2002–descriptive study	7	“No new data”	[47]
Le Bell et al.	2002*	Occlusal interferences–TMD signs and symptoms	40	“Significant”	[24]
Maloney et al.	2002	Jaw movement devices–TMD signs and symptoms	22	“Effective”	[32]
Bettega et al.	2002	Surgical procedures–correct occlusion	23	“Differences”	[3]
Raphael and Marbach	2001	Occlusal appliances–widespread body pain	69	“Improvement”	[41]
Glaros et al.	2000	Biofeedback–TMD pain	32	“Significantly higher”	[15]
de Andrade et al.	1998	Surgical procedures–TMD signs and symptoms	13	Significant	[11]
Kirveskari et al.	1998*	Occlusal interferences–TMD signs and symptoms	41	Significant	[21]
Rodrigues-Garcia et al.	1998	Orthodontic surgical procedures–TMD signs and symptoms	45	“Other factors responsible”	[43]
Davies and Gray	1997*	Occlusal appliances’ wearing time–TMD signs and symptoms	19	“All marked improvement”	[10]
Karjalainen et al.	1997*	Occlusal adjustment–TMD signs and symptoms	14	Significant	[20]
Obrez and Stohler	1996	Muscle irritation–range of mandibular movements	36	Significant	[38]
Vallon et al.	1995*	Occlusal adjustment–TMD signs and symptoms	16	Significant	[50]
Tsolka and Preiskel	1993*	Occlusal interferences–EMG and kinesiographics	20	Not significant	[46]

Table 2: Continued.

Author	Year	Characteristics of the trial	Citation	Effect/result	Reference number
List and Helkimo	1992*	Acupunture/occlusal appliance–TMD signs and symptoms	42	"No differences"	[28]
Tsolka et al.	1992*	Occlusal adjustment–TMD signs and symptoms	21	"No differences"	[45]
Lundh et al.	1992*	Occlusal appliances–TMD signs and symptoms	77	"No differences"	[29]
Johansson et al.	1991*	Acupunture/occlusal appliance–TMD signs and symptoms	65	"No differences"	[19]
Gray et al.	1991*	Occlusal appliances–TMD signs and symptoms	12	"No differences"	[16]
Kirveskari et al.	1989*	Occlusal adjustment–TMD signs and symptoms	29	Yes/no significant	[22]
Lundh et al.	1988	Occlusal therapy/appliance–disk displ. with reduction	55	"Differences"	[30]
Lipp et al.	1988	Intubation procedures–TMD signs and symptoms	7	"Temporary effect"	[27]
Wenneberg et al.	1988*	Occlusal adjustment/appliance–TMD signs and symptoms	34	"More effective"	[51]
Puhakka and Kirveskari	1988*	Occlusal adjustment–globus symptoms	20	"Significant association"	[39]
Forssell et al.	1986*	Occlusal adjustment/appliance–TMD signs and symptoms	30	"Effective treatment"	[14]
Raustia	1986	Acupuncture/tomography stomatognathic treatment	6	Paper not available	[42]
Kirveskari and Puhakka	1985*	Occlusal adjustment–globus symptoms	11	"Significant association"	[23]
Manns et al.	1985	Occlusal apliances–EMG activity	30	"Study suggests"	[33]
Dahlstrom and Carlsson	1984*	Biofeedback/occlusal apliance–TMD signs and symptoms	25	"No differences"	[9]
Dahlstrom	1984*	Biofeedback/occlusal apliance–TMD signs and symptoms	3	"A positive correlation"	[7]
Manns et al.	1983*	Occlusal appliances–EMG activity	52	"More effective"	[34]
Dahlstrom et al.	1982*	Occlusal appliance/biofeedback–TMD signs and symptoms	36	No significant differences	[8]

*Exclusively occlusion-orientated studies.

Occlusion, Biopsychosocial Model, Evidence Based Medicine, Evidence Based Dentistry, and Pyramid of Evidence. Results were further filtered by the type of the study (clinical trial, controlled clinical trial, and randomized controlled trial) and/or sorted by the year of publication and frequency of citation. The results of the "occlusion" searches are presented in 3 tables, 2 figures, and an eight-point summary.

3. Results

During the recent 67-year period, there are only 35 papers published concerning the biopsychosocial model and "TMD," 86 different trials, of which 52 randomized controlled trials (Table 2) [3–54] and 21 different studies with the keywords "Evidence Based Dentistry" (Table 3) [55–75] focused on all 6 "TMD" terms and "occlusion." Further refining the 35 BPSM studies with the search term "evidence based dentistry" results in 3 studies by Ohrbach and Dworkin [76], Simmons [77], and Goldstein [78]. One of the 35 BPSM papers is an RCT by Andrew et al. [79].

It is almost impossible to abstract an extensive RCT into single keywords regarding the results of the study. Nevertheless, the combination of the columns "characteristics of the trial" and "effect/result" is an attempt to realize this. Further explanations of the study results are presented in Discussion. Researchers are invited to further scan, screen, and study the collected papers by themselves to verify the presented conclusions.

Without underestimating the value of papers that will not be addressed in further detail here, the search, presented in Table 3, revealed a number of papers to pay more attention to. First of all, the review papers by Ash [55], both papers by Carlsson [58, 59], the paper of Moreno-Hay and Okeson [69], and the meta-analysis by Fricton et al. [65] are of particular interest. These papers should not only be cited in all future TMD literatures but should also be included in any future study design or at least in Discussion. Of course, the annual reviews of the American Academy of Restorative Dentistry by Donovan et al. [62, 63] are very informative and must have been "a hell of a job" to compose for the experts. Unfortunately, they describe, with all due respect to the 8 authors, only a selection of the available papers. The 2014 review concerning TMD and occlusion refers to 17 papers, and the 2016 review refers to 22 papers including the bruxism section. The total number of TMD papers in the included years of their study is, respectively, 825 (in 2013) and 932 (in 2015). In conclusion, less than 0.5% of all TMD papers are documented and discussed. In the result section of the abstract in 2016, the authors formulate the following: *"The reviews are not meant to stand alone but are intended to inform the interested reader about what has been discovered in the past year. The readers are then invited to go to the source if they wish more detail."* On one hand, this selection is most probably beneficial for the dental practitioner. On the other hand, a researcher following this advice is directed to only 0.5% of the preselected TMD papers and misses the

Table 3: Web of Science search in the Medline database in the period 1950–2017 for all "TMD" terms ($n = 21,686$) refined with the keywords "Evidence Based Dentistry (EBD)" ($n = 60$) and "Occlusion" ($n = 21$) chronologically by the first author, title/characteristics of the study, number of citations, type of the study, and reference number [55–75], which is presented in a chronological order of the year of publication.

First author	Year	Title/characteristics of the study	Citation	Study type	Reference number
Weinberg	1976	TMJ function and occlusion concepts	23	Article	[74]
Becker	1995	Occlusion etiology of TMD	5	Article	[56]
Ey-Chmielewska	1998	Ultrasonic techniques for painful TMD, with ultrasonic exam aid	1	Comp. + CT + CCT	[64]
Ash	2001	Paradigms of TMD and occlusion	18	Review	[55]
Gremillion	2002	Orofacial pain, a pain-oriented study	6	Review	[66]
Rinchuse et al.	2005	EBD versus experience-based views on TMD + occlusion	26	Article	[72]
Dawson	2005	"EBD-based versus experience-based views on occlusion and TMD"	2	Letter + comment	[60]
Rinchuse and Kandasamy	2006	Centric relation: orthodontics	35	Review	[71]
Luther	2007	TMD and occlusion: orthodontics	11	Review + evaluation	[68]
Carlsson	2009	Review of prosthodontic dogmas	72	Review + meta-analysis	[58]
Carlsson	2010	TMD and occlusion dogmas	27	Review	[59]
Fricton	2010	Critical appraisal of TMD-RCTs	14	Meta-analysis	[65]
Blackwood	2010	"After 50 years in practice, the evidence is convincing"	0	Letter + comment	[57]
Roehm	2010	"Gnathology lessons from a 1969 Oldsmobile engine"	0	Letter + comment	[73]
Hudson	2010	"Myths of orthodontic gnathology"	0	Letter + comment	[67]
Pensak	2011	"One has to wonder": orthodontic and neuromuscular balance	0	Letter + comment	[70]
Donovan	2014	Annual review of the American Academy of Restorative Dentistry	1	Review	[62]
Wiens and Priebe	2014	Occlusion article: occlusal concepts in prosthetic dentistry	5	Review	[75]
Moreno-Hay	2015	Occlusal dimensions: a review	4	Review	[69]
Donovan et al.	2016	Annual review of the American Academy of Restorative Dentistry	1	Review	[63]
de Kanter	2016	TMD prevalence and etiology: a historical article in Dutch	0	Review	[61]

other 99.5%. Also, the Luther study [68] might have been of interest for our study topic. However, the paper was not specifically focused on RCTs, and its conclusions are based on papers of a lower level of evidence.

Finally, 5 of the selected papers in this search are letters or comments, with 4 of them disputing the Rinchuse 2005 orthodontic-orientated TMD papers. All of the letters and comments concerned about orthodontic-related TMD aspects.

In the period 1977–2017, a total of 20,340 "TMD" papers were published, starting with 160 papers in 1977 to almost a thousand (903) in 2016. Figure 1 shows a temporary increase in the period 1982–1992. A similar increase seems to be present in the papers about "TMD" refined with "occlusion." Most "TMD"-"occlusion" papers were published in 1985 (90) and 1991 (104). In that 11-year period, on average, 70 papers were published yearly.

The "TMD" refined with "occlusion" curve does not follow the curve of evidence-based dentistry papers. However, the number of EBD papers did increase in line with the total number of "TMD" papers. In the recent decade, EBD papers also increased substantially to approximately 180 papers yearly. It might be prudently concluded from these data that apart from the 21 papers presented in Table 3, the EBD papers were apparently not proportionally focused on "occlusion".

A clear discrepancy is visible between the periods of increased activity in the number of papers of the topics "TMD" + "occlusion" and the EBD curve, whereas the curves of "TMD" + EBD and the trial curves of "TMD" + "occlusion" are fluctuating more or less constantly over the 40-year period (EBD papers ranging from 0 to 8 with a top in 2010 and "occlusion" trials ranging from 0 to 7 with a top in 2003, resp.).

The increase of the number of EBD studies is not followed by a progression of both the studies of "TMD" + occlusion (all trials) ($n = 86$) and the "TMD"-related EBD ($n = 58$). Regarding the 11-year period of increased attention to the "occlusion" and "TMD" topics from 1982 to 1992, all 14 exclusively "occlusion"-oriented RCTs were published. This is the same number of RCTs as that in the 22-year period from 1993 to 2015.

Figure 2 clearly shows the similarity of the curves of evidence-based medicine (EBM), evidence-based dentistry (EBD), and the topic "pyramid of evidence" (PoE), popular terms in today's research (the correlation between the number of publications over the years is, resp., EBM-EBD:

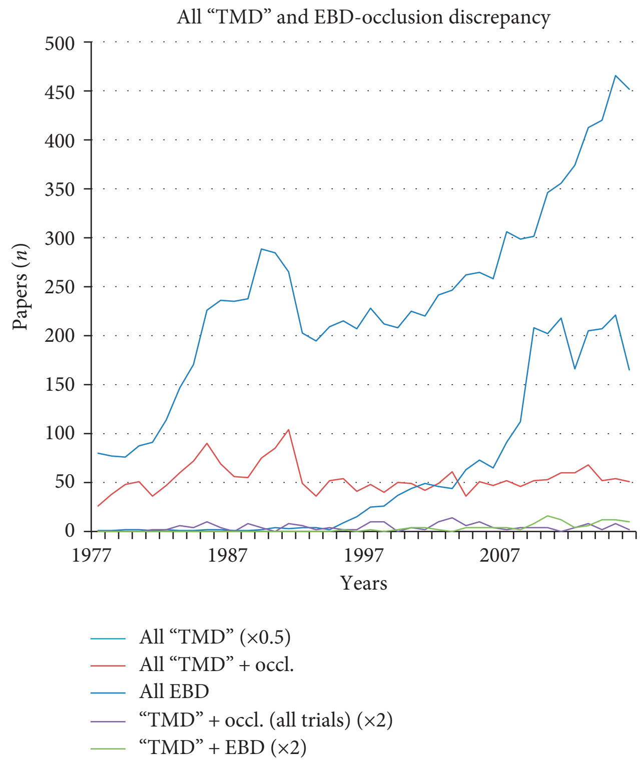

Figure 1: Web of Science search in the Medline database in the period 1977–2016 showing curves of all "TMD" papers (0.5 × all "TMD"), all evidence-based dentistry (EBD) papers, all " TMD" and "occlusion" papers, the "TMD" + EBD papers, and "TMD" + "occlusion" all trials papers.

0,922, EBM-PoE: 0.900, and EBD-PoE: 0.934). All 3 topics became more important as the subject of research and scientific interest in the past 2 decades. The onset of interest in evidence-based research papers started in 1995.

In 1977, one single paper with the keyword EBD, two EBM papers, and zero PoE papers were found. In 1995, at the start of the "hype," 9 EBD papers, 154 EBM papers, and 7 PoE papers were published. In 2015, the number of papers substantially grew to 221 for EBD, 5689 for EBM, and 20 for PoE yearly.

Finally, in a search focused on the topic "Trials" in the Medline database in the period 1950–2017, more than half a million (clinical/controlled/randomized controlled) trials appeared to be present. Refined with the keywords "Evidence Based Dentistry," 417 studies could be selected. A further refining with "occlusion" resulted in 8 studies.

A summary of all trials in the Medline database in the period 1950–2017 refined with the search terms Evidence Based Dentistry and Occlusion:

(1) "Evidence-based clinical practice guideline for the use of pit-and-fissure sealants" by Wright et al. [80]

(2) "Does altering the occlusal vertical dimension produce temporomandibular disorders? A literature review" by Moreno and Okeson [69]

(3) "Is there enough evidence to regularly apply bone screws for intermaxillary fixation in mandibular fractures?" by Bins et al. [81]

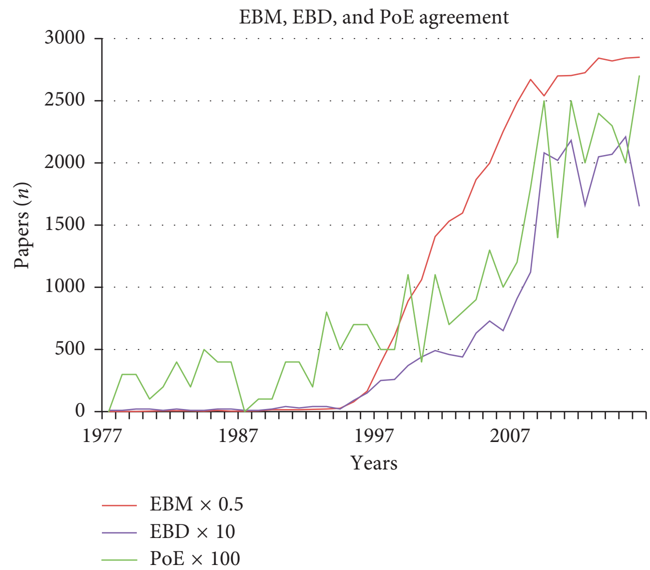

Figure 2: Web of Science search in the Medline database in the period 1977–2016 showing curves of all evidence-based medicine (EBM × 0.5) papers, all evidence-based dentistry (EBD × 10) papers, and all pyramid of evidence (PoE × 100) papers.

(4) "Occlusion on oral implants: current clinical guidelines" by Koyano and Esaki [82]

(5) "Bilateral balanced articulation: science or dogma?" by Farias-Neto and Carreiro [83]

(6) "Complete denture occlusion: an evidence-based approach" by Farias-Neto and Carreiro [84]

(7) "Critical appraisal of methods used in randomized controlled trials of treatments for temporomandibular disorders" by Fricton et al. [65]

(8) "Association between orthopedic and dental findings: what level of evidence is available?" by Hanke et al. [85]

As a result of this search, only 2 papers addressing the "occlusion" topic of our study were found: the Moreno/Okeson study and the Fricton study. After replacing "occlusion" by "TMD" in the second refining step of the same EBD search, this revealed only 3 studies: the Keenan 2015 study [86], the Forssell and Kalso 2004 study [87], and again the Moreno/Okeson 2015 study [69]. In the perspective of our study, the study of Forssell entitled "Application of principles of evidence-based medicine to occlusal treatment for temporomandibular disorders: are there lessons to be learned?" is also relevant.

4. Discussion

Despite the substantial number (2419) of published papers about "TMD" and "occlusion," there are still controversy and contradictory opinions on the interaction between "occlusion" and "temporomandibular disorders."

What could be an explanation for the still ongoing discussion? Why has the scientific world not yet reached consensus? For a one-to-one link between a disorder and a factor, the 2419 occlusion papers, or otherwise, the 52 RCTs, the highest level of research in the pyramid of evidence [88], should have been more than sufficient to elucidate the link between both. However, research is still going on, and the number of papers is still increasing.

A possible explanation for the ongoing controversy about "occlusion" and "temporomandibular disorders" is definition-based.

Ever since Goodfriend described functional disturbances of the stomatognathic system in the Dental Cosmos of 1932 [89], several terms were used to describe deviations from the optimal and healthy normal status of the stomatognathic system. Currently, the term "temporomandibular disorders" (TMDs) is generally accepted and most frequently used to represent disturbances and dysfunction of the stomatognathic system (Table 1). Moreover, in 2014, this term became the "golden standard" for the disorder's diagnostic criteria and taxonomy through a series of workshops and symposia, a panel of clinical and basic science pain experts, reaching a consensus to differentiate TMD into 5 pain-related temporomandibular disorders (3 disorders of muscular origin, 1 of joint origin, and 1 TMJ headache-provocated disorder) and 5 intra-articular temporomandibular disorders [90].

Considering the topic "occlusion" in the dental literature, this term is used for 4 different entities: (1) the anatomic or "orthodontic" jaw relation: the Angle classification, (2) static contact between the teeth of the upper and lower jaws, (3) dynamic contact between the teeth of the upper and lower jaws, for example, cuspid guidance versus group function, articulation, and occlusal interferences, and (4) the prosthetic classifications, more specifically, the complete/incomplete dentition versus complete dentitions and the presence of fixed/removable prosthetics.

Based on purely statistical fundamentals, there are at least $10^4 = 10{,}000$ different possibilities for research and RCT studies (TMD: the 10 distinguished disorders as described by Schiffman et al. in combination with the 4 occlusion entities).

It can be concluded that due to the phenomenon of the multiple catch-all or container concepts of both "occlusion" and "TMD," there are many different options to research. In addition, considering the etiology, the cause and effect relation, and vice versa, there are almost inexhaustible possibilities.

In summary, the 52 RCTs of the Medline database over the period 1977–2017 only represent approximately 0.5% of these 10,000 possible study options. In addition, there are also RCTs in this 52-RCT search collection dealing with other topics than exclusively "occlusion." This is a consequence of the generally accepted multifactorial and multicausal character of "TMD."

Considering the multifactorial character, 40 years ago, in 1979, De Boever [91] described the well-known multifactorial etiological approach for CMD. He distinguished five theories: the mechanical displacement theory, the neuromuscular theory, the psychophysiologic theory, the muscle theory, and the psychological theory. De Boever stated that none of the theories as such give an adequate explanation of the cause and the symptoms of CMD. He concluded that the etiology of functional disturbances is multifactorial and is a combination of dental, psychological, and muscular factors.

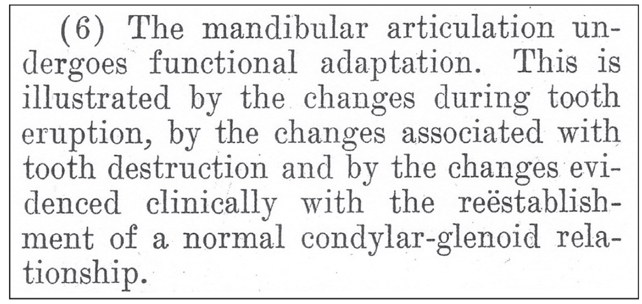
(6) The mandibular articulation undergoes functional adaptation. This is illustrated by the changes during tooth eruption, by the changes associated with tooth destruction and by the changes evidenced clinically with the reëstablishment of a normal condylar-glenoid relationship.

FIGURE 3: Original fragment in *Dental Cosmos*, volume LXXIV, no. 6, June page 534, 1932.

This is in line with the "biopsychosocial" theory published in 1987 by Marbach and Lipton, "Biopsychosocial factors of the temporomandibular pain dysfunction syndrome. Relevance to restorative dentistry" [92]. More recently, Ohrbach and Dworkin published a paper with the modern multifactorial approach, presenting the biopsychosocial model of illness, addressing more focus on the psychosocial domain [76].

Considering the adaptation capacity, already in the early years of dental literature in 1932, 85 years ago, Goodfriend stated the following in his concluding remarks: *"The mandibular articulation undergoes functional adaptation"* [89] (Figure 3).

In 2005, Michelotti et al. accordingly wrote the following: *"None of the subjects developed signs and/or symptoms of TMD throughout the whole study, and most of them adapted fairly well to the occlusal disturbance"* [35]. Recently, in 2015, with respect to the capacity of the stomatognathic system to adapt to a recovered or new vertical dimension, Moreno and Okeson wrote the following: *"Permanent occlusal changes should only be attempted after the patient has demonstrated adaptability at the new vertical dimension"* [69].

The stomatognathic system of patients appears to be able to accept and adapt to occlusal alterations.

In conclusion, for almost a century, the scientific world confirms and agrees with the existence of the adaptation capacity of the structures of the stomatognathic system.

Focusing on the aim and the subject of this paper—research about the contradictory role of "occlusion" in relation to "TMD"—the following conclusions about "occlusion" in relation to "TMD" can be abstracted after a more in-depth study of the 52 selected RCTs and the results of the other described searches:

(i) The role of occlusion in the etiology of "TMD" is not absolutely assessed.

(ii) Occlusal interferences affect "TMD."

(iii) "TMD" is multifactorial, and subsequently, it will be affected by different treatment modalities (the biopsychosocial model of illness approach).

(iv) "TMD" fluctuates over time.

(v) Adaptation is an important quality of the human being; in this respect, it is more specific of the stomatognathic system.

The still existing confusion and contradiction in the dental literature about the role of "occlusion" in "TMD" is probably caused by the approach of some mainly American gnathologists/researchers who maintain that since occlusal interferences affect TMD, all occlusal varieties and "abnormalities" cause TMD signs or symptoms and therefore have to be treated preventively. Such an approach to patients does not account for the interindividual variation, as present all over the world and in this context as described by Ramfjord and Ash [93, 94].

Since it will take about a generation to fundamentally change treatment strategies and opinions [95], the profession will still be confronted in the next decades by the often-used concluding statements, sentences, and words in scientific papers: "more research is still necessary," "the contradictory role of occlusion," and "the controversy."

With respect to the possible role of "occlusion" in the etiology of "TMD," the scientific world has to accept that it will most probably never ever be more elucidated than it is at present. In all probability, there will never be an ethics commission approving "occlusal experiments" in healthy young people to study the onset or incidence of "TMD" signs or symptoms over time.

The only possibility to make any progress is to study in detail the available studies and to respect and implement practitioners' experiences.

It is one of the challenging and obliging tasks of universities, researchers, and dental societies to achieve this progress by performing an objective, accurate, and critical study of the existing literature. This will then result in studies with a sound methodological standard. Accurate reviewing of submitted papers in peer-reviewed journals is also important to achieve this aim. All this might result in less "scientific" papers and consequently less (governmental) granting, but on the other hand, also in a higher level, standard and quality of the published papers.

It will create an achievable way for practitioners to stay up-to-date with the literature to the application of evidence-based dentistry in their daily dental practice and not be overwhelmed by an ocean of conflicting information and endless discussions about scientific topics.

The conclusion of this review is to stop trying to find the exact etiologic role of "occlusion" in the perspective of "TMD" and concentrate on a critical study of the available scientific and clinical information and integrate them.

5. Management Section

Based on the available "TMD" papers and experiences from the daily dental practice, first, some general elementary starting issues are detailed below to provide the general practitioner some support and clues for the treatment of TMD patients. Subsequently, practical clinical examples and tips of each issue are presented:

(1) Each patient is unique.

(2) Respect the biological variation in form/appearance and (the coherent) function.

(3) Adaptation is possible within defined biologic limits and contains a time factor or aspect.

(4) Be alert to recent (dental) treatments or events that might interrelate with the onset of the complaints or problems.

(5) Try to differentiate and diagnose the different entities of TMD and adjust your treatment modality accordingly.

(6) Be reluctant with irreversible treatment options and direct the treatment as much as possible to a predictable, reliable, and proven result with a known determined prognosis.

(7) Consider and take into account the opinion or idea of the patient about the possible cause of the complaint or problem.

Observe and consider that not only the anatomy and morphology of each individual diverge but also the regular everyday use of the stomatognathic system differs from one another. The biologic variation is huge, even within distinguished ethnic groups. The functions of the stomatognathic system: communicating (talking, laughing, kissing, and making love), eating (biting and chewing), supporting (TMJ's orthodontic abnormalities), stress processing (bruxism, grinding, and clenching), and aesthetics, differ significantly between individuals. There may be clues present between the complaints and the observed problems with the functions of the stomatognathic system of the patient in question. The patient's age and gender also affect the prevalence of TMD (De Kanter et al. [96] and, more recently, Lovgren et al. [97]). Also, women are on average smaller than men, have less muscle mass, and have on average a more limited maximum mouth opening. In daily life, they will meet the limits of function and maximum mouth opening more frequently than men. For example, US Big Macs and French baguettes have the same size for both genders. Also, some physical intimacies and sexual activities in the most prevalent heterogeneous relationships for men and women differ substantially with respect to the maximum mouth opening and the limits of the temporomandibular joints [98].

Adaptation is possible within certain biological limits; however, including the accessory time component hereby is an important and essential factor. Clinical experience reveals that this time component influences the eventual exceedance of adaptation in two ways. In patients with restored dentitions, the presence of different restoration materials, materials with a different hardness and wear component, will not wear equally over time. As a result, even after a long period of the application of the restoration, the tooth restored with the most resistant and hard restoration material might cause an uncomfortable feeling, become more or less painful, and provoke complaints and TMD resembling signs or symptoms. These strong tooth-related complaints are difficult to distinguish from endodontic problems. Apical X-rays might be an aid to reveal the correct diagnosis in these cases. For one reason or another, no (further) intrusion of the concerning tooth occurs as a possible mechanism of compensation or adaptation. This tooth also apparently does not abide the overall biological, natural, and functional wear of the other adjacent teeth. Subsequently, as a mechanism of adaptation, their mobility increases slightly. These patients indicate most of the time that the tooth is feeling a little bit higher and more sensitive. Based on clinical experience, these, a little more than physiologic mobile teeth, show most often interferences at chewing movements, at articulation, and not in the static occlusal contact position. These are mostly indirect restorations such as (solitaire/single) crowns, abutment teeth for removable casted partial prosthetics, or the occlusal clasps of removable partial dentures. These so-called "iatrogenic occlusal interferences" will manifest only over time. It is advisable to eliminate the disturbance by selective grinding and reshaping and adjusting the contour of these restored teeth or clasps. The recently developed device "Tekscan®" may be a useful aid to substantiate this, also in the treatment of "occlusion-sensitive" subjects [99].

Exceeding the adaptation capacity might also occur in a specific and limited period of time, during the eruption of the wisdom molars, more specifically, the eruption of the 3rd mandibular molars. Although the eruption pattern of the 3rd molars shows a wide range, the majority erupts between the age of 17 and 26 years [100, 101]. Especially when the process of the eruption is slightly disturbed, occasionally, the distal part of the second molar might become dislocated and pressed up distally resulting in a slight tipping along the mesiodistal axis and cause a physiologic-based occlusal interference in the most posterior region of the mouth. The closer a (slight) static occlusal interference is to the temporomandibular joints, the bigger will be the change in the vertical dimension and influence on the closure of the mouth especially in the anterior region. As a consequence, this will affect the musculature. Furthermore, the TMJs will go out of balance as a compensation mechanism, deflecting from their physiologic position. Any outmost slight change in the vertical dimension posterior will have more impact on the TMJs and the musculature and result in a more extreme change in the vertical dimension than would ever be possible with the same dimensional changes more anterior.

The distal interference causes tilting of the concerning TMJ and might initiate grinding and wear of the contralateral cuspids in a short period of time, as a parafunction, mostly unconsciously at night. In combination with the mostly irritated operculum, patients compensate for this with an unnatural, divergent chewing pattern. This unnatural chewing pattern occurs in unnatural positions within the TMJs and the articular discs, resulting in dislocation, joint sounds, and pain in and around the TMJs. Counseling, information, advice about extraction, or preferably the extraction procedure itself is desirable. Some adaptation time after the extraction of the third molar, the affected and worn top of the cuspid might be restored using the composite etch technique. If, for any reason, the third molar will not be extracted, treatment of the painful operculum is recommended. Both the further eruption of the third molar and the occlusal condition have to be monitored or treated.

With respect to the onset of TMD or TMD-related complaints, it is advised to be alert to recent dental procedures or events that might be associated with the complaints. This includes extractions, particularly extractions of mandibular teeth. Damaging or even luxation of the TMJs might have occurred. Also, long-lasting dental treatment procedures when the patient had to have the mouth opened extremely wide and for a long time may have this effect. Equally, the intubation procedures for general anesthesia/surgical interventions are notorious and suspected. As a result, the TMJs might have been extremely strained and stretched, and the musculature might have been traumatized and injured. Recovery of these attacks on the TMJ tissues requires time and has to be treated by getting as much rest as possible. This means no excessive function, temporary use of soft or liquid foods, and/or temporary medication for pain relief.

Recently inserted prosthetic devices also might provoke complaints of a TMD character such as tenderness of the chewing muscles, biting on the cheek or lips during chewing, joint sounds, or even pain in or around the TMJs and the masticatory muscles. In case, after accurate inspection, no shortcomings or imperfections of the prosthetic provisions and no deviations in the static and active dynamic occlusion can be determined, the adaptation capacity has to be appealed. The patient has to be informed and counseled and explained that more time is necessary to adapt to the new situation. Not infrequently, the patient is not convinced of this approach and appears to be unhappy with the aesthetics or comfort of the new devices. The patient explains and interprets this by a lack of the support function and the presence of chewing problems.

Frequently, the patient's interpretation of those shortcomings is gratefully strengthened by the treatment and repetitive corrections of the occlusion by the general practitioner. A treatment not addressing the real cause or problem will never ever be successful. In extreme cases, placebo adjustments might be applied to address and permeate this problem.

From a historical perspective, TMD patients show different, nowadays better distinguished functional disorders. It is important for the dental practitioner to assess the most possible specific diagnosis. If the diagnosis is correct, a conforming, matching therapy and treatment is available. If the treatment was successful, then the diagnosis was the right one. Crucial for this is a good and complete examination of the patient. Anamnesis and clinical examinations, not only intraoral but also from the head and neck region, are very important and indispensable.

Important signs might be observed as nonverbal expressions such as the overall body posture, the position of the head in relation to the chest, shoulders up or down, and patients' handshake with a firm or soft hand. How does the patient communicate? How clearly does he or she express himself or herself? Is there a (recent) trauma in his or her history? How many different professionals have previously been consulted? Is the location of the pain clearly pointed to with one finger, for instance, the joint, or do the patient's hands encircle the entire head? Are other joint problems present such as hypermobility of knees, ankles, wrists, or elbows? Is there a history of rheumatic diseases?

All this information is important to assess a correct and specific diagnosis.

Whenever the general practitioner is not able to reach a right circumscribed diagnosis, other experts have to be consulted before any treatment is proposed. The advice of a specialized gnathologist might be required, or a physiotherapist specialized in TMJ problems might be consulted mainly for muscular problems, or a (clinical) psychologist.

There is plenty of literature available describing the patient's anamnesis and clinical examination protocols [102, 103].

Occasionally, even after intensive examinations and interdisciplinary consultation, a general practitioner might not be convinced of a right treatment approach of the specific TMD. In that situation, it is advised to be cautious with (irreversible) treatment options. One has to treat as predictably as possible. In progressive bruxism cases, preventive occlusal splints are necessary. The application of occlusal appliances is also recommended as indispensable reversible tools to test, restore, and establish a physiologically accepted natural and healthy comfortable balance in the stomatognathic system.

Whenever a patient is not aware of a TMD problem, but the dental practitioner recognizes signs of TMD at the regular checkups of the patient, it is important to find out whether the patient himself or herself has any idea or assumption about the cause or the existence of the assessed TMD phenomenon [104]. If not, it is advised to be very cautious with active treatment, and informing the patient absolutely has to be the first step. Try to formulate understandable and acceptable arguments about your concern as a dental practitioner concerning the patient's dental health and the possible benefit of the proposed treatment. When the patient lacks the conviction about an intervention, it is better to (temporarily) abandon the proposed treatment. In these cases, it is preferred to evaluate and monitor the determined deviation by means of repetitive produced cast models of the dentition or chronological assessed digital files of it.

6. Epilogue

This study at the end of the professional career of the first author is the final spin-off from the PhD thesis: Prevalence and Etiology of Craniomandibular Dysfunction. An Epidemiological Study of the Dutch Adult Population [105]. In this present paper, we tried to present research and experiences from the dental practice in a symbiosis. Some final interesting and, in our opinion, wise quotes from experts in this field to remember are the following:

"More emphasis should be placed on patient-centred criteria of what is perceived to be important to patients' function, satisfaction, and needs, as well as dentists' views of what is significant for improvement in dental health" Ash [55].

A final comment of Klineberg to the Forssell Paper [106] about evidence-based medicine with respect to TMD occlusal treatment is the following: "*It is clear, that even without a role in TMD etiology, the occlusion retains an important role in most aspects of dental practice*" [106].

And last, but certainly not least, also the most recent statement of these 3 from Carlsson is the following [59]: *"In a longer perspective, many of today's "truths" will be questioned, and dogmas that lack strong evidence will eventually be abandoned. But to achieve this goal it is necessary for open-minded educators and researchers to question and analyse current practice methods in all areas of clinical dentistry."*

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Clinical Study

Electromyographic Analysis of Masticatory Muscles in Cleft Lip and Palate Children with Pain-Related Temporomandibular Disorders

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Aim. The aim of this study was to assess the electrical activity of temporalis and masseter muscles in children with cleft lip and palate (CLP) and pain-related temporomandibular disorders (TMD-P). *Methods*. The sample consisted of 31 CLP patients with a TMD-P (mean age 9.5 ± 1.8 years) and 32 CLP subjects with no TMD (mean age 9.2 ± 1.7 years). The children were assessed for the presence of temporomandibular disorders (TMD) using Axis I of the Research Diagnostic Criteria for TMD (RDC/TMD). Electromyographical (EMG) recordings were performed using a DAB-Bluetooth Instrument (Zebris Medical GmbH, Germany) in the mandibular rest position and during maximum voluntary contraction (MVC). *Results*. The rest activity of the temporalis and masseter muscles was significantly higher in TMD-P group compared with non-TMD children. A significant decrease in temporalis muscle activity during MVC was observed in TMD-P patients. There was a significant increase in the Asymmetry Index for temporalis and masseter muscle rest activity in the TMD-P group. *Conclusion*. Cleft children diagnosed with TMD-P have altered masticatory muscle activity, and this can affect their muscle function.

1. Introduction

Cleft lip and palate (CLP) is one of the most common congenital deformities of the craniofacial area requiring long-term functional and aesthetic rehabilitation [1]. Complete clefts of the lip and/or palate are immediately recognizable disruptions of normal facial structure [2]. In addition to dysfunctional facial expressions, patients with CLP may have serious functional problems with sucking, swallowing, breathing, chewing, speaking, hearing, and social integration [3, 4].

The prevalence of malocclusions in CLP patients is relatively high [5]. The most common occlusal disorders in patients with clefts are crossbites and class III malocclusions [6, 7]. Malocclusions, particularly of the transverse type where disrupted symmetry of the dental arches can be clinically observed, are a potential cause of functional disorders of the stomatognathic system [8]. Hence, patients with CLPs are potentially at risk of developing temporomandibular disorders (TMD), due to psychosocial burdens and malocclusions predisposing them to this condition [6, 9]. This is consistent with previous reports [10–12]. The importance of a patient's lower socioeconomic status as a likely important factor in the development of TMD in CLP patients has also been noted [13].

Temporomandibular disorders (TMD) are a collective term embracing a number of clinical problems affecting the masticatory muscles, the temporomandibular joint (TMJ), and associated structures [14]. Pain-related temporomandibular disorders (TMD-P) are the most prevalent conditions among TMD [15]. They comprise myalgia, arthralgia, and headaches attributed to TMD [16]. The primary manifestations of TMD-P are pain of a persistent, recurring, or chronic nature in the masticatory muscles, TMJ, or in adjacent structures [17, 18]. The other major symptoms include limitation in the range of mandibular motion and joint noises [14, 17]. The pain may radiate to different regions, such as the dental arches, ears, temples, forehead, occiput, and the cervical region of spine or shoulder girdle [18]. The aetiology of pain-related TMD is considered to be multifactorial and to result from a complex interaction between biological, psychological, social, and environmental variables [19, 20].

The prevalence of TMD signs and symptoms in children and adolescents in the general population ranges from 1 to 50%, and TMD-P from 1% to 22% [21–26]. The prevalence of objective and subjective symptoms of TMD in children with CLP is relatively higher [13].

Surface electromyography (sEMG) is the study of muscle function based on an analysis of the electrical signals produced during muscular contraction. The sEMG method is painless and innocuous, and these are important factors when conducting studies involving children [27, 28]. It has been widely used in research settings for the assessment and follow-up of patients with TMD [29, 30], and numerous studies have demonstrated altered electromyographical (EMG) values in the masticatory muscles of patients with TMDs [31–34]. Subjects diagnosed with TMD-P alter the recruitment of their jaw muscles [35]. Free nerve endings act as nociceptors activated by noxious stimulation such as temporomandibular joint (TMJ) overloads and/or masticatory muscle ischemia, if it is prolonged and associates with muscle contractions [36, 37]. A correlation has been observed between a decrease in the motor unit firing rate and muscle pain intensity, although the central mechanisms involved remain unclear [38]. Maximum EMG activity is greater in pain-free subjects than in patients with pain-related TMD [33, 39]. Nevertheless, to the authors' knowledge, until now there have been no EMG studies on masticatory muscle activity in cleft lip and palate subjects with a TMD-pain diagnosis. The identification of the electromyographic pattern of the mastication muscles is necessary in order to achieve functional improvement in the stomatognathic system, particularly in cleft children. For these reasons, it is essential to determine temporalis and masseter muscle activity in cleft lip and palate children with pain-related TMD by means of electromyography (EMG).

The aim of this study was to determine whether the electrical activity of temporalis and masseter muscles in children with complete CLP and pain-related TMD differs from that observed in CLP individuals with no TMD. The null hypothesis was that there are no differences between CLP individuals with TMD-P and non-TMD with regard to the electrical activity of the temporalis and masseter muscles in the mandibular rest position and during maximum voluntary teeth clenching.

2. Material and Methods

The clinical research was registered as a case-control study in the ClinicalTrials.gov database and assigned the number NCT03308266.

2.1. Study Sample. The sample comprised 63 children with cleft lip and palate and mixed dentition. In accordance with the outcomes of Axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) [17], the children were divided into two groups: a TMD-pain group and a non-TMD group. The groups were matched for age and gender. The TMD-pain group included 31 children (15 girls and 16 boys) aged between 6.4 and 13.9 (mean 9.5 ± 1.8) with complete cleft lip and palate and a pain-related TMD diagnosis. The control group consisted of 32 subjects (14 girls and 18 boys) aged between 6.7 and 11.7 years (mean 9.2 ± 1.7) with CLP and no TMD diagnosis. The subjects were selected from a total of 90 patients who had been referred to three Cleft Care Centres in Szczecin, Poznań, and Wrocław, Poland, between November and December 2015. All had undergone lip and palate surgery at one of four different Plastic Surgery Clinics in Poland according to the following protocols: A. a two-stage lip and palate repair procedure, that is, a lip operation at the age of 3–6 months, followed by palate closure (hard and soft palate in one-step procedure) at the age of approximately 12 months; B. single-stage lip and palate repair in children at the age of about 6 months, that is, the lip and hard and soft palate were closed in a single operation. The application of the adopted inclusion and exclusion criteria resulted in 27 of the subjects being excluded from the study and 63 of the participants qualifying for further examination. The inclusion criteria for the TMD-pain group were as follows: meeting Axis I of the RDC/TMD diagnosis criteria with pain (arthrogenous or myogenous TMD), children of both sexes with mixed dentition, undergoing lip and palate surgery, the presence of a cleft lip and palate without a syndrome, a sequence or karyotype abnormalities, and consent to participate voluntarily in the study. The inclusion criteria for control group were as follows: children without any TMD diagnosis according to the RDC/TMD protocol, children of both sexes with mixed dentition, undergoing lip and palate surgery, the presence of a cleft lip and palate without a syndrome, a sequence, or karyotype abnormalities, and consent to participate voluntarily in the study. The exclusion criteria for both groups included: meeting Axis I of the RDC/TMD diagnosis criteria without pain, the presence of systemic or rheumatologic diseases, a history of cervical spine or temporomandibular joint (TMJ) surgery, trauma or malformations, and completed orthodontic or masticatory motor system dysfunction treatment.

Masticatory motor system function was assessed on the basis of a clinical examination and electromyographic procedures.

2.2. Clinical Examination. Anamnestic interviews were conducted, which covered the patients' general medical history and provided detailed information on the patients' masticatory motor systems, including subjective TMD symptoms, such as jaw pain during function, frequent headaches, jaw stiffness/fatigue, difficulty in opening the mouth wide, teeth grinding, and TMJ sounds. The children were assessed for the presence of temporomandibular disorders using Axis I of the Research Diagnostic Criteria for TMD (RDC/TMD) by a single trained examiner. This helped ensure standardized procedures for epidemiological studies, unified TMD diagnostic and exploratory criteria, and a comparison with the results of other similar studies [17, 40]. The clinical signs were assessed using the RDC/TMD criteria, including pain on palpation, mandibular range of motion (mm), associated pain (jaw opening pattern, unassisted opening, maximum assisted opening, mandibular excursive, and protrusive movements), sounds coming from the TMJ, and tenderness induced by muscle and joint palpation. Generally, the RDC/TMD criteria classify forms of TMD into three diagnostic categories:

(i) Group I: muscle disorders (Group Ia with myofascial pain and Group Ib with myofascial pain with limited opening);

(ii) Group II: disc displacement (Group IIa with reduction, Group IIb without reduction with limited opening, and Group IIc without reduction but without limited opening);

(iii) Group III: arthralgia (Group IIIa) or arthritis (Group IIIb/IIIc).

RDC/TMD specifies distinct operational criteria for each TMD subtype; for example, a myalgia diagnosis is made if a person reports pain in the face or mastication muscles at rest or during function, as well as the presence of pain upon palpation at 3 or more sites. An arthralgia diagnosis includes pain upon palpation of the TMJ and joint-related pain during movements of the opening mouth, mandibular excursive, and protrusive movements; a diagnosis of arthritis includes pain in addition to reported clicking sounds upon palpation. Thus, every TMD subject could have both a masticatory muscle pain diagnosis and/or a TMJ pain diagnosis.

Replicate measurements of clinical signs of TMD were recorded for twenty randomly selected children in order to assess intraexaminer reliability. For this purpose, intraclass correlation coefficients (ICCs) were calculated for both continuous and dichotomous variables of the RDC/TMD examination. The considered ICC values were as follows: $ICC < 0.4$ which corresponds to poor reliability; $0.4 \le ICC \le 0.75$—fair to good reliability; $ICC > 0.75$—excellent reliability [41, 42].

The intraoral examination included an analysis of the dental arch shape on three planes together with a reciprocal analysis of both dental arches. The following occlusal characteristics were evaluated: sagittal relationship of the permanent first molar according to Angle's classification, posterior crossbite, overbite, overjet, and lateral open bite.

2.3. Electromyographical Examination. We followed the methods by Szyszka-Sommerfeld et al. [43]. The EMG recordings were taken with a DAB-Bluetooth Instrument (Zebris Medical GmbH, Germany) by a single experienced researcher. During the recordings, each patient sat in a comfortable chair without a head support and was instructed to assume a natural head position [44]. This position allows us to eliminate or limit any unintentional movements from other parts of the body.

Surface EMG signals were detected with four silver/silver chloride (Ag/AgCl), disposable, self-adhesive, bipolar electrodes (Naroxon Dual Electrode, Naroxon, USA) with a fixed interelectrode distance of 20 mm. The electrodes were precisely positioned on the anterior temporalis muscle and the superficial masseter on both the left and the right sides parallel to the muscular fibres. The placement of the electrodes was exactly the same as previously described by Ferrario et al. [45] The temporalis anterior muscle: vertically along the anterior margin of the muscle; the masseter muscle: parallel to the muscular fibres with the upper pole of the electrode located at the intersection between the tragus-labial commissura and exocanthion-gonion lines. A reference electrode was applied inferior and posterior to the right ear.

The surface of the patient's skin was cleaned of impurities and degreased with a 70% ethyl alcohol solution by wiping it several times with disposable cotton wool. Slight reddening of the skin after cleaning is a clinical indicator that the site has been properly prepared. To confirm that the tested area had been properly prepared, an impedance test was performed with Metex P-10 a measuring device (Metex Instruments Corporation, Korea) with an accuracy of 2%. This device measures the resistance between a pair of electrodes for a period of 5 minutes from the placing of the electrodes. Further examinations would be conducted if the test produced a positive result (low skin tissue impedance).

The EMG recordings were taken 5 minutes later. The electrical activity of the temporalis and masseter muscles was then measured during the course of three different tests:

(1) Rest activity of the masticatory muscles in the clinical rest position;

(2) Maximum voluntary clench (MVC) in the intercuspal position where the patient was asked to clench as hard as possible for 5 seconds;

(3) Maximum voluntary clench (MVC) with two 10-mm thick cotton rolls placed on the mandibular second premolars and molars or on the mandibular second milk molars and the first permanent molars and the

patient was asked to clench as hard as possible for 5 seconds.

To avoid any effects of fatigue, a rest period of at least 5 minutes was allowed between each of these recordings. The EMG recordings were repeated at least three times to ascertain stability. The first recordings were eliminated as a "learning" sequence since they were frequently observed to be dissimilar to the other two repetitions. In a single subject, all EMG data were the arithmetic means of these last two surface EMG recordings. The patients were allowed to relax for 1 minute between each activity.

The DAB-Bluetooth Instrument was interfaced with a computer, which presented the data graphically and recorded it for further analysis. The EMG signals were amplified, digitized, and digitally filtered. The basic component of the data analysis was the normalization process. Normalization involved referring the raw results (the mean values of the EMG potentials) to the data obtained from each patient after clenching on two cotton rolls (reference values) according to the following formula: mean values (μV) during rest position or MVC/mean values (μV) during MVC with two 10 mm cotton rolls × 100%. For each muscle, the EMG potentials were expressed as a percentage of the MVC value using cotton rolls (unit μV/μV%). This procedure was essential for the preliminary processing of raw data to ensure intercomparisons and further analysis. In order to compare EMG recordings among different subjects, it was necessary to relate all measurements to the electrical muscle activity detected during certain standardization recordings, such as MVC. The EMG potentials collected in MVC are reported to have the highest repeatability. Among the various protocols, MVC on cotton rolls is reported to have the lowest interindividual variability, and a method based on this standardization is now commonly used [45–48]. According to this protocol, normalized EMG data will provide information on the impact of occlusion (teeth contact) on neuromuscular activity, while avoiding individual variability (anatomical variations, physiological and psychological status, etc.) and technical variations (muscle cross-talk, electrode position, skin and electrode impedance, etc.).

Finally, the Asymmetry Index (As, unit %) was recorded to assess asymmetry between the activity of the left and right jaw muscles according to a formula ranging from 0% (total symmetry) to 100% (total asymmetry) [49].

$$\mathrm{As} = \frac{\sum_{i=1}^{N} \left| R_i - L_i \right|}{\sum_{i=1}^{N} \left(R_i + L_i \right)} \cdot 100 \qquad (1)$$

To investigate the repeatability of the recording protocol, duplicate EMG evaluations were performed on the 20 subjects by the same operator, after a gap of 15 minutes between the two recordings. We asked the subjects to remain relaxed during this 15-minute break once the electrodes had been removed from their muscles and to walk around the laboratory if they needed to. The results of the first and second set of experiments demonstrated the repeatability of the EMG measurements. The data were presented as the mean values of the electrical activity of the temporalis and masseter muscles in rest position and during MVC. The repeatability of electrode positioning was maintained by using a standard procedure for positioning the electrodes. To assure standard results during the EMG examination, the electrodes were placed accurately at the area of muscle belly contraction [50].

2.4. Statistical Analysis. The homogeneity of variance was evaluated using the Levene test. The normality test applied was the Kolmogorov–Smirnov test. The results of the EMG recordings and the repeatability of the EMG measurements were analysed using Student's t-test and the Mann–Whitney U test to determine differences between the mean values of the independent variables. The chi-square test was used to determine differences in the prevalence of malocclusions between the groups of participants. The level of significance was set at $P = 0.05$.

3. Results

The reliability value for the RDC/TMD clinical examination ranged from good to excellent (from 0.62 to 1.0). Table 1 presents the distribution of TMD-P subjects according to their RDC/TMD diagnosis. Myofascial pain with no limited mouth opening (Group Ia) and arthralgia (Group IIIa) were diagnosed in 38.7% of the TMD-P patients, while 9.7% of the children were diagnosed with myofascial pain with limited mouth opening (Group Ib) and 12.9% of the subjects received a mixed TMD-pain diagnosis (Groups Ia and IIIa or Ib and IIIa).

The occlusal characteristics for both groups of children are presented in Table 2. There were no significant differences between TMD-pain group and control subjects in terms of the prevalence of malocclusions ($P > 0.05$).

Table 3 shows the results of the repeatability of the recording protocol. The differences between first and second evaluations of the electrical potentials of the masticatory muscles were not statistically significant in the case of any of the aforementioned activities ($P > 0.05$).

Analysis of the EMG recordings showed that the rest activity of both the temporalis and the masseter muscles was higher in subjects with CLP and TMD-P compared with non-TMD subjects (for temporalis muscles, $P = 0.0102$; for masseter muscles, $P = 0.0188$) (Table 4).

A significant increase was observed in the Asymmetry Index in relation to the rest activity of the temporalis ($P = 0.0218$) and masseter muscles ($P = 0.0010$) in patients with TMD-P compared with non-TMD children (Table 4).

Temporalis muscle activity during MVC was significantly lower in children from the TMD-pain group compared with children with no TMD ($P = 0.0477$). There were no significant differences in masseter muscle activity during MVC between the TMD-pain group and control subjects ($P = 0.3163$) (Table 5).

There were no differences between TMD-P and non-TMD subjects in terms of the Asymmetry Index for the temporalis and masseter muscles during MVC (temporalis muscle $P = 0.0858$, masseter muscle $P = 0.0773$) (Table 5).

Table 1: The distribution of TMD-pain subjects according to RDC/TMD diagnosis.

Diagnosis	TMD-pain group (n = 31)	
	n	%
Myofascial pain without limited mouth opening (Group Ia)	12	38.7
Myofascial pain with limited mouth opening (Group Ib)	3	9.7
Arthralgia (Group IIIa)	12	38.7
Group Ia and IIIa	3	9.7
Group Ib and IIIa	1	3.2

Table 2: The occlusal characteristics in the children studied.

Variable		TMD-pain group		Non-TMD group	
		n	%	n	%
Vertical overlap	Normal[1]	12	38.7	19	59.4
	Increased[2]	7	22.6	7	21.9
	Absence[3]	12	38.7	6	18.7
Overjet	Normal[4]	8	25.8	13	40.6
	Increased[5]	7	22.6	7	21.9
	Anterior crossbite	17	54.8	13	40.6
Posterior crossbite	No	7	22.6	12	37.5
	Yes	24	77.4	20	62.5
Angle class	I	10	32.3	17	53.1
	II	7	22.6	5	15.6
	III	14	45.2	10	31.2
Lateral open bite	No	22	71.0	24	75.0
	Yes	9	29.0	8	25.0

[1]Upper incisors is one-third of the clinical crown of lower incisors; [2]categorized as ≥3 mm; [3]the overlap absence (anterior open bite); [4]upper central incisors did not exceed 3 mm; [5]categorized as ≥3 mm.

Table 3: The results of the repeatability of the recording protocol.

Region	Activity	1 examination		2 examination		P value
		Mean	SD	Mean	SD	
Temporalis muscles	Rest	6.06	2.12	6.21	2.07	0.916
	MVC	109.63	41.01	109.98	41.09	0.994
Masseter muscles	Rest	5.25	2.10	5.41	2.14	0.948
	MVC	107.41	34.29	107.82	34.22	0.993

In the rest position, differences between girls and boys in the TMD-pain and control groups with regard to the Asymmetry Index of the masseter muscles were statistically significant (for girls-$P = 0.0080$ and for boys-$P = 0.0478$) (Table 4). During MVC, a significant difference was observed in the Asymmetry Index of the masseter muscles between girls from the TMD-pain and the non-TMD group ($P = 0.0330$) (Table 5).

4. Discussion

The present clinical study was designed to evaluate the electrical potentials of the masticatory muscles in cleft lip and palate children with pain-related temporomandibular disorders. Muscle activity was analysed in the mandibular rest position and during maximum isometric contraction (MVC). The EMG recordings showed that children diagnosed with CLP and pain-related TMD have greater temporalis and masseter muscle activity at rest, reduced temporalis muscle activity during maximum voluntary contraction, and a higher Asymmetry Index for the temporalis and masseter muscles in the rest position.

We used surface electrodes in this examination. They have the advantage of being noninvasive and for this reason are better tolerated by patients [51]. The repetition of the main experiment confirmed the repeatability of electrode positioning, as well as the entire protocol. No study on method error was performed with regard to the positioning of subjects in the "natural head position". On the other hand, we employed a method that is considered one of the most repeatable, especially in adults (data about children are not so clear).

The study revealed hyperfunction of both temporalis and masseter muscles at rest position in patients with CLP and TMD-pain diagnoses. This means that, at rest, the EMG activity of the masticatory muscles was higher in CLP children with pain-related TMD than in subjects with no TMD. This behaviour may be explained by the need for greater muscle recruitment in individuals with TMD and pain when the mandible is at rest [52, 53]. This is probably due to sensorial-motor interactions, of which pain can modify the generation of action potentials and, eventually, myoelectric activity [54]. Riise [55] found that the activity of the temporalis muscle in the rest position was higher when occlusal interferences existed. In the long term, hyperactivity may be followed by structural adaptations, such as tooth movement, muscular reactions, and remodelling of the temporomandibular joints or it could lead to pathologic changes in the masticatory system.

Reduced temporalis activity in the cleft group diagnosed with TMD-pain during MVC suggests that there is an alteration in masticatory muscle recruitment compared to children without TMD. These alterations may be employed as an effective protective mechanism for damaged TMJs [56]. The specific recruitment of the temporalis muscle appears to be the result of descending central modulation subsequent to nociceptive stimuli of the affected TMJ and/or myofascial and/or periodontal nociceptors [36].

A higher Asymmetry Index for the temporalis and masseter muscles at rest in the TMD-P group indicates differential left-right muscle activity. Moreover, the increased Asymmetry Index in TMD-P patients may confirm a higher frequency of unilateral TMD in this group.

The results of the study indicate that in comparison to non-TMD cleft patients children diagnosed with CLP and TMD-P have altered masticatory muscle activity. As mentioned earlier, CLPs are strongly associated with the presence of malocclusions [5], which in turn could be a potential cause of TMD and can affect electrical muscle activity [8, 11, 12, 57]. Nevertheless, the prevalence of malocclusions in this study was similar in both children with TMD-P and in non-TMD children. However, other malocclusion-related

Table 4: Electrical activity of the masticatory muscles at clinical mandibular rest position in the children studied.

Region	Variable	Gender	TMD-pain group			Non-TMD group			P value
			n	Mean	SD	n	Mean	SD	
Temporalis muscles	Electrical activity (μV/μV%)	Females	15	6.79	1.43	14	5.80	1.24	0.0554
		Males	16	7.53	2.43	18	6.06	1.95	0.0596
		Total	31	7.17	2.01	32	5.94	1.66	0.0102*
	Asymmetry index (%)	Females	15	15.81	7.66	14	10.19	4.97	0.1557
		Males	16	16.13	7.62	18	9.94	4.68	0.0807
		Total	31	15.99	7.02	32	10.06	4.33	0.0218*
Masseter muscles	Electrical activity (μV/μV%)	Females	15	5.18	2.37	14	3.98	1.97	0.1516
		Males	16	6.08	2.11	18	4.64	2.01	0.0509
		Total	31	5.64	2.25	32	4.35	1.98	0.0188*
	Asymmetry index (%)	Females	15	14.35	7.01	14	5.53	2.44	0.0080*
		Males	16	12.04	6.67	18	6.08	3.42	0.0478*
		Total	31	13.25	6.69	32	5.81	2.46	0.0010*

*Statistically significant difference.

Table 5: Electrical activity of the masticatory muscles at maximal voluntary contraction (MVC) in the children studied.

Region	Variable	Gender	TMD-pain group			Non-TMD group			P value
			n	Mean	SD	n	Mean	SD	
Temporalis muscles	Electrical activity (μV/μV%)	Females	15	99.83	37.05	14	110.55	40.04	0.4607
		Males	16	102.98	26.68	18	129.78	48.20	0.0576
		Total	31	101.46	31.61	32	121.37	45.17	0.0477*
	Asymmetry index (%)	Females	15	15.93	7.30	14	7.53	3.03	0.0607
		Males	16	5.81	2.48	18	5.91	2.87	0.9563
		Total	31	10.71	5.21	32	6.62	2.93	0.0858
Masseter muscles	Electrical activity (μV/μV%)	Females	15	98.24	31.53	14	102.56	31.33	0.7144
		Males	16	103.01	35.33	18	115.29	41.76	0.3649
		Total	31	100.70	33.08	32	109.72	37.54	0.3163
	Asymmetry index (%)	Females	15	15.31	7.32	14	8.09	4.85	0.0330*
		Males	16	6.75	3.34	18	6.59	3.38	0.9418
		Total	31	10.89	5.59	32	7.24	3.50	0.0773

*Statistically significant difference.

factors, for example, the severity of malocclusion, were not determined. Further research would be needed to explore the association between TMD and muscle EMG activity in CLP subjects including factors that may contribute to TMD problems and changes in EMG pattern (e.g., malocclusion).

It is important to note that the children who participated in the study were still in the developmental stage. The alterations in masticatory muscle electrical activity showed by EMG recordings in children with TMD-P affect their muscle function. The altered muscle function in a growing stomatognathic system can result in malocclusion, or in the exacerbation of an already existing malocclusion, and this will be a significant risk factor promoting the development or progression of TMD problems in the future. Early investigation of the electromyographic characteristics of children could facilitate the development of treatment strategies aimed at normalizing muscle activity so as to achieve functional improvement in these patients. Of course, further studies that could be repeated for the same group of children in the future would provide evidence for a validity of EMG on the progression of their TMD.

This is the first report concerning masticatory muscle activity in children diagnosed with CLP and TMD-P based on the RDC/TMD criteria. As there have been no similar studies, it is difficult to compare our results with others. Nevertheless, the data obtained in our study could be referred to Li et al. [12], who evaluated masticatory muscle activity in patients with unilateral cleft lip and palate and anterior crossbite. The examined group included 29 individuals with CLP ranging in age from 11 to 21 years. Among them, 22 cleft patients had one or more symptoms of TMD on clinical examination. The control group consisted of 28 volunteers with no cleft abnormalities and normal occlusion. They found that compared to noncleft controls, patients with unilateral CLP had the following parameters for temporalis and masseter muscles: higher activation levels in the rest position, lower activity recorded during maximum clenching in the intercuspid position, and a higher Asymmetry Index.

An analysis of masticatory muscle EMG activity in children with TMD was the subject conducted by Chaves et al. [58]. They assessed the EMG activity of the masseter, temporalis, and suprahyoid muscles in 34 children aged 8–12 years: 17 children with TMD and 17 without TMD. The results of this study demonstrated a lower mean electromyographic ratio for masseter muscles and anterior temporalis muscles (sEMG-M/AT ratio) during maximum voluntary clenching in the TMD group. These results can be explained by three factors acting together: the lower mean raw activity of the masseter muscle compared to the anterior temporalis muscle in the TMD children, the lower mean raw activity of the masseter muscle in the TMD group compared to the control group, and the higher mean raw activity of the anterior temporalis muscle in the TMD group compared to the non-TMD group.

The relationship between TMD and TMD-P and the electrical activity of the masticatory muscles in adult females has been described by Rodrigues et al. [54] and Berni et al. [33]. They analysed the EMG potentials of the anterior temporalis, masseter, and suprahyoid muscles at rest position and during MVC on parafilm. They both found that EMG activity of the masticatory muscles at rest was higher in a TMD group than in a control group with no TMD. Rodrigues et al. [54] observed no differences with regard to MVC between such groups. However, Berni et al. [33] reported significantly lower activity in the masseter muscle. Similarly, Tartaglia et al. [34] and Liu et al. [59] found that temporalis and masseter muscle activity was significantly lower in TMD subjects than in non-TMD patients during MVC. Moreover, Liu et al. [59] observed greater EMG activity at rest position in the anterior temporalis muscle.

Khawaja et al. [15] assessed associations between masticatory muscle activity levels both when awake and during sleep among pain-related TMD diagnostic groups. Twenty-six adult subjects were classified into those diagnosed with TMD-P (myalgia and arthralgia) and those who were diagnosed with no pain. The data suggest a tendency towards increased masseter muscle activity in the TMD-pain group both when awake and during sleep. However, the same tendency was not noted in the temporalis muscle. They observed that temporalis muscle activity was only found to be higher in the pain-related TMD diagnoses group at extreme activity levels (<25% and ≥80% ranges).

The importance of such a parameter as muscular symmetry was noted by Liu et al. [59] and Tartaglia et al. [34]. Tartaglia et al. [34] found that symmetry in the temporalis muscles was greater in the control group than in TMD patients. Liu et al. [59] reported that asymmetry of the masseter muscle during MVC was significantly pronounced in TMD patients compared to normal subjects. The asymmetry of the anterior temporalis muscle was more pronounced in TMD patients during 70% MVC and was estimated at 28.6%, compared with 19.6% in normal subjects.

The results of the aforementioned studies suggest that an association exists between TMD and pain-related TMD and masticatory muscle EMG activity. Our study also revealed the influence of TMD-P on masticatory muscle EMG potentials in children with cleft lip and palate. Cleft children diagnosed with TMD-P have altered temporalis and masseter muscle activity compared with non-TMD subjects. From a clinical point of view, what is important is the fact that alteration of the pattern of muscle electrical activity in TMD-P patients can affect muscle fatigue, and can, as a consequence, have an impact on every function they perform in the stomatognathic system [60]. Such knowledge is essential when it comes to developing treatment protocols to normalize muscle activity and improve muscle function in these patients. However, we ought to be aware of the study's limitations, such as the relatively small number of subjects involved. In addition, the groups studied cover a comparatively wide age range. Hence, some differences between patients may result from variations in neuromuscular system development. Another possible limitation of the study might be the fact that the TMD-pain group included both joint- and muscle-related pain disorders, since EMG activity may vary in these subgroups of patients. In this context, further studies involving a larger number of patients are needed to confirm the study results.

5. Conclusions

The EMG recordings showed that in comparison to non-TMD cleft patients, children diagnosed with CLP and pain-related TMD have greater temporalis and masseter muscle activity at rest, reduced temporalis muscle activity during maximum voluntary contraction, and a higher Asymmetry Index for the temporalis and masseter muscles in the rest position. The altered masticatory muscle activity in TMD-P children can affect their muscle function.

Ethical Approval

The present study was previously approved by the Local Bioethics Committee of the Medical University and assigned number KB-0012/08/15. All the children's parents were informed about the examination procedures and gave their consent to all the procedures performed.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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Research Article

Low-Level Laser Therapy for Temporomandibular Disorders: A Systematic Review with Meta-Analysis

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Objectives. We systematically reviewed randomized controlled trials (RCTs) of the effect of low-level laser therapy (LLLT) versus placebo in patients with temporomandibular disorder (TMD). *Methods*. A systematic search of multiple online sources electronic databases was undertaken. The methodological quality of each included study was assessed using the modified Jadad scale, and the quality of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system. *Results*. A total of 31 RCTs were included. Total modified Jadad scale scores showed that the methodological quality was high in 30 studies and low in 1 study. Combining data from all clinically heterogeneous studies revealed positive effects of LLLT on pain relief, regardless of the visual analogue scale (VAS) score or the change of VAS score between the baseline and the final follow-up time point, while dosage analyses showed discrepant results about the effects of high or low doses for patients with TMD. Follow-up analyses showed that LLLT significantly reduced pain at the short-term follow-up. Temporomandibular joint function outcomes indicated that the overall effect favored LLLT over placebo. *Conclusion*. This systematic review suggests that LLLT effectively relieves pain and improves functional outcomes in patients with TMD.

1. Introduction

Temporomandibular disorder (TMD) is a set of clinical conditions that includes disorders of the temporomandibular joint (TMJ) and/or the masticatory muscles [1]. The most common symptoms are pain, joint noises, and restricted mandibular movement [2]. A variety of other symptoms may occur, such as tinnitus, abnormal swallowing, and hyoid bone tenderness [3, 4]. These symptoms compromise quality of life (QoL) [5], sleep [6], and the psychological well-being, leading to anxiety, stress, depression, and a negative effect on social function, emotional health, and energy level [7]. The incidence of signs and symptoms of TMD varies from 21.5% to 50.5%, and they occur more frequently among women than men [8–10].

The etiopathogenesis of TMD remains unclear. In general, it is thought that the origin of TMD is multifactorial, including biomechanical, neuromuscular, biopsychosocial, and biological factors [11]. Therefore, the mainstay of treatment for TMD is a multidisciplinary approach that includes physical therapy modalities such as manual therapy [12], electrotherapy [13], ultrasound [14], transcutaneous electrical nerve stimulation (TENS) [15], or laser therapy [16].

Among the various physical therapy modalities, low-level laser therapy (LLLT) has recently been put under the spotlight because of its easy application, short treatment time, and few contraindications. Many prospective clinical trials have been performed to evaluate the efficacy of LLLT. However, the results have been controversial [16–21]. Some authors have reported the superiority of LLLT over placebo [16, 20, 21], while others have found no significant differences between LLLT and placebo [17–19].

Over the past recent years, a number of systematic reviews with or without meta-analysis have analyzed the efficacy of LLLT for TMD [2, 22–27]. Based on the included studies, which were all published before 2010, four systematic reviews concluded that there was no definite evidence to support the use of LLLT in the management of TMD [22–25]. On the contrary, one meta-analysis published in 2014 concluded that applying LLLT to the masticatory muscle or joint capsule has a moderate analgesic effect on TMJ pain [2]. In 2015, another meta-analysis provided evidence that using LLLT has limited efficacy in reducing pain, but can significantly improve the functional outcomes of patients with TMD [26]. However, there is no solid evidence to support or refute LLLT for TMD.

Since the latest published meta-analysis, many new randomized controlled trials (RCTs) have been conducted, which may accumulate evidence on the use of LLLT for TMD [4, 28–31]. Therefore, in this systematic review with meta-analysis, we reevaluated the effect of LLLT versus placebo in patients with TMD. The results of this study may provide practical recommendations for clinical physicians who treat patients with TMD.

2. Methods

2.1. Search Strategy and Selection Criteria. This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [32, 33] and Cochrane handbook for systemic reviews [34]. We systematically searched PubMed, EMBASE, CINAHL, ClinicalTrials.gov, the Cochrane Library database, AMED, Toxline, PEDro, ProQuest Digital Dissertations, PsycBite, SCOPUS, Current Contents Connect, Web of Science, and the WHO Trial Registry for RCTs comparing LLLT with a placebo intervention in patients with TMD.

The following search terms were used: "temporomandibular disorder(s)" OR "temporomandibular joint disorder(s)" OR "temporomandibular joint dysfunction" OR "TMJ disorder (s)" OR "TM disorder(s)" OR "temporomandibular joint pain" OR "temporomandibular pain" OR "TM pain" OR "TMJ pain" OR "TMD" OR "temporomandibular osteoarthritis" OR "myofascial pain" OR "craniomandibular disorder(s)" OR "mandibular dysfunction" AND "laser" OR "laser therapy" OR "low level laser therapy" OR "low intensity laser therapy (LILT)" OR "low energy laser therapy (LELT)" OR "LLLT" OR "infrared (IR) laser" OR "IR laser" OR "diode laser" OR "helium-neon laser" OR "HeNe laser" OR "gallium-arsenide laser" OR "GaAs laser" OR "gallium-aluminium-arsenide laser" OR "GaAlAs laser." The last search was performed on May 16, 2017.

Inclusion criteria were as follows: (1) RCTs involving patients with TMD; (2) articles published or informally published in English or Chinese; and (3) primary studies or studies in which LLLT was compared with placebo or sham laser, with similar appearance to the active treatment but without laser irradiation, in patients with TMD; and (4) studies of LLLT for myogenous or arthrogenous temporomandibular pain, or both, regardless of age and gender. Studies including cointerventions were allowed if applied equally to both the LLLT and placebo groups.

Exclusion criteria were as follows: (1) nonrandomized or crossover studies; (2) total number of study participants (in the LLLT and placebo groups combined) less than 10; (3) meeting abstracts that did not report data for the outcomes of interest; and (4) studies involving patients with systemic diseases (i.e., fibromyalgia and rheumatoid arthritis) or pain not related to TMD (i.e., neuralgia, toothache, and psychological disturbances).

2.2. Study Selection. Two independent reviewers (Xu and Jia) initially screened and identified relevant titles and abstracts. Full-text articles were obtained for all eligible studies, and these were assessed independently by Jin and Li against an inclusion and exclusion checklist. Disagreements were resolved by discussion until consensus was reached; if this approach failed, a third party (Cao) was consulted. The reference lists of all retrieved studies were manually examined to identify any studies missed by the electronic literature search. We also contacted all principal investigators or corresponding authors of the identified studies for additional information where necessary.

2.3. Outcome Measures. The primary outcome of interest was pain intensity, as expressed by visual analogue scale (VAS) score (at the final follow-up time point) or the change of VAS score (between the baseline and the end of the follow-up) in the LLLT and placebo groups.

The secondary outcomes included the change of TMJ function between the baseline and the end of the follow-up, oral function (masticatory performance), electromyographic (EMG) activity, adverse effects, pressure pain threshold (PPT), joint noises, tinnitus, quality of life (QoL), and psychological satisfaction in the LLLT and placebo groups.

TMJ function was assessed in terms of maximum active vertical opening (MAVO), maximum passive vertical opening (MPVO), lateral excursion (LE), and protrusion excursion (PE), expressed in millimeters.

2.4. Data Extraction. We used data from the longest follow-up time point for each trial. Data were extracted and cross-checked independently by Li and Wang using a standard data extraction form that contains general information (authors, publication year), subject number, treatment-related information, and relevant clinical outcome data. Authors were contacted to clarify further information where necessary. In three RCTs that examined more than one laser dose, the placebo group was divided into two equal-sized groups to avoid "double counting" to allow inclusion of two independent comparisons within the meta-analysis [30, 35, 36].

Data from the included studies were pooled for further meta-analysis where appropriate. If available, means and standard deviations for outcome measures were extracted or calculated based on the published data with RevMan 5.0 software as supplied by the Cochrane Collaboration. Means and standard deviations were used to calculate mean differences (MDs) and 95% confidence intervals (CIs) in the meta-analysis.

2.5. Assessment of Methodological Quality. All included studies were assessed for methodological quality using the modified Jadad scale [37]. Two reviewers (Xu and Jia)

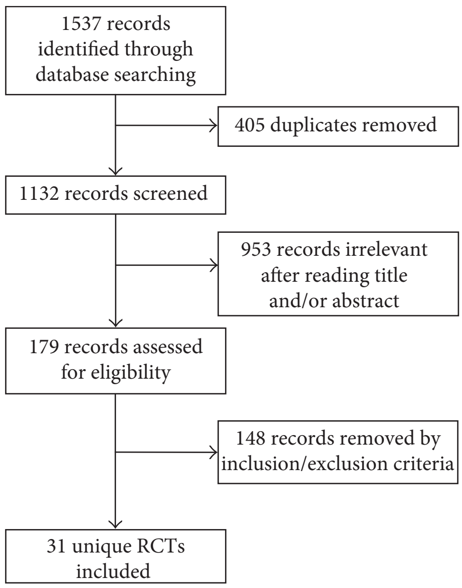

Figure 1: The study selection process for the systematic review.

performed the assessment independently, and discrepancies between reviewers were resolved by consensus. Studies achieving four or more points (from a maximum of eight) were considered to be of high quality, while studies scoring below four were considered to be of low quality.

2.6. Statistical Analysis. Dichotomous outcomes were expressed as relative risks (RRs) and continuous outcomes were expressed as the weighted mean differences (WMDs), both were presented with 95% CIs. Pooled effect sizes were based on the results of pain intensity (assessed by VAS) as well as MAVO, MPVO, LE, and PE values in millimeters. Revman 5.0 Software was used to summarize the effects and to construct the forest plots for all comparisons. Heterogeneity was examined according to the I^2 statistic alongside the chi-squared test; if I^2 was greater than 50%, the random-effects model was applied [38]. Qualitative analysis was performed if studies failed to provide data to be pooled for analysis. Publication bias was assessed by examination of funnel plots for primary outcomes. A symmetric funnel plot represented lower risk of bias and vice versa. Because interstudy heterogeneity precluded a meta-analysis in some outcomes, narrative synthesis of related studies was employed.

2.7. Subgroup and Sensitivity Analysis. Subgroup and sensitivity analysis were planned in the presence of heterogeneity. Subgroup analysis was performed to evaluate the effect of the intervention at different laser dosages and follow-up periods (short-term and long-term effects). Sensitivity analysis was performed for testing the robustness of the pooled effect size where appropriate. Effects were examined according to methodological quality, to ensure that the analysis was not biased by a low-quality study or a study with a large population.

2.8. Evaluation of Quality of Evidence. The quality of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system [39], which is based on five domains (limitations of the study design, inconsistency, indirectness, imprecision, and publication bias).

3. Results

3.1. Search Results. The study selection process is shown in Figure 1. A total of 1537 records were identified from searches. No unpublished manuscripts were identified. After excluding 1506 records, a total of 31 articles that met the inclusion criteria were included in the present systematic review.

3.2. Characteristics of the Included Studies. General information and technical features of the included studies are summarized in Tables 1 and 2, respectively. All studies were RCTs published in English, except one Chinese study. Participants received a total of 3 to 20 treatment sessions. There were seven different types of laser among the 31 included studies. Gallium-aluminium-arsenide laser (GaAlAs) was applied in 20 studies [1, 16, 17, 19–21, 28, 29, 31, 35, 36, 40–48], gallium-arsenide laser (GaAs) in six studies [30, 49–53], and neodymium-doped yttrium aluminum garnet (Nd:YAG) in two studies [4, 54]. Helium-neon laser (HeNe) [18], indium-gallium-aluminum-phosphide laser (InGaAlP) [53], and diode laser [4] were applied each in one study. The laser type was not mentioned in two studies [55, 56]. The shortest wavelength of laser was 632.8 nm and the longest was 1064 nm. Laser dosage varied from 1.5 J/cm^2 to 112.5 J/cm^2; four studies did not report the dosage [20, 21, 31, 50].

Two studies including cointerventions applied equally to both LLLT and placebo groups: in one study, LLLT was combined with piroxicam [28]; in the other study, it was combined with oral motor (OM) exercises [40]. Two studies investigated the combination of two types of laser: one study applied InGaAlP (660 nm) and GaAs (890 nm) [53], while the other applied Nd:YAG (1064 nm) and diode laser (810 nm) [4]. One study combined GaAlAs at two wavelengths (650 nm/830 nm) [21]. There were four studies using only one laser type, but at two or three laser dosages [35, 36, 44, 45]. There was one study which applied one type of laser, but at two application sites [30]. The majority of the included studies compared LLLT and placebo groups, except for four studies involving other interventions, namely, ibuprofen [20], occlusal splint [54], needling [55], and physiotherapeutic and drug protocol (PDP) [47]. The final follow-up time point varied from immediately to 3 months after completing the treatment. Application sites were generally the TMJ and/or temporomandibular muscles. One study added remote acupuncture points [16].

The majority of the included studies provided pain intensity data. Thirteen RCTs investigated mouth opening (MO) [17, 19–21, 28, 30, 36, 44, 46, 49, 51, 55, 56], nine focused on LE [17, 19–21, 30, 36, 46, 49, 51], six focused on PE [17, 19, 21, 30, 36, 51], seven focused on PPT

Table 1: General information and modified Jadad score in the included trials.

Study	Research location	n	Treatment design	Aspect evaluated	Evaluations/follow-up	Evaluation methods	Modified Jadad score
Conti [17]	Brazil	20	Laser (10) versus placebo (10)	PI, mandibular function	After each treatment	VAS, MO, LE, PE	5
Kulekcioglu [49]	Turkey	35	Laser (20) versus placebo (15)	PI, mandibular function, joint sounds,	Before, after, and 1 month after treatment	VAS, MO, LE, auscultation	5
Venancio [19]	Brazil	30	Laser (15) versus placebo (15)	PI, mandibular function, pain sensitivity	Immediately before the first, third, and fifth treatment sessions, and at the follow-up appointments after 15, 30, and 60 days of the end of treatment	VAS, MO, LE, PE, PPT	5
Mazzetto [41]	Brazil	48	Laser (24) versus placebo (24)	PI	Before treatment, after the 4th and 8th applications, and 30 d after the last application.	VAS	6
Cunha [42]	Brazil	40	Laser (20) versus placebo (20)	PI, TMD status	Before treatment and after the last treatment	VAS, DI, CMI, palpation index	5
Carrasco [1]	Brazil	14	Laser (7) versus placebo (7)	PI, masticatory efficiency	Before treatment, after the 8th application, 30 days after the last application	VAS, colorimetric capsule method	5
Emshoff [18]	Austria	52	Laser (26) versus placebo (26)	PI	Before treatment and 2, 4, and 8 weeks after the first laser therapy	VAS	7
Lassemi [50]	Iran	48	Laser (26) versus placebo (22)	PI, joint sounds	Before treatment, immediately, 2 and 4 days after treatment	VAS, stethoscope	3
Carrasco [43]	Brazil	60	Laser (30, 3 parameter groups, 10 in each group) versus placebo (30)	PI	Before treatment, after the 4th and 8th applications, 15 days and 1 month after the last application	VAS	5
Shirani [53]	Iran	16	Laser (the combination of two wavelengths, 8) versus placebo (8)	PI	Before and immediately after treatment, 1 week after treatment, and on the day of feeling complete pain relief	VAS	6
Marini [20]	Italy	99	Laser (39) versus ibuprofen versus (30) placebo (30)	PI, mandibular function, morphologic structural analysis of TMJ	PI at baseline, 2, 5, 10, and 15 days after treatment. Mandibular function at baseline, 15 days and 1 month after treatment. MRI at baseline and at the end of the treatment.	VAS, MO, LE, MRI	6
Sattayut [35]	England	30	Low energy laser (10) versus high energy laser (10) versus placebo (10)	PI, pain sensitivity, mandibular movements, EMG activity	Baseline and 1, 3, 5, and 8 days after treatment	VAS, PPT, EMG, McGill pain questionnaire	6
Silva [36]	Brazil	45	Low energy laser (15) versus high energy laser (15) versus placebo (15)	PI, madibular movements	Before treatment, immediately after the first, fifth, tenth treatments, and 5 weeks after completing the applications	VAS, MO, LE, PE	6

Table 1: Continued.

Study	Research location	n	Treatment design	Aspect evaluated	Evaluations/follow-up	Evaluation methods	Modified Jadad score
Ferreira [16]	Brazil	40	Laser (20) versus placebo (20)	PI	Before intervention, monthly until intervention completed	VAS	7
Ahrari [44]	Iran	20	Laser (10) versus placebo (10)	PI, madibular movements	Before intervention, after six applications, at the end of treatment, and 1 month after the last application	VAS, MO	6
Demirkol [54]	Turkey	30	Laser (10) versus occlusal splint (10) versus placebo (10)	PI	Before treatment, immediately and 3 weeks after treatment	VAS	4
Röhlig [51]	Turkey	40	Laser (20) versus placebo (20)	PI, functional examination, pain sensitivity	Before treatment and after the last applications	VAS, MO, LE, PE, PPT	8
Wang [21]	China	42	Laser (21) versus placebo (21)	PI, functional examination	Before treatment, immediately, 1 month and 2 months after treatment	VAS, MO, LE, PE	5
Carli [28]	Brazil	32	Laser + piroxicam (11) versus laser + placebo piroxicam (11) versus placebo laser + piroxicam (10)	PI, functional examination	Before treatment, after the first, second, third, and fourth treatment sessions, and 30 days after last treatment.	VAS, MO	8
Fornaini [31]	Italy	24	Laser (12) versus placebo (12)	PI	Before treatment, 1 and 2 weeks after treatment	VAS	5
Sancakli [30]	Turkey	30	Laser I (10) versus laser II (10) versus placebo (10)	PI, mandibular mobility, pain sensitivity	Before treatment and after the completion of therapy	VAS, MO, LE, PE, PPT	7
Frare [52]	Brazil	18	Laser (10) versus placebo (8)	PI	Before and immediately after all sessions of laser applications	VAS	4
Venezian [45]	Brazil	48	(1): Laser I (12) versus placebo I (12) (2): Laser II (12) versus placebo II (12)	PI, EMG activity	PI: before treatment, immediately and 30 days after treatment EMG: before and immediately after treatment	VAS, EMG	6
Mazzetto [46]	Brazil	40	Laser (20) versus placebo (20)	PI, mandibular movements	Before treatment, immediately, 7 and 30 days after applications	VAS, MO, LE	4
Uemoto [55]	Brazil	21	Laser (7) versus needling group (7) versus placebo (7)	PI, EMG activity, pain sensitivity, madibular movements	Before treatment, after four sessions with intervals ranging between 48 and 72 h	VAS, EMG, PPT, MO	4
Madani [56]	Iran	20	Laser (10) versus placebo (10)	PI, madibular movements, joint sounds	Before treatment, after 6 and 12 applications and 1 month after last application	VAS, MO, perceiving joint sounds by the fingertips	6
Maia [29]	Brazil	21	Laser (12) versus placebo (9)	PI, masticatory performance, pain sensitivity	MP and PPT, before treatment, at the end of treatment and 30 days after treatment VAS, at the same time as above and was also measured weekly	VAS, optical test material, PPT	5

Table 1: Continued.

Study	Research location	n	Treatment design	Aspect evaluated	Evaluations/follow-up	Evaluation methods	Modified Jadad score
Cavalcanti [47]	Brazil	60	Laser (20) versus PDP (20) versus placebo (20)	Presence or absence of pain	Before treatment, at each week till the fourth week after treatment	Muscle tenderness palpation and the questionnaire of fonseca	4
Magri [48]	Brazil	91	Laser (31) versus placebo (30) versus control (30)	PI, pain sensitivity, the sensory and affective dimensions of pain	Before treatment, after each treatment and 30 days after last treatment	VAS, PPT, SF-MPQ	7
Demirkol [4]	Turkey	46	Nd:YAG laser (15) versus diode laser (16) versus placebo (15)	The severity of the tinnitus	Before treatment, immediately and 1 month after treatment	VAS	4
Machado [40]	Brazil	82	GI: laser + OM exercises (21) versus GII: pain relief strategies + OM exercises (22) versus GIII laser placebo + OM exercises (21) versus GIV: laser (18)	PI, TMD severity, and orofacial myofunctional status	Before treatment, immediately and 3 months after last treatment	ProTMDmulti-part II questionnaire, orofacial myofunctional evaluation with scores	5

CMI: craniomandibular index; DI: dysfunction index; EMG: electromyography; LE:_lateral excursion; ME: masticatory efficiency; MO: mouth opening; MRI: magnetic resonance imaging; *n*: number; OM: oral motor; PDP: physiotherapeutic and drug protocol; PE: protrusion excursion; PI: pain intensity; PPT: pressure pain threshold; SF-MPQ: short form McGill Pain Questionnaire; TMD:_temporomandibular disorder; TMJ:_temporomandibular joint; VAS: visual analogue scale.

[19, 29, 30, 35, 48, 51, 55], three focused on joint noises [49, 50, 56], two focused on masticatory efficiency [1, 29], and one focused on subjective tinnitus [4]. Three studies applied EMG as a study parameter [35, 45, 55].

3.3. Quality Assessment. A summary of the quality assessment using the modified Jadad scale scores is shown in Table 1. Total scores showed that the quality of 30 studies was high, with a minimum of 4 points and a maximum of 8 points. One study had low quality (3 points) [50] (Supplementary Material Appendix A).

3.4. Effects of Laser Therapy. The 31 RCTs showed mixed results, as reported by the authors, with two-thirds reporting positive effects favoring LLLT and one-third reporting inconclusive results or no effect. Twenty-two studies provided sufficient data to calculate effect sizes for key outcome measures and were included in the meta-analysis. Subgroup analysis was performed for laser dose and follow-up period using the random-effects model. Studies were subcategorized into low dosage (≤50 J/cm^2) versus high dosage (>50 J/cm^2) and into short-term follow-up (≤2 weeks) versus long-term follow-up (>2 weeks). For all studies, we only collected data from the final follow-up time point.

3.5. Primary Outcomes. All 22 studies, except three [4, 40, 47], used VAS to assess pain as one of the primary outcome measures. However, as a result of data detectability, only 19 studies were subjected to meta-analysis.

3.5.1. VAS Score. Seventeen of the included studies provided VAS scores at the final follow-up time point. Meta-analysis of data from 643 participants across 17 studies indicated a statistically significant reduction in total pain scores in LLLT versus placebo groups. The overall effect for pain favored LLLT (WMD = −14.05; 95% CI = −25.67 to [−2.43]; $P = 0.02$; $I^2 = 96\%$), yet with substantial heterogeneity. Subgroup analysis showed significant differences between LLLT and placebo groups at high dosage (WMD = −10.42; 95% CI = −19.67 to [−1.17]; $P = 0.03$; $I^2 = 51\%$) and unknown dosage (WMD = −33.75; 95% CI = −57.18 to [−10.33]; $P = 0.005$; $I^2 = 98\%$). However, there were no significant differences between the two groups at low dosage (WMD = −9.22; 95% CI = −18.78 to 0.34; $P = 0.06$; $I^2 = 85\%$) (Supplementary Material Appendix B).

There were significant differences between the two groups at the short-term follow-up (WMD = −14.66; 95% CI = −21.04 to [−8.29]; $P < 0.00001$; $I^2 = 71\%$). However, LLLT failed to show significant favorable effects on pain scores at long-term follow up compared to the placebo (WMD = −14.84; 95% CI = −35.35–5.68; $P = 0.16$; $I^2 = 97\%$) (Supplementary Material Appendix B).

3.5.2. Mean Difference of VAS Score. The mean difference of VAS score (change scores from baseline) between the baseline and the final follow-up time point was used [17, 42, 49, 53]. When the data were missing, we calculated them using the published relevant data with RevMan 5.0 software [1, 16, 18–21, 28, 30, 31, 35, 41, 43, 50, 51, 54]. Analysis of data from 679 subjects (19 studies) revealed a significant difference between the LLLT and placebo

Table 2: Parameters of LLLT and outcomes in the included trials.

Study	Laser type	Treatment time/number of total sessions/number of sessions week^{-1}	Application sites	Power	Dosage (J/cm^2)	Outcome
Conti [17]	GaAIAs 830 nm	40 s/3/1	TMJ and/or muscles	79 mW	4	LLLT = placebo
Kulekcioglu [49]	GaAs 904 nm	180 s/15/–	TMJ and/or muscles	17 mW	3	LLLT > placebo (MO, LM) LLLT = placebo (PI, TMJ sounds)
Venancio [19]	GaAlAs 780 nm	10 s/6/2	TMJ	30 mW	6.3	LLLT = placebo
Mazzetto [41]	GaAIAs 780 nm	10 s/8/2	TMJ (external auditory meatus)	70 mW	89.7	LLLT > placebo
Cunha [43]	GaAlAs 830 nm	20 s/4/1	TMJ and/or muscles	500 mW	100	LLLT = placebo
Carrasco [1]	GaAlAs 780 nm	60 s/8/2	TMJ	70 mW	105	LLLT > placebo (PI on palpation) LLLT = placebo (ME: masticatory efficiency)
Emshoff [18]	HeNe 632.8 nm	120 s/20/2-3	TMJ	30 mW	1.5	LLLT = placebo
Lassemi [50]	GaAs 980 nm	60 s/2/2	TMJ and muscles	NA	NA	LLLT > placebo
Carrasco [43]	GaAlAs 780 nm	60 s/8/2	Muscles	50/60/70 mW	25/60/105	LLLT = placebo
Shirani [53]	InGaAlP 660 nm and GaAs 890 nm	360 s/6/2 600 s/6/2	Muscles	17.3 mW and 1.76 mW	6.2 and 1.0	LLLT > placebo
Marini [20]	GaAIAs 910 nm	20 min/10/5	TMJ	400 mW	NA	LLLT > placebo
Sattayut [35]	GaAIAs 820 nm	–/3/–	TMJ and/or muscles	60 mW or 300 mW	21.4 or 107	LLLT > placebo (high energy) LLLT = placebo (low energy)
Silva [36]	GaAIAs 780 nm	30 s or 60 s/10/2	TMJ and/or muscles	70 mW	52.5 or 105.0	LLLT > placebo
Ferreira [16]	GaAIAs 780 nm	90 s/12/1	TMJ and muscles	50 mW	112.5	LLLT > placebo
Ahrari [44]	GaAIAs 810 nm	120 s/12/3	Muscles	50 mW	3.4	LLLT > placebo
Demirkol [54]	Nd:YAG 1064 nm	20 s/10/5	Muscle	250 mW	8	LLLT > placebo
Röhlig [51]	GaAs 820 nm	10 s/10/3-4	Muscle	300 mW	8	LLLT > placebo
Wang [21]	GaAIAs 650 nm/830 nm	15 min/6/6	TMJ	300 mW	NA	LLLT > placebo
Carli [28]	GaAlAs 830 nm	28 s/4/2	TMJ and muscles	100 mW	100	LLLT = placebo
Fornaini [31]	GaAlAs 808 nm	15 min/14/7	TMJ	250 mW	NA	LLLT > placebo
Sancakli [30]	GaAs 820 nm	10 s/12/3	Muscle	300 mW	3	LLLT > placebo
Frare [52]	GaAs 904 nm	16 s/8/2	TMJ and external auditory meatus	15 mW	6	LLLT > placebo
Venezian [45]	GaAIAs 780 nm	20 or 40 s/8/2	Muscles	50/60 mW	25 or 60	LLLT = placebo
Mazzetto [46]	GaAlAs 830 nm	10 s/8/2	TMJ	40 mW	5	LLLT > placebo
Uemoto [55]	Laser type NA, 795 nm	–/4/–	Muscle	80 mW	4 or 8	LLLT > placebo (only 4 J/cm^2)
Madani [56]	Laser type NA, 810 nm	120 s/12/3	TMJ and muscles	50 mW	3.4	LLLT = placebo
Maia [29]	GaAlAs 808 nm	19 s/8/2	Muscle	100 mW	70	LLLT > placebo

Table 2: Continued.

Study	Laser type	Treatment time/number of total sessions/number of sessions week^{-1}	Application sites	Power	Dosage (J/cm^2)	Outcome
Cavalcanti [47]	GaAlAs780 nm	20 s/12/3	TMJ and muscles	70 mW	35.0	LLLT > placebo
Magri [48]	GaAlAs 780 nm	10 s/8/2	TMJ and muscles	TMJ, 20 mW; muscle, 30 mW	5 or 7.5	LLLT = placebo
Demirkol [4]	Nd:YAG laser (1064 nm), diode laser (810 nm)	20 s or 9 s/10/5	External auditory meatus	250 mW	8	LLLT > placebo
Machado [40]	GaAlAs 780 nm	45 min/12/1–0.5	TMJ and muscles	60 mW	60 ± 1.0	LLLT = placebo

GaAlAs: gallium-aluminium-arsenide laser; Ga-Ar: gallium argon; GaAs: gallium-arsenide laser; HeNe: helium-neon laser; InGaAlP: indium-gallium-aluminum-phosphide laser; LLLT: low-level laser therapy; NA: not available; Nd:YAG: neodymium-doped yttrium aluminum garnet; TMJ: temporomandibular joint.

groups (WMD = 15.43; 95% CI = 3.61–27.26; $P = 0.01$; $I^2 = 98\%$). Subgroup analysis showed significant differences at low dosage (weighted mean difference = 15.09; 95% CI = 5.37–24.80; $P = 0.002$; $I^2 = 93\%$) and unknown dosage (WMD = 36.31; 95% CI = 10.63–61.98; $P = 0.006$; $I^2 = 99\%$). However, there were no significant differences between the two groups at high dosage (WMD = 5.52; 95% CI = −5.52 to 16.56; $P = 0.33$; $I^2 = 80\%$) (Supplementary Material Appendix B).

In term follow up subgroup, similar to VAS score, there was significant differences between the two groups in the short-term follow up subgroup (WMD = 17.66; 95% CI = 9.94–25.38; $P < 0.00001$; $I^2 = 90\%$), but not at long-term follow up compared to the placebo (WMD = 13.85; 95% CI = −7.73 to 35.43; $P = 0.21$; $I^2 = 99\%$) (Supplementary Material Appendix B).

3.5.3. Sensitivity Analysis. The pooled results were in favor of LLLT based on the above-mentioned main findings (see Supplementary Material Appendix C), after excluding low-quality [50] and/or extreme value and maximal weight value (large population) studies [20].

3.6. Secondary Outcomes

3.6.1. Functional Outcomes. The secondary outcomes included the change of TMJ function from baseline to the end of the follow-up in LLLT and placebo groups. TMJ function was assessed in terms of MAVO, MPVO, LE, and PE. These four outcomes all indicated that the overall effect favored LLLT over placebo: MAVO (WMD = 6.37; 95% CI = 2.82–9.93; $P = 0.0004$; $I^2 = 95\%$), MPVO (WMD = 6.96; 95% CI = 1.99–11.93; $P = 0.006$; $I^2 = 92\%$), LE (WMD = 3.52; 95% CI = 2.63–4.40; $P < 0.00001$; $I^2 = 90\%$), and PE (WMD = 1.77; 95% CI = 0.09–3.45; $P = 0.04$; $I^2 = 95\%$).

Most of these outcomes showed significant differences between the LLLT and placebo groups, except for MAVO and PE at low dosage and PE at unknown dosage. In addition, there were no MPVO data in the high-dosage subgroup. All data of TMJ function in follow-up subgroups showed significant differences between the LLLT and placebo groups, except for MAVO at the short-term follow-up (Supplementary Material Appendix D).

3.6.2. PPT. Seven studies investigated pain by measuring PPT [19, 29, 30, 35, 48, 51, 55], expressed as mm, kpa, or kg/cm^2. It is impossible to estimate the overall effect size across the different scales. Four studies showed a significant change [29, 30, 35, 51], while two reported no change of PPT in the LLLT group compared to the placebo group [19, 48]. In another study [55], a significant improvement was observed in the LLLT group only at a dosage of 4 J/cm^2 ($P = 0.0156$), but not at 8 J/cm^2 ($P = 0.4688$).

3.6.3. EMG Activity. Three studies measured EMG activity before and after treatment [35, 45, 55]. LLLT did not promote any changes in EMG activity [45, 55]. However, in another study [35], EMG records in the maximum voluntary clenching (cEMG) of the MLILT (a modified high-energy LILT) group were significantly higher after the final treatment than those of the placebo group ($P = 0.022$, 95% CI = 5.96–68.66 microV), but there was no significant difference of cEMG between the CLILT (a conventional low-energy LILT) and placebo groups.

3.6.4. Oral Function Outcome Measures. Masticatory efficiency was evaluated in two studies [1, 29]. However, the used methods were different, for the results were considered inadequate for meta-analysis. Although both studies indicated that masticatory performance might be better after LLLT treatment, only one study [29] showed a significant improvement in masticatory performance in the LLLT group at the end of treatment compared with baseline values ($P < 0.01$).

3.6.5. Joint Noises. Three studies investigated joint noises following LLLT [49, 50, 56]. Two studies reported that LLLT could not reduce joint noises [49, 56]. Lassemi et al. reported LLLT could reduce "Click" compared to placebo [50], but the conclusion is questionable due to the low quality of the methodology.

3.6.6. Tinnitus. One study evaluated subjective tinnitus [4]. The study applied two types of LLLT in bilateral subjective tinnitus with TMD, namely, LLLT with Nd:YAG (1064 nm) and LLLT with a diode laser (810 nm). Both Nd:YAG and diode laser were effective for the treatment of subjective tinnitus related to TMD.

3.6.7. QoL and Psychological Satisfaction. None of the included studies reported QoL or psychological satisfaction as an outcome measure.

3.7. Adverse Effects. Nine of the 31 included studies reported no adverse effects related to laser application during or after the treatment period [4, 16, 28, 30, 47, 51–54]. The other studies lacked information regarding the adverse effects of laser exposure.

3.8. Publication Bias. Considering the heterogeneity of the studies, funnel plots were drawn according to different outcome measures. Visual assessment of funnel plots did not show considerable asymmetry in pain (VAS score), LE, and PE, indicating that the publication-related bias was low for these outcomes. However, there was asymmetry in MAVO and MPVO outcomes, indicating that the publication bias was high for these two outcomes (Supplementary Material Appendix E).

3.9. Quality of Evidence. The present meta-analysis investigated a total of six types of outcomes (including 29 subgroup analyses stratified by laser dosage and follow-up period) about pain intensity and mandibular function. The GRADE assessment of the level of evidence for these outcomes is shown in Supplementary Material Appendix F. The quality of the evidence was judged to range from very low to moderate. All domains affected low grades except indirectness.

4. Discussion

This systematic review and meta-analysis summarized RCTs that compared the effect of LLLT with placebo for the treatment of TMD. The results of the studies indicated that LLLT was effective in reducing TMD pain compared to placebo. In addition, LLLT could improve functional outcomes. Combining data from all clinically heterogeneous studies demonstrated positive effects of laser on pain relief, regardless of VAS score or the change of VAS score between the baseline and the final follow-up time point, while dosage subgroup analyses showed discrepant results about high or low dosage for TMD patients. The follow-up subgroup analysis showed more consistent results, suggesting LLLT significantly reduced pain at the short-term follow-up both in the VAS score and the change of VAS score. However, there was no significant difference at the long-term follow-up between LLLT and placebo. TMJ function outcomes, assessed in terms of MAVO, MPVO, LE, and PE (the changes between baseline and the end of follow-up) indicated that the overall effect favored LLLT over placebo. Most (five out of 7) studies indicated PPT improved by LLLT, but most (two out of 3) studies showed no change in EMG activity.

The use of LLLT has been seen as a complementary option for the treatment of TMD [16, 20, 21, 26] due to its analgesic, anti-inflammatory, and regenerative effects with no reported adverse effects and good acceptance by patients [16, 28, 30, 51, 53, 54, 57, 58]. In view of the lack of robust evidence about the effects of LLLT on TMD, recent systematic reviews did not reach a consensus [2, 22–27]. Here, we update the clinical evidence for the effects of LLLT on TMD.

Our results regarding the analgesic effect of LLLT are consistent with findings of Chang et al. [2], in contrast to those of Chen et al. [26], but the results regarding functional outcomes (motion) were in accordance with those of Chen et al. [26]. The strengths of our systematic review are the larger number of studies and the inclusion of the most recent publications since the last review in the subject.

As pain is the principal complaint of patients with TMD, pain is the most common reason why patients with TMD seek medical help. Pain occurs at any stage of TMD and pain reduction contributes to ameliorating jaw motion [26, 59], chewing [60], and masticatory performance [29]. Therefore, our primary outcome measure was pain intensity. Given the heterogeneity of the included studies, meta-analyses were performed using subgroups of studies according to the dosage and follow-up time. Although the overall effects of LLLT on pain were positive in both the VAS score and the change of VAS score, subgroup analysis reached contrary conclusions for high dosage versus low dosage in these two parameters. It is difficult to draw precise conclusions regarding an effective dosage window from these studies due to the contrary conclusions from subgroup analysis (analyzed by actual VAS score or the change of VAS score) and the wide dosage range employed. Four of the included studies [35, 36, 43, 45] compared high dosage with low dosage, but only one study [35] showed the superiority of high dosage, while the others showed no differences between the two dosages. The mechanism underlying the therapeutic effects of LLLT is under debate [61, 62]. The magnitude of the laser effect seems to also depend on the dosage of laser [63]. Bjordal et al. [64] believed that the controversy on the efficacy of LLLT on TMD laid in the disagreement on the dosage of laser. Laser acupuncture has been suggested to be a dosage-dependent modality [65, 66], suggesting that the energy delivered to the target point by laser acupuncture has to reach a threshold in order to produce a desired effect. Thus, the dosages used in the included studies may explain the observed differences in outcomes.

With regard to the relationship between laser effectiveness and follow-up period, Law et al. found that long-term follow-up effects increased in three types of musculoskeletal disorders (myofascial pain/musculoskeletal trigger points, lateral epicondylitis, and temporomandibular joint pain) [67]. Pooled effect sizes were doubled during the follow-up period compared to those at the end of intervention, suggesting that laser may have delayed or long-lasting effects. However, our follow-up subgroup analysis showed a more consistent result, contrary to Law et al., both of pain evaluation methods showing significant differences only in short-term follow up between the laser and placebo groups. In one trial conducted by Carli et al. [28], laser, piroxicam, and placebo significantly improved the VAS score. An evaluation at 30 days after the end of the treatment showed that the laser did not have a residual effect, and piroxicam was more effective than the laser to reduce the level of muscular pain in patients with TMJ arthralgia. These results illustrate that laser may have a short-lived effect, which is consistent with our follow-up subgroup analysis data. However, because of the high degree of heterogeneity, this finding needs to be explored in further research. Nonetheless, the present systematic review and others support the continued use of laser for treating TMD/musculoskeletal pain.

Besides the subjective pain assessments, the objective clinical outcomes include TMJ function, PPT, EMG, and masticatory performance. The overall effects in MAVO, MPVO, LE, and PE favored LLLT over placebo. In most studies, LLLT increased PPT, but did not affect EMG activity. Only one study [29] showed that LLLT improved masticatory performance at the end of treatment compared with baseline values, but other study [1] showed no significant effects.

Skin surface application of laser (trigger points/tender points) was used in most of the included studies, external auditory meatus was used in some studies [4, 41, 52], and only one study added remote application sites at acupuncture points [16]. We are unable to perform analysis on different sites for the variety and the complexity of these application sites.

It is worth to mention that using the combination of two wavelengths [21, 53] yields positive result. Shirani et al. [53] combined GaAs and InGaAlP lasers, usually applied for deep-lying disorders and superficial disorders, respectively. Another study [21] applying GaAlAs at 650 nm and 830 nm also obtained good effects, implying that the combination of two laser wavelengths may be beneficial to patients with TMD. During TMD treatment with LLLT, the variability of laser type, frequency, dosage, exposure time, application area, number of laser sessions, and therapy duration may increase heterogeneity in effects. Thus, the findings of clinical studies must be interpreted against the background. Using proper laser parameters is important to obtain better effects, as suggested by Law et al. [67] Additionally, due to the multifactorial etiology of TMD, including biopsychosocial and biological factors [11], about one-third of the patients report eating problems and feelings of depression or dissatisfaction with life [68]. However, none of the included studies focused on psychological assessment. TMD diagnosis has been standardized based on research diagnostic criteria for temporomandibular disorders (RDC/TMD) that constitute a multidimensional diagnostic research tool adopted worldwide [69, 70]. This standardization has improved reproducibility among clinicians and has facilitated the comparison of results among researchers [16, 28, 44]. It is important to establish standardized therapy regimens about TMD through evaluating relevant behavioral, psychological, and psychosocial factors (e.g., pain status variables, depression, nonspecific physical symptoms, and disability levels) [69, 70]. In addition, the effect of laser can be further evaluated by adding QoL and patient satisfaction as outcome measures.

Nine of the 31 included studies explicitly stated that no adverse effects were observed [4, 16, 28, 30, 47, 51–54]. The other studies lacked information regarding the adverse effects of laser exposure. Nevertheless, it is thought that LLLT is safe. LLLT is noninvasive and has few or none adverse effects, which may contribute to increased patient comfort.

This systematic review has some limitations. First, the methodological quality varied among the included studies. Second, there was a high degree of heterogeneity because of differences in TMD diagnosis, laser style, laser parameters, treatment regimens, outcome measurements, and follow-up time, which hindered some comparisons between studies. Furthermore, discrepancies also existed in the inclusion and exclusion criteria. Third, although we tried to obtain full data, some data were missing because some of the studies reported continuous variables such as MAVO or MPVO without SD, while others used box plots or histograms to represent the data. Moreover, most of the included studies had small sample sizes (≤60 subjects), which limited the generalizability of the conclusions. Fourth, although a systematic search of multiple databases was undertaken, some unpublished grey literature might have been missed. In addition, some of the included studies were not used in the meta-analysis. Thus, potential publication bias and selection bias could not be eliminated. We only included English and Chinese language articles, which could induce a language bias. Pooled analysis of all kinds of TMD (muscular origin, articular origin, or a combination of both) degraded the level of conclusion because of the poor description of TMD type in some studies. Given the above reasons, the findings from this study should be interpreted cautiously.

5. Conclusion

The results of this systematic review and meta-analysis are encouraging. Despite the above-mentioned limitations, the overall effect illustrated that LLLT effectively relieves pain in the treatment of TMD. LLLT may induce a short-term effect only, but the existing evidence does not allow us to determine an effective dosage window. Moreover, LLLT also improves the functional outcomes in TMD. In view of the high discrepancy among the included studies, this systematic review highlights the need for more well-designed RCTs with larger sample sizes to evaluate the efficacy of LLLT. Future research should carefully define the study population and provide the rationale for the parameters chosen. This would facilitate not only replication in the clinical setting, but also improve trial homogeneity and allow data to be pooled for meta-analysis. Furthermore, it is necessary to examine different laser parameters, treatment regimens, evaluation times, and outcome measures because it is noninvasive, safe, easy-to-use, and cheap.

Conflicts of Interest

The authors declare that they have no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplementary Materials

Appendix A: quality assessment of the included studies according to modified jadad score. Appendix B: forest plots of primary outcomes (pain). Appendix C: primary outcomes/pain-sensitivity analysis. Appendix D: forest plots (functional outcomes). Appendix E: funnel plot. Appendix F: GRADE evidence profile for pain and functional outcomes. (*Supplementary Materials*)

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Clinical Study

Assessment of the Short-Term Effectiveness of Kinesiotaping and Trigger Points Release Used in Functional Disorders of the Masticatory Muscles

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Chronic face pain syndrome is a diagnostic and therapeutic problem for many specialists, and this proves the interdisciplinary and complex nature of this ailment. Physiotherapy is of particular importance in the treatment of pain syndrome in the course of temporomandibular joint functional disorders. In patients with long-term dysfunction of masticatory muscles, the palpation examination can localize trigger points, that is, thickening in the form of nodules in the size of rice grains or peas. Latent trigger points located in the muscles can interfere with muscular movement patterns, cause cramps, and reduce muscle strength. Because hidden trigger points can spontaneously activate, they should be found and released to prevent further escalation of the discomfort. Kinesiotaping (KT) is considered as an intervention that can be used to release latent myofascial trigger points. It is a method that involves applying specific tapes to the patient's skin in order to take advantage of the natural self-healing processes of the body. The aim of the study was to evaluate the effect of the kinesiotaping method and trigger points inactivation on the nonpharmacological elimination of pain in patients with temporomandibular disorders. The study was conducted in 60 patients (18 to 35 years old). The subjects were randomly divided into two subgroups of 30 people each. Group KT (15 women and 15 men) were subjected to active kinesiotaping application. Group TrP, composed of 16 women and 14 men, was subjected to physiotherapy with the release of trigger points by the ischemic compression method. The results show that the KT method and TrP inactivation brought significant therapeutic analgesic effects in the course of pain-related functional disorders of the muscles of mastication. The more beneficial outcomes of the therapy were observed after using the KT method, which increased the analgesic effect in dysfunctional patients.

1. Introduction

Chronic myofascial pain syndrome is a diagnostic and therapeutic problem for many specialists, such as dentists, laryngologists, neurologists, neurosurgeons, general surgeons, anesthetists, psychiatrists, and oncologists [1]. This indicates the interdisciplinary and complex nature of these diseases. The prevalence of dysfunctional pain syndrome is estimated at around 12% of the adult population and 50% of the elderly population; it is more frequent in women between 20 and 40 years of age [2]. The percentage of women with headache associated with temporomandibular dysfunctions reaches up to 15%, and 10% in men [3]. Pain intensity varies from dull to acute. In people gnashing their teeth at night (occlusal parafunction, bruxism), morning pain in the joint and muscles is characteristic; it intensifies while eating and disappears during the day. In people clenching their teeth during the day, the pain may be most intense in the evening [4]. Signs and symptoms associated with temporomandibular dysfunctions include the pathological wear of the teeth as a result of bruxism, increased muscle tone in the masticatory muscles, overgrowth of the masseter, tinnitus, and changes in the psychological profile [5]. Differential diagnosis of pain in the course of temporomandibular dysfunction should exclude other pathologies of the temporomandibular joint, as well as tumours of the zygomatic bone, neoplasms of the nose, mandible, and parapharyngeal area, systemic connective tissue diseases, giant cell arteritis (mandible claudication), cluster headache, and reflex sympathetic dystrophy of the face [6].

The role of occlusal and nonocclusal parafunctions is emphasized potential etiological factors, along with malocclusion, missing teeth in the lateral areas, macro- and microinjuries of the joint, stress leading to hyperactivity of the masticatory muscles, the activation of masticatory muscles by the route descending from the limbic system and reticular formation, the lack of effective contraction of both lateral pterygoid muscles, and rheumatic diseases [7].

The multiple manifestations of the symptoms lead to a multitude of treatment methods and indicate that there is still no consensus in understanding the pathophysiology of the underlying TMD mechanisms. Because of the heterogeneity of the causes, the treatment of pain syndrome in the course of temporomandibular dysfunction should have a multiprofile character [8, 9].

Temporary pain relief can be obtained by pharmacological treatment with nonsteroidal anti-inflammatory drugs. Drugs that reduce muscle tone, antidepressants, and intra-articular steroids are also used. Dental treatment includes the use of, among others, flexible or hard occlusal splints [10–12]. Physiotherapy is of particular importance in the treatment of pain syndrome in the course of temporomandibular joint functional disorders. Positive therapeutic effects are obtained using botuline, laser therapy, heat therapy, light therapy, electrotherapy, electromagnetic field, manual therapy, proprioceptive neuromuscular motion paving, kinesiotherapy, relaxation techniques, autogenic training, and biofeedback to change of parafunctional behaviors [13, 14].

In patients with long-term dysfunction of masticatory muscles, the palpation examination can localize trigger points, that is, thickening in the form of nodules in the size of rice grains or peas. These are muscle fibres with increased tension, felt as thickening in the course of the muscle fibres. Latent trigger points located in the muscles can interfere with muscular movement patterns, cause cramps, and reduce muscle strength. Because hidden trigger points can spontaneously activate, they should be found and released to prevent further escalation of the discomfort [15]. Physiotherapeutic treatment is primarily based on the inactivation of trigger points by various techniques, such as compressive mobilization, positional release, myofascial relaxation, active relaxation technique, postisometric relaxation technique, or integrated neuromuscular inhibition technique (INIT) [16, 17]. Among the commonly used methods, we should also mention deep tissue massage and passive stretching of the muscles. Kinesiotaping is considered an intervention that can be used to release latent myofascial trigger points. This method involves the use of specific tapes applied to the patient's skin in order to take advantage of the natural self-healing processes of the body. It is very often applied as an element supportive of the therapeutic effect. The action of the method is mainly based on normalizing muscle tension, supporting the work of joints, improving the function of weakened muscles, and increasing microcirculation at the application site [18–20].

2. Study Objective

The aim of the study was to evaluate the effect of the kinesiotaping method and trigger points inactivation on the nonpharmacological elimination of pain in patients with temporomandibular disorders.

3. Materials and Methods

3.1. Material: Inclusion and Exclusion Criteria. The study was conducted during the years 2015-2016 in 60 patients (18 to 35 years old). All qualified patients suffered from painful functional disorders within the masticatory muscles of myofascial characteristic. Patients were also tested by the research diagnostic criteria for temporomandibular disorders (RDC/TMD) introduced by Dworkin and LeResche in 1992 [21]. This enables the standardization of the procedures of epidemiological studies, the unification of TMD diagnostic and exploratory criteria, and the comparison of results of other similar studies. The results of the study were based on the RDC/TMD Axis I diagnostic criteria. All researchers have been trained and calibrated in accordance with the adopted norms presented on the official website of the International RDC/TMD Consortium [22].

The exclusion criteria were as follows: regular drug therapy, mental illness, coagulopathy, diabetes, or chronic infections. The subjects were not addicted to nicotine, alcohol, or drugs. The participants with joint clicking and a clinical diagnosis of disc displacement were also excluded, and they were asked to refrain or not to use self-treatment during the therapy.

The study was approved by the Bioethics Committee of the Pomeranian Medical University in Szczecin (KB–0012/36/15). It is in accordance with ethical standards; all participants signed written informed consent and were acquainted with the technique and the course of the research.

3.2. Method. The subjects were randomly divided into two subgroups of 30 people each. Group KT (15 female and 15 male) were subjected to active kinesiotaping application (K-Active Tape Classic, 50 mm × 17 m; Nitto Denko Corporation, Japan) (Figure 1). Subjects undergoing therapy were

Figure 1: The muscular application of KT to the area of the masseter.

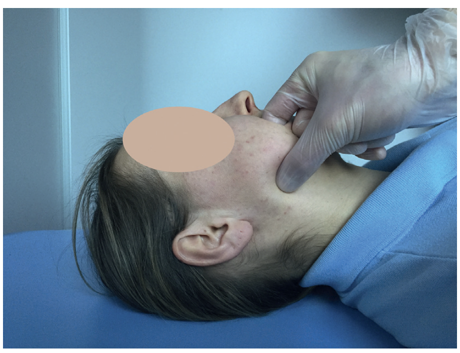

Figure 2: The release of TrP by the ischemic compression method.

diagnosed with excessive strain of masseter muscles and muscular pain, without limitations in the movements of the mandible and without disc derangement and joint pain. The muscular application was used for the region of the masseter with a tape (5 cm wide) cut into 2 parts, called tails, which covered the treatment sites without tension. The base was located in the region of the temporomandibular joint. The upper tail ran across the buccal surface of the face towards the nose, while the lower tail was directed towards the chin and thus included the masseter. This type of application raised the surface of the skin, which was translated into a decrease in the tension of the affected area. All participants of the study were obliged to wear the kinesiology tape for a period of 5 days and were advised to carry out everyday activities without unnecessary care.

Group TrP, composed of 16 women and 14 men, was subjected to physiotherapy with the release of trigger points by the ischemic compression method, which was based on applying pressure to the active trigger point until it was switched off, that is, the pain disappeared (Figure 2). Subjects undergoing therapy were diagnosed with excessive strain of masseter muscles and muscular pain, without limitations in the movements of the mandible and without disc derangement and joint pain. The localization of the trigger points, on average 4 on the right and on the left side, was done palpably with the dental arches clenched, using a pliers grip covering the dense tissue inside and outside the cheek with the thumb and index finger. Trigger point therapy was performed within the upper and lower attachment of the masseter, on the right and left sides. The procedure of deactivation of trigger points was performed three times, on the first, third, and fifth days of therapy.

Before performing the physiotherapeutic procedures in groups KT and TrP and after their application, all patients were subjected to diagnostic actions, including the measurement of pain intensity using the visual analogue scale (VAS). Two dentists were involved in the selection of participants. Only one physiotherapist performed KT applications and TrP therapies. The therapeutic effectiveness of the two methods was verified by comparing the mean values of pain intensity before and after performing the physiotherapeutic procedures. Changes in pain intensity were considered as dependent variable, while the therapy used and patients' gender and age were considered as independent variables.

Prior to the examination, each patient gave written consent to participate in the therapy and was provided with information about the technique and the course of the tests. The protocol was developed in accordance with the latest version of the World Medical Declaration of the Helsinki Association [23]. The patients were also informed about the principle of anonymity of the tests.

4. Statistical Analysis

The statistical analysis included determining the physiotherapeutic effects, examining the influence of gender and patient's age on the outcomes, and comparing the analgesic efficacy of the treatment methods. In order to check the efficacy of the therapy, mean pain values were compared before and after performing the procedures. The statistical significance of the change in mean values was verified using the paired sample Welch t-test. The linear regression models were also used to examine the influence of gender and age on treatment efficacy.

The hypothesis about greater analgesic efficacy of KT compared to TrP was additionally tested. For this purpose, the mean values of absolute and relative pain intensity changes obtained from two groups of patients were compared using the unpaired sample Welch t-test. (The Welch t-test is a generalization of Student's t-test for populations with different variances. Significant differences in the value of variance were observed in the measurements taken before and after the treatment, as well as in the comparison of changes after the use of both therapeutic methods.)

5. Results

5.1. Physiotherapeutic Effects. The basic statistics of patients' age and measurements for the methods applied in particular groups of patients are summarized in Table 1.

The t-test confirms the statistical significance of both therapeutic methods in reducing pain symptoms (Table 2.)

5.2. Comparison of the Analgesic Effect of KT and TrP. In order to compare the analgesic effect of KT and TrP, absolute change in pain level AbsCh was calculated for each

Table 1: The basic statistics of patients' age and pain intensity measurements before and after the application of both methods.

Characteristic / Measurement	KT: Age (years)	KT: Pain (VAS units) Before	KT: Pain (VAS units) After	TrP: Age (years)	TrP: Pain (VAS units) Before	TrP: Pain (VAS units) After
All patients						
Minimum	18	3	1	18	4	2
Maximum	35	10	6	35	9	7
Mean	25.87	6.50	3.10	27.37	6.27	4.17
SD	4.86	1.74	1.35	5.08	1.41	1.36
Male patients						
Minimum	18	4	1	18	4	3
Maximum	32	8	5	35	9	7
Mean	26.07	5.93	2.93	28.93	6.57	4.50
SD	4.92	1.44	1.10	5.36	1.55	1.30
Female patients						
Minimum	19	3	1	19	4	2
Maximum	35	10	6	34	8	6
Mean	25.67	7.06	3.27	26.00	6.00	3.88
SD	4.97	1.87	1.58	4.51	1.25	1.37

KT, kinesiotaping; TrP, trigger point therapy.

Table 2: The significance of therapeutic methods' test results.

Method	Pain (VAS units, mean ± SD) Before	Pain (VAS units, mean ± SD) After	t-statistic	p value
KT	6.50 ± 1.74	3.10 ± 1.35	14.92	<0.001
TrP	6.27 ± 1.41	4.17 ± 1.36	8.23	<0.001

patient as the difference of measurement after and before treatment. In addition, to account for the different levels of initial pain in the two groups of patients entering therapy, relative change RelCh was also calculated:

$$\text{AbsCh} = \text{pain after} - \text{pain before},$$
$$\text{RelCh} = \frac{\text{AbsCh}}{\text{pain before}}. \quad (1)$$

Relative change shows what fraction of patient's initial pain was eliminated during treatment.

Although both methods proved to be efficacious, the mean values of the changes after KT and TrP suggest that the KT method gives greater improvement in the reduction of pain. The unpaired sample Welch t-test confirms this (Table 3).

5.3. Study of the Influence of Gender and Patient's Age on Therapeutic Outcomes. The therapeutic outcomes obtained by using both methods (KT and TrP) in the group of male and female patients were compared by analyzing the mean values of changes using the t-test. For both methods, no significant differences were found in the treatment effects between male and female patients.

In the linear regression models, the absolute change in pain intensity was a dependent variable. For both therapy methods, the models with age, gender, and their cross-factor as independent variables were examined. There were no significant variables in any model (t-statistic values less than 1).

Table 3: Comparison of the analgesic effect of KT and TrP results.

Characteristic	KT Mean ± SD	TrP Mean ± SD	t-statistic	p value
AbsCh	−3.40 ± 1.24	−2.10 ± 1.40	−3.80	<0.001
RelCh	−0.53 ± 0.15	−0.32 ± 0.21	−4.31	<0.001

6. Discussion

Face and oral pain syndromes lasting longer than 6 months are a multidisciplinary issue. Close cooperation between neurologists, laryngologist, physiotherapists, psychiatrists, and dentists can help in identifying the causes of these ailments and avoiding the misdiagnosis or false causal relationship. The diagnostic and therapeutic management of facial pain depends on the suspected cause of pain and the accompanying symptoms. It is important to remember that every chronic condition, including pain, causes an impact on the psychological and social status of patients and reduces the quality of life [24].

The study presents cooperation between physiotherapists and dentists by investigating the impact of kinesiotaping and inactivation of trigger points applied to the area of the masseter in the course of functional disorders of the muscles of mastication, with particular emphasis on pain. The original research revealed a significant reduction of pain. The results of the study confirm the observations of other authors who have given special attention to the influence of the kinesiotaping method on the human body.

Youngsook identified changes in myofascial pain and examined the range of movement in the temporomandibular joint after the application of the kinesiotaping method in patients with latent myofascial trigger points within the sternocleidomastoid muscle [25]. He concluded that pain intensity significantly decreased, and the range of motion in the temporomandibular joint considerably increased. Wei-Ting et al. suggest that the KT method can be used as a regular therapy or as a complement to the treatment of myofascial pain [26]. The therapeutic value of the kinesiotaping method in the muscular application is emphasized in the publications of other authors who include this method in the algorithm for treating pain originating from different muscles. Öztürk et al., who used the application of active tapes in patients with myofascial pain syndrome, demonstrated a statistically significant improvement in pain intensity and strength of the upper trapezius muscle [27].

Kalichman et al. described the case of a patient suffering from meralgia paresthetica with symptoms of numbness, paresthesia, and pain in the anterolateral part of the thigh. After using the KT method for 4 weeks, the symptoms significantly regressed and the quality of life improved [28]. Using KT in patients with an acute cervical spine injury, Osterhues showed an immediate decrease in pain intensity in the study group [29].

There are also critical opinions about the use of the kinesiotaping method which we have to take into consideration. Montalvo et al. conducted a meta-analysis of the available literature on KT to assess its efficacy in pain management therapy in patients with musculoskeletal injuries. Articles published between 2003 and 2013 were selected by searching SPORTDiscus, Scopus, ScienceDirect, CINAHL, Cochrane Library, PubMed, and PEDro databases with the terms kinesio tap*, kinesiology tap*, kinesiotap*, and pain. Thirteen articles investigating the effects of kinesiology tape application on pain with at least level II evidence were selected. Combined results of this meta-analysis indicate that KT may have a limited potential to reduce pain in individuals with musculoskeletal injury. The authors suggest using KT in conjunction with or instead of more conventional therapies. However, further research that compares KT to other clinical interventions is needed to evaluate its efficacy [30].

Morris et al. conducted a systematic review of RCTs investigating the use of KT in the management of clinical conditions. A systematic literature search was performed in the following databases: CINAHL, MEDLINE, OVID, AMED, ScienceDirect, PEDro, www.internurse.com, SPORTDiscus, British Nursing Index, www.kinesiotaping.co.uk, www.kinesiotaping.com, Cochrane Central Register of Clinical Trials, and ProQuest.

The review included articles published until April 2012. Evaluation of the risk of bias and the quality of evidence was conducted in accordance with the Cochrane methodology. Eight RCTs met the full inclusion criteria. Six of these included patients with musculoskeletal conditions. There was limited to moderate evidence that KT is no more clinically effective than sham or usual care tape/bandage. There was limited evidence from one moderate quality RCT that KT in conjunction with physiotherapy was clinically beneficial for plantar fasciitis-related pain in the short term. There are, however, serious concerns about the internal validity of this RCT. There is currently insufficient evidence to support the use of KT over other clinical interventions [31].

Parreira et al. conducted a systematic review comparing KT to sham KT. Twelve randomized trials with 495 participants in total were included in the review. The efficacy of KT was assessed in patients with shoulder pain in two trials, knee pain in three trials, chronic low back pain in two trials, neck pain in three trials, plantar fasciitis in one trial, and multiple musculoskeletal conditions in one trial. The methodological quality of the studies that met the inclusion criteria was moderate, with a mean score of 6.1 points on the 10-point PEDro scale. The study found that KT was better than sham KT/placebo and active comparison groups. However, the effect sizes were small and probably not clinically significant or of low quality [32].

In their research, Tremblay and Karam concluded that the application of KT had little effect at the neuromuscular level. The changes in sensory feedback assigned to an elastic tape are probably insufficient to modulate corticospinal excitability in the functional sense [33]. Therefore, more research should be carried out to explain the effectiveness of the KT method in the elimination of TMD-related ailments, which is very difficult due to the need to perform random configurations and double-blind tests. The cosmetic defect caused by sticking active tapes to the skin of the face is also important. Therefore, the analgesic action is local, and its main goal is to enlarge the space between the skin and soft tissues in order to expand the movement space, facilitate the circulation of blood and lymph, and increase the rate of tissue healing, as suggested by Skirven et al. [34].

The pain associated with TMD often reduces the activity of the masticatory muscles. The implementation of the appropriate set of exercises significantly improves the action of analgesic methods and all physical fitness parameters [35]. Because of the multidimensional nature of the problem, patients with musculoskeletal pain of the face should be treated by an interdisciplinary team. There is increasing evidence that psychosocial factors have a significant impact on therapeutic outcomes and may also affect the symptoms reported by patients. Taiminen et al. found that many patients complaining of chronic headache are also diagnosed with a psychiatric or personality disorder that blurs the manifestation of the disease, which considerably affects the treatment [36]. Because a few health care workers believe that they are able to help them on their own and that these people require multidisciplinary treatment, Hals et al. indicate that these patients are often marked as "difficult" [37].

7. Conclusions

(1) The methods of kinesiotaping (KT) and TrP inactivation have brought significant analgesic effects to the treatment of painful forms of functional disorders of the masticatory muscles.

(2) The more beneficial results were observed after using the KT method, which increased the analgesic effect in dysfunctional patients.

(3) No influence of gender or patient's age on the treatment results was reported.

(4) There is also a need to develop algorithms for the diagnosis and treatment of oral and facial pain syndromes with a strict definition of the role of dentists and physiotherapists.

Data Availability

All interested in the results and the course of the research are encouraged to contact via e-mail with the Independent Unit of Propaedeutic and Dental Physical Diagnostics, in which the tests were carried out and all data are stored.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Temporomandibular Disorders Related to Stress and HPA-Axis Regulation

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Temporomandibular disorders (TMDs) are characterized by pain and dysfunction in the masticatory apparatus and the temporomandibular joint (TMJ). Previous trauma, stress symptoms, psychosocial impairment, and catastrophizing have been related to TMD. To assess if the hypothalamic-pituitary-adrenal (HPA) axis is upregulated in TMD patients, we performed a cross-sectional study with saliva from 44 TMD patients and 44 healthy sex- and age-matched controls for cortisol (F) and cortisone (E) with liquid chromatography-tandem mass spectrometry. Furthermore, we calculated the F/E ratio for the evaluation of 11β-hydroxysteroid dehydrogenase activity. We also assessed anxiety/depression and pain catastrophizing scores from a questionnaire that participants completed prior to the examination. We found that F ($P = 0.01$), E ($P = 0.04$), the F/E ratio ($P = 0.002$), and the sum of glucocorticoids ($E + E$) in saliva ($P = 0.02$) were significantly higher in the TMD group. Anxiety/depression and catastrophizing scores were also significantly higher in the TMD group ($P < 0.0001$). Our findings indicate that patients with TMDs may have an upregulated HPA axis with higher F secretion from the adrenal cortex. Anxiety/depression and pain catastrophizing scores were significantly higher in the TMD group, and psychological factors may contribute to chronic upregulation of the HPA axis.

1. Introduction

Temporomandibular disorders (TMDs) are a group of disorders associated with pain and dysfunction affecting the temporomandibular joint (TMJ) and the masticatory apparatus [1, 2]. TMDs occur predominantly in women, who are especially likely to experience more severe symptoms. TMD-associated comorbidities include fibromyalgia, irritable bowel syndrome, and depression, with trauma and stress symptoms frequently present as well [3]. Psychosocial impairment within a TMD, such as somatization and depression, is linked with pain-related disability as well as the duration of pain [4]. The Orofacial Pain Prospective Evaluation and Risk Assessment (OPPERA) study found that psychosocial factors (e.g., somatic awareness, distress, catastrophizing, pain amplification, and psychosocial stress) had a significantly higher prevalence in subjects with a TMD compared to healthy individuals [2, 5].

During the last few decades, use of physiological markers for assessing psychosocial-related disorders has increased. Stress activates the hypothalamic-pituitary-adrenal (HPA) axis, which results in a cascade of reactions leading to increased secretion of cortisol from the adrenal cortex. Research examining the HPA axis response to stress has yielded contradictory results. A meta-analysis of chronic stress and HPA-axis activity found that HPA response to stress varies with the nature and controllability of stressful stimuli as well as the individual psychiatric response [6]. The role of stress in the etiology and persistence of TMD remains unclear. However, dysregulation of the HPA axis has been correlated with TMD in several studies [7–9]. Accordingly, analysis of cortisol (F) levels in saliva may provide a means for examining HPA-axis activity.

Salivary F levels follow circadian fluctuations, and these variations can be used to create a curve depicting unbound free and total cortisol in serum [10]. However, previous analyses of F in saliva from TMD patients have given variable results. Some researchers have found elevated F values in association with TMD [11, 12], while others have not found any significant difference in comparison to a control group [13]. Analyses using immunoassay methods [11–15] have also been undertaken to measure F in saliva from subjects with a TMD. These methods do not separate cortisol (F) and cortisone (E), which have structural similarities but unequal biological activities. Recent F and E analyses based on liquid chromatography-tandem mass spectrometry (LC-MS/MS) are now available [16].

The primary objective of this study was to assess the stress levels in TMD patients based on an upregulated HPA axis and compare the results with healthy individuals. Secondary objectives were to analyze the saliva for F and E and the scores for self-reported anxiety/depression and catastrophizing from a questionnaire. The hypothesis was that TMD patients have an upregulated HPA axis shown by increased psychological scores and increased level of cortisol in saliva.

2. Materials and Methods

2.1. Study Design. The present study is a clinical cross-sectional study, which was a part of a multidisciplinary investigation of TMD patients at Haukeland University Hospital, sponsored by the Norwegian Ministry of Health [17]. Ethical approval was granted by the Regional Ethical Review Board South East (2015/930), in accordance with the Helsinki Declaration (1964). A written informed consent was received from all subjects.

2.2. Participants. All TMD patients ($n = 60$) were referred by their general practitioner to the National TMD project in Bergen, Norway. The subjects were from all regions in Norway and were consecutively included in the project during the years of 2013–2015. Patients were included, examined, and evaluated based on the severity and duration of symptoms, both for pain and dysfunction and for consequences. Six specialists representing several disciplines, who created an individual treatment proposal for each patient, performed the examination. The investigation included pain intensity and duration, functional impairment (general and jaw-specific), effect on quality of life, and presence of extended periods of sick leave. Inclusion criteria were long-term TMD-related pain. Furthermore, inclusion was based on the examination; thus, patients with and without functional impairment were included. Exclusion criteria were non–TMD-related orofacial pain, relevant drug dependence problems, and obvious psychiatric diagnoses.

A healthy sex- and age-matched control group ($n = 60$) was recruited for comparison with the TMD patients, during 2016. A majority of the control group consisted of employees and students from the Department of Clinical Dentistry at the University of Bergen, who were not affiliated with the study research group. The remaining members of the control group were recruited from the general population in Bergen, Norway. The subjects gave their informed consent to participate in the study. Inclusion criteria for the control group was age 20 years or older and age- and sex-matched with the TMD patient group. Exclusion criteria were TMD symptoms or other musculoskeletal pain and symptoms in the head and neck area. Individuals in the control group were anonymized.

2.3. Questionnaire. TMD patients completed a comprehensive questionnaire prior to clinical examination. The questionnaire covered medical history, socioeconomic history, and lifestyle factors and included tools to assess psychosocial factors, specifically the Hospital Anxiety and Depression Scale (HADS) [18] and a 2-item version of the Coping Strategies Questionnaire [19] regarding catastrophizing. The healthy individuals completed a shortened version of the same questionnaire.

2.4. Saliva Samples and Analyses. Saliva samples were collected in the morning with the Salivette Cortisol Code Blue test kit (Sarstedt Darmstadt, Germany) and stored at −80°C until analysis. F and E were determined by liquid chromatography-tandem mass spectrometry (LC-MS/MS) at the Core Facility for Metabolomics, University of Bergen. Sample processing was completely robotized (Hamilton Robotics, Inc., Reno, NV, USA). Briefly, 20 μL of internal standard (Cortisol-2,3,4-$^{13}C_3$) was added to 100 μL of human saliva, which was subjected to liquid-liquid extraction with 480 μL of ethylacetate-heptane (80 : 20, v/v). The supernatant (380 μL) was subsequently washed with 50 μL of sodium hydroxide (0.1 M). Next, 280 μL of supernatant was removed and evaporated to dryness under nitrogen flow and then reconstituted in 100 μL of a 0.01% aqueous solution of formic acid : methanol (50 : 50, v/v). Samples were then analyzed on a Waters ACQUITY UPLC system connected to a Waters Xevo TQ-S tandem mass spectrometer (Waters, Milford, MA, USA). The compounds were separated on a C-18 BEH phenyl column from Waters (100 × 2.1 mm column, 1.7 mm particle size), which was developed by gradient elution over 5.5 min, using an aqueous solution of formic acid and acetonitrile as mobile phases. Formic acid adducts were detected in negative multiple reaction-monitoring mode. A potential source of bias is that the TMD patients likely experienced more stress prior to the examination compared to the controls because the majority of the controls were examined at their ordinary workplace.

2.5. Statistical Analyses. All statistical analyses were performed in STATA. Mean, median, range, and standard deviation (SD) for all variables in both groups were calculated. A paired t-test was used to calculate the P value of no difference in F, E, F/E ratio, and $F + E$ between the TMD group and the control group. A Wilcoxon signed rank test was used to calculate the P value of no difference in HADS and catastrophizing scores between the TMD group and the

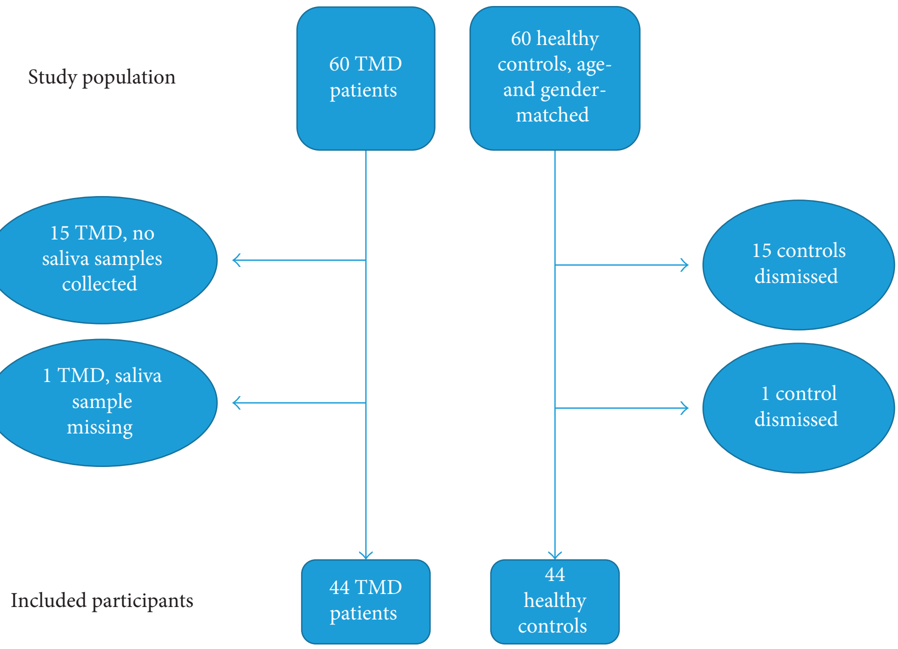

Figure 1: Flow chart of the study population: TMD patients and healthy controls.

control group. A linear multiregression between F and psychosocial factors in both groups was performed as well as a linear correlation (R) with associated P values between GC levels and psychosocial factors.

3. Results

3.1. Demographic Data. The multidisciplinary investigation [17] consisted of 60 patients, all experiencing severe TMD symptoms, and 60 healthy control subjects. Because no saliva sampling was done for the first 15 TMD patients and one saliva sample was missing from the patient group, the population in the present study ended up with 44 TMD patients and 44 healthy controls (Figure 1). The patients were aged 20–69 years, with a mean age of 44 years. The control subjects were aged 23–71 years with a mean age of 46 years. Both groups consisted of 38 women and 6 men.

3.2. Saliva Samples and Analyses. The TMD patient group had a mean saliva-sampling time point of 2 h, 52 min after awakening. The saliva samples were mostly collected at 9:00 AM but a few were collected at 11:00 AM owing to logistic factors. All subjects in the control group collected saliva 2 h, 45 min after awakening, matching the mean sampling time of the TMD patient group. Saliva samples from the control group were collected between 8:00 AM and 10:00 AM.

The transitions monitored under LC-MS/MS analyses were 405.22→329.24 for E and 407.24→331.26 for F. The linearity range was 0.7–100 nmol/L for E and 0.3–50 nmol/L for F. Accuracy was between 87% and 110%, and total imprecision was <10%.

3.3. Stress Scores and Glucocorticoids in Saliva. Our most important finding was that F in saliva was significantly higher in the TMD group compared to the control group ($P = 0.01$) (Table 1). E ($P = 0.04$), the F/E ratio ($P = 0.002$), and the sum of GC ($F + E$) in saliva ($P = 0.02$) were also significantly higher in the TMD group. Stress scores from questionnaires were significantly higher in the TMD group, including pain catastrophizing ($P < 0.0001$) and HADS ($P < 0.0001$) (Table 2). Pain catastrophizing score in the TMD group was negatively correlated with E and $F + E$ ($P = 0.033$ and $P = 0.047$, resp.); however, no association between F and pain catastrophizing was found (Table 3). In the control group, we observed a significant correlation between depression score and $F + E$ ($P = 0.045$). No other associations between the GC levels in saliva and psychosocial factors were found in the control group (Table 4).

4. Discussion

In this study, we found that F and E levels in saliva are significantly higher in TMD patients compared to healthy individuals. Our results were obtained by LC-MS/MS analysis. Compared with immunoassays, LC-MS/MS has much higher specificity and thus permits identification and quantification of F and E [16, 20, 21]. To our knowledge, this study is the first to determine F in TMD by LC-MS/MS and the first to investigate the sum and ratios of different GCs in TMD patients. However, the LC-MS/MS indicates significantly lower F levels than immunoassays due to a lower incidence of cross-reactions [22]. The correlation between LC-MS/MS and immunoassays is poor [16], and the F and E levels measured in this study are consequently not directly comparable to those from previous studies of TMD patients using immunoassays. Accordingly, our study may also contribute to the general assessment of salivary levels of F and E in healthy and diseased subjects.

F levels in healthy individuals follow circadian fluctuations. The lowest value occurs during early sleep and levels

Table 1: Glucocorticoid levels in saliva of TMD patients and healthy controls, analyzed with liquid chromatography-tandem mass spectrometry (LC-MS/MS). A paired t-test resulted in significant higher levels of cortisone (E) and cortisol (F), as well as the ratio of F/E and the sum of $F+E$, in TMD patients.

Glucocorticoids	Cortisone (E) (nmol/L)	Cortisol (F) (nmol/L)	F/E (ratio)	$F+E$ (nmol/L)
TMD ($n = 44$)				
Mean	26.31	7.17	0.26	33.48
Median	24.83	6.29	0.26	31.37
Range	13.17–47.05	2.24–27.04	0.14–0.66	15.41–67.77
SD	8.61	4.56	0.09	12.49
Control ($n = 44$)				
Mean	22.91	4.90	0.20	27.81
Median	21.56	3.81	0.18	25.35
Range	10.54–74.38	1.42–28.21	0.10–0.53	15.68–102.59
SD	9.74	4.37	0.09	13.91
P value (paired t-test)	0.041	0.01	0.002	0.02

Table 2: Results from the questionnaires Hospital Anxiety and Depression Scale (HADS) and Coping Strategies Questionnaire regarding catastrophizing, assessed in the TMD patients and controls. A signed rank test resulted in significant higher score on all parameters in the TMD patient group.

Psychosocial scores	Mean	Median	Range	SD	P value (signed rank)
Catastrophizing (0–12)					<0.0001
TMD	7.88	8.0	1–12	2.95	
Control	1.39	0.0	0–11	2.64	
Anxiety (A) (0–21)					0.0002
TMD	7.73	7.0	0–20	5.11	
Control	3.35	2.0	0–12	3.22	
Depression (D) (0–21)					<0.0001
TMD	6.28	5.0	0–19	5.07	
Control	1.70	1.0	0–9	2.32	
$A+D$ (HADS) (0–42)					<0.0001
TMD	14.25	13.0	0–39	9.76	
Control	5.05	3.5	0–19	4.85	

rise until awakening and then rise even faster in the cortisol awakening response. The peak value occurs approximately 30–45 min after awakening [23, 24]. Our saliva samples had a mean sampling time 2 h, 52 min after awakening in the TMD group and 2 h, 45 min in the control group. Accordingly, F levels from our patients and controls were not directly comparable to previous TMD studies because of the diurnal decrease in F levels after peaking in addition to lower F levels being expected from LC-MS/MS compared with immunoassays.

Many studies have reported elevated F levels in TMD patients compared to healthy individuals. A significantly higher daytime F value in plasma was reported in subjects with TMD compared to healthy controls [14]. Analysis of saliva from TMD patients also revealed elevated F levels [11, 12]. Significant higher F levels as a response to experimental stress in subjects with TMD has also been reported [15]. In contrast, some researchers have not found significant differences in salivary F levels related to TMD [13]. In a study examining hair F concentration, even lower values of F were found in subjects with TMD [7].

Elevated or lowered basal F levels may reflect changes in the regulation of the HPA axis, which is discussed in other TMD studies and in several studies of stress-related and chronic pain disorders [7, 9, 14, 15, 25–32]. A significantly higher rise in salivary F in response to experimental stress has been reported in a TMD group compared to a healthy control group [15]. An opposite finding within a subgroup separate from the TMD group in the same study showed slightly lower, but nonsignificant, salivary F levels compared to the control group at all measuring points. No significant differences in basal F levels existed between the TMD and control groups before the stress exposure [15]. However, no difference in salivary F levels was reported as a response to experimental pain in a TMD group compared to a control group. Nevertheless, an association between high pain-catastrophizing scores and high F response to pain was observed although basal morning F was lower in association with high pain catastrophizing in both TMD and controls [25]. In our study, we showed that not only F, but also E and the sum of both GCs ($F+E$), was significantly higher in the TMD group. This finding means that the total sum of GCs is higher in the TMD group and supports the theory of an upregulated HPA axis, with higher F secretion from adrenal cortex. The high level of the inactive hormone E may be the result of enzymatic conversion of F by 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD-1) in the glandula parotis.

Table 3: Linear correlation (R) with associated P values between glucocorticoid levels and psychosocial factors in the TMD group. Pain-catastrophizing score was significant, negatively correlated with E and the sum of glucocorticoids ($F + E$) ($P = 0.033$ and $P = 0.047$, resp.). No significant association between F and pain catastrophizing was found, neither any significant associations between the other parameters of glucocorticoid levels in saliva and psychosocial factors.

TMD group	Cortisone (E)	Cortisol (F)	F/E-ratio	$F + E$
Catastrophizing score				
R	−0.323	−0.230	−0.080	−0.305
P value	0.033	0.138	0.611	0.047
Anxiety (A) score				
R	−0.089	0.125	0.247	−0.016
P value	0.566	0.420	0.107	0.919
Depression (D) score				
R	−0.091	0.036	0.128	−0.049
P value	0.563	0.821	0.415	0.753
$A + D$ (HADS) score				
R	−0.042	0.123	0.211	0.016
P value	0.785	0.426	0.169	0.919

Table 4: Linear correlation (R) with associated P values between glucocorticoid levels and psychosocial factors in the control group. Depression score was significantly associated with the sum of glucocorticoids ($F + E$) ($P = 0.045$). No significant associations between the other parameters of glucocorticoid levels in saliva and psychosocial factors were observed.

Control group	Cortisone (E)	Cortisol (F)	F/E-ratio	$F+E$
Catastrophizing score				
R	0.111	0.147	0.175	0.124
P value	0.473	0.340	0.256	0.422
Anxiety (A) score				
R	0.187	0.171	0.044	0.185
P value	0.225	0.266	0.778	0.231
Depression (D) score				
R	0.313	0.269	0.010	0.304
P value	0.039	0.077	0.519	0.045
$A + D$ (HADS) score				
R	0.273	0.242	0.077	0.268
P value	0.073	0.113	0.620	0.079

Another possible explanation of higher F levels in TMD patients may arise from suppressed negative feedback of the HPA axis, as seen in major depression [27]. An exaggerated F response to CRH as well as higher basal F levels has been reported for patients with irritable bowel syndrome [28]. Since we did not perform any suppression tests in our study, we could not evaluate the negative feedback of the HPA axis for comparison.

The F/E ratio is an indicator of 11β-HSD activity, which has previously been measured in early morning saliva sample and found to be 0.24 [33], 0.15 [34], and 0.20 [35]. The active molecule F is converted to an inactive form E in parotid tissue by the enzyme 11β-HSD-1 and a reverse conversion by 11β-HSD-2. Our calculations resulted in a F/E ratio of 0.26 in TMD patients compared to 0.2 in controls. The difference may be explained by decreased activity of 11β-HSD-2 in TMD patients or 11β-HSD-2 saturation at a high substrate concentration [35]. Enzyme saturation has previously been indicated by scatter plots with curve fitting [33, 35], showing that the increase in salivary E is nonlinear with the increase of salivary F at high F concentrations. For example, an elevated F/E ratio was reported in a study of apparent mineralocorticoid excess [36], and F/E ratios in urine were reported to be significantly higher in depressed patients compared to healthy individuals [37]. In fetoplacental tissue, 11β-HSD-2 has a key function in neurobehavioral development, and loss of its function has resulted in lifelong anxiety in mice [38]. Given that 11β-HSD-2 is supposed to protect the mineralocorticoid receptor from GC binding [39], examining blood pressure in TMD patients in future studies could be interesting.

Psychosocial factors such as stress, anxiety, and depression may influence the HPA axis as well, although the response seems unclear and inconsistent. Stress may potentially be an important factor in the etiology of TMD [11]. The prevalence of physical and psychological stressors in TMD is high, and they may contribute to dysregulation of the HPA axis [8]. However, no significant differences in salivary morning F were reported from a study of 30 young women with TMD, although the TMD subjects appeared more psychologically distressed compared to healthy individuals [13]. Subjects with TMD also had a significantly higher stress score, despite apparently lower F levels, which were measured through hair analysis [7]. However, F levels in hair may reflect stress and F output over time, while salivary F reflects the same variables at the point of measurement. The TMD patients in our study scored significantly higher on HADS and pain-catastrophizing questionnaires, which could reflect higher stress levels that potentially contribute to an upregulation of the HPA axis. Still, we did not find any significant correlation between anxiety, depression, or catastrophizing scores and F levels. This outcome may be due to the presence of many other factors influencing F levels. Nevertheless, we found a significantly negative association between pain-catastrophizing score and both E and the sum of GCs ($F + E$). F was also lower with higher pain catastrophizing in the TMD group, but the association was nonsignificant. Nevertheless, the findings from our study are comparable with a previous study in which lower basal F was associated with high pain catastrophizing [25]. Nonsignificantly higher catastrophizing scores in a subgroup of TMD patients with low F levels have also been reported [15]. However, we did not see lower F levels correlated to anxiety or depression in the TMD group. In the control group, we observed a significant correlation between depression score and $F + E$, though the majority in the control group had a depression score that ranged zero to very low, and the association has probably low scientific value. We could not find any other correlations between GC levels and any psychological factor in the control group. A recent review on stress in chronic pain patients highlighted that several types of HPA-axis dysregulation can occur in chronic stress and pain conditions, leading to a HPA-axis stress response that cannot be determined by basal F levels only [40].

The role of stress in the etiology of TMD remains unclear. The effect of stress in TMD patients may result in a complex and multifactorial response by biological systems, including neuroendocrine function and psychosocial and physical adjustments [9].

5. Conclusion

In summary, we report that a group of TMD patients had significantly higher F and E levels compared to a healthy control group. This finding may indicate that TMD patients have an upregulated HPA axis. Anxiety/depression and pain-catastrophizing scores were significantly higher in the TMD group, and they may potentially indicate chronic upregulation of the HPA axis. Based on these results, the hypothesis that TMD patients have an upregulated HPA axis may be approved. More research is needed to confirm the activity of the HPA axis in TMD patients. In future studies, it would be interesting to collect samples at several time points to compare their diurnal F rhythm. Examination of the F response to experimental stress would be expedient, as would suppression by dexamethasone and further investigation of 11β-HSD; blood pressure would be of great interest.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflicts of interest with respect to the authorship and/or publication of this article.

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Research Article

Temporomandibular Disorders among Dutch Adolescents: Prevalence and Biological, Psychological, and Social Risk Indicators

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Aims. To assess the prevalence rates of pain-related temporomandibular disorders (TMDs) and temporomandibular joint (TMJ) sounds in a large group of Dutch adolescents, aged between 12 and 18 years and to determine if the same biological, psychological, and social risk indicators are related to both TMD pain and TMJ sounds. *Methods*. In this cross-sectional questionnaire survey, 4,235 questionnaires were analyzed, with an about equal gender distribution. *Results*. The overall prevalence of pain-related TMDs was 21.6% (26.1% for girls and 17.6% for boys) and that of TMJ sounds was 15.5% (19.3% for girls and 11.7% for boys). Logistic regression analyses revealed that the following variables appeared to be the strongest predictors of TMD pain: female gender, increasing age, sleep bruxism, biting on lips and/or cheeks, stress, and feeling sad. Regarding self-reported TMJ sounds, the multiple regression model revealed that female gender, increasing age, awake bruxism, and biting on lips and/or cheeks were the strongest predictors. *Conclusions*. TMDs are a common finding among Dutch adolescents. Except for the psychological factors that appeared to be associated with TMD pain only, pain-related TMDs and TMJ sounds shared similar biological risk indicators.

1. Introduction

Temporomandibular disorders (TMDs) is a collective term that embraces a variety of temporomandibular joint (TMJ) disorders, masticatory muscle disorders, headache disorders, and disorders affecting the associated structures [1, 2]. One way of classifying the different types of TMDs is by dividing them into two broad categories: (1) pain-related TMDs and (2) intra-articular TMDs [2]. Regarding the first category, pain can originate from the TMJs, but more frequently, the masticatory muscles are involved [3, 4]. Pain-related TMDs are usually transient over time and resolve without serious long-term effects [5, 6]. Intra-articular TMDs are expressed by biomechanical signs like TMJ sounds (clicking and crepitation), jaw locking, and limited mouth opening [2]. TMJ sounds are the most common expression of intra-articular TMDs [7] and usually occur without pain or jaw movement limitation [8, 9]. Even though both categories of TMDs are primarily present among young and middle-aged adults [10, 11], studies performed on children and adolescents seem to indicate that the prevalence of pain-related forms of TMDs increases with increasing age in this age group [11–13]. Likewise, several studies on intra-articular TMDs report an increase of TMJ sounds in the young population [8, 14, 15].

It is generally believed that a variety of biological, psychological, and social factors may reduce the adaptive capacity of the masticatory system, thus resulting in TMDs [6, 16]. Since pain-related TMDs and TMJ sounds represent clusters of related disorders in the masticatory system [6], this would imply that overlap exists among the risk indicators for both categories of TMDs. For instance, it is commonly believed that teeth grinding or jaw clenching (i.e., bruxism) causes TMD pain due to overloading of the musculoskeletal structures [17]. At the same time, bruxism-induced overloading of the TMJs that exceeds the normal adaptive capacity might result in more TMJ sounds due to degenerative changes of the anatomical structures, or a tendency of the disc to be dislodged off the condyle [18, 19]. Surprisingly, many risk assessment studies on TMDs in the young population focused on one category of TMDs only (e.g., [8, 13, 20]), whereas in others, the various signs and symptoms of TMDs were merged into one overall TMD diagnosis (e.g., [21–23]). As it is, however, generally agreed that TMDs represent a nonspecific umbrella term, it is essential to differentiate pain-related TMDs from intra-articular TMDs. The aims of the present study, therefore, were (1) to assess the prevalence rates of self-reported pain-related TMDs and TMJ sounds in a large group of adolescents aged between 12 and 18 years, (2) to determine their associations with biological, psychological, and social risk indicators, and (3) to determine if the same risk indicators are related to both categories of TMDs.

2. Materials and Methods

2.1. Data Collection. This investigation was designed as a cross-sectional, population-based study. During three subsequent semesters, participants were drawn from among adolescents attending nine Dutch secondary schools that were willing to participate in this investigation. Because of time demand or other priorities at that time, 23 schools declined participation. All approached schools were dispersed over the southern and western parts of Netherlands and were situated in urban areas. Prior to the data collection, the parents/legal representatives received an information letter about the study. The children and/or the parents/legal representatives had the right to refuse participation.

On the day of data collection, a questionnaire was handed over to the schools' pupils and collected several minutes later, before the lessons started. This questionnaire contained 17 items that covered demographic items, sleep and awake bruxism, signs and symptoms of TMDs, and psychosocial and behavioural factors [24]. Most questions were derived from already existing questionnaires, like the Dutch translation of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) [25] and an oral habits questionnaire [26]. During the time the questionnaires were completed, the pupils were supervised by the class teacher and the investigators to ensure that the questionnaires were completed individually. Due to this approach, the participation rate was 100%. The institutional review board of the Academic Centre for Dentistry Amsterdam (ACTA) and the school boards of the participating schools approved the data collection procedures. Prior to the investigation, the feasibility of the research process was field-tested in a pilot study. In addition, the test-retest reliability of the employed questionnaire was assessed, yielding fair-to-good to excellent reliability scores. For detailed information about the data collection methods, see van Selms et al. [24].

2.2. Outcome Variables

(i) Orofacial pain, indicative of TMD pain, was assessed by means of the following question: "Have you had pain in the face, jaw, temple, in front of the ear or in the ear?" (no, yes). The question referred to the presence of pain within the last month.

(ii) The presence of TMJ sounds was assessed using the question "Does your jaw make a clicking or popping sound when you open or close your mouth, or while chewing?" (no, yes). The question referred to the presence of TMJ sounds within the last month.

Since no clinical diagnoses were established in this study, the term "pain-related TMDs" has to be interpreted as "pains indicative of TMD pain" and "TMJ sounds" as "self-perceived TMJ sounds."

2.3. Independent Variables

2.3.1. Biological Items

(i) Age (years) and sex (0, "male"; 1, "female").

(ii) The presence of sleep bruxism was assessed using the question "Have you been told, or did you notice yourself, that you grind your teeth or clench your jaws when you are asleep?" The presence of awake bruxism was assessed using the question "Do you grind your teeth or clench your jaws during the day?" These questions referred to the last month, and the pupils could choose between no, yes, or unknown. Other oral activities that may be stressful to the masticatory system were asked by the following four questions: Do you chew on chewing gum? Do you bite your nails? Do you bite on pens/pencils? Do you bite your lips/cheeks? Again, these questions referred to the last month, and the answer possibilities were no, occasionally, regularly, often, and very often.

(iii) The following exogenous aspects were assessed: "Do you smoke cigarettes?" and "Do you drink alcohol?" (both questions: no, occasionally, regularly, often, and very often).

2.3.2. Psychological Items

(i) An impression of the psychological status was assessed by means of the following two questions "Are you stressed?" and "Are you feeling sad?" (both questions referred to the last month: no, occasionally, regularly, often, and very often).

2.3.3. Social Items

(i) Ethnic background was classified following the method of Statistics Netherlands (CBS), using the country of birth from both parents. This procedure resulted in a classification into two subgroups, namely, native Dutch (i.e., both parents were born in Netherlands, regardless of the country of birth of the subject; coded "0") and nonnative Dutch (i.e., all other subjects; coded "1").

(ii) Educational level was characterized by the type of the secondary educational system that was followed. Depending on their abilities, Dutch children around the age of 12 can choose for either vmbo, vmbo/havo, havo, havo/vwo, or vwo. The vmbo diploma gives access to advanced vocational education, the havo diploma to polytechnic education, and the vwo diploma to university education. The 5-point Likert scale item educational level was recoded into a dichotomous variable (vwo (1) versus the other levels (0)).

2.4. Data Analysis. Descriptive statistics included frequency distributions of each of the independent variables. In order to determine the prevalence rates of TMD pain and TMJ sounds, the prevalence data were stratified by gender and age and ratios were calculated. The chi-square test was performed to test the association between TMD pain and TMJ sounds as depicted in a 2×2 contingency table. To determine the association between the outcome variables and each of the independent variables, hierarchical logistic regression analyses were performed. First, single regression analyses were executed to determine the associations between each of the various predictors and the outcome variable. Regarding the ordinal variables, initial analyses were based on the full range of the 5-point Likert response options, and linearity of their effect on the presence of TMD pain was checked by analysis of dummy variables. When the regression coefficients of the dummy variables consistently increased or decreased, linearity was considered present. In case of a nonlinear association, the variable was dichotomized. Second, independent variables that showed at least a moderate association with the outcome measure were entered in a multiple regression model. Due to the fact that the large sample size may impact the corresponding P values, a more conservative level of significance was chosen (i.e., P value < 0.05 instead of P value < 0.1). Subsequently, the variables with the weakest association with the outcome variable were removed from the multiple regression model. This was repeated in a backward stepwise manner until all variables that were retained in the model showed a P value < 0.01; for each removed independent variable, the P-to-Exit is reported. Of the independent variables included in the final model, the odds ratios and their confidence intervals are reported. All analyses were conducted using the IBM SPSS Statistics 24 software package (IBM Corp., Armonk, NY). The data in the multiple regression model were checked for multicollinearity, using a tolerance value < 0.10 and a variance inflation factor > 10.

3. Results

Initially, a total of 4,285 pupils, with ages ranging from 10 to 22 years, completed the questionnaire. Since the present study focuses on TMD pain during adolescence, the data of pupils under twelve years (children) and above eighteen years (adults) were excluded ($n = 42$; <1% of the total number). An additional eyeball verification of the paper questionnaires was performed in order to check the face validity of the data. In case a pupil deliberately had noted only extremes on all single items, this questionnaire was removed from further analysis ($n = 8$). Therefore, the final sample consisted of 4,235 adolescents with a mean age of 14.5 (±1.6) years (Table 1). Of the 3,940 adolescents who completed the question about gender, 1,966 (49.9%) were girls. In addition, 82.0% of the adolescents were classified as native Dutch, and 43.7% of the pupils followed the highest educational level (vwo).

Of the 3,935 adolescents who completed the questions about gender and TMDs, the overall prevalence of pain-related TMDs was 21.6% (26.1% for girls and 17.6% for boys). The overall prevalence of TMJ sounds was 15.5% ($n = 3,920$; 19.3% for girls and 11.7% for boys). The prevalence rates of both TMD pain and TMJ sounds, stratified by age and gender, revealed that girls had higher rates at all ages studied and that the prevalence tended to increase with age for both genders (Figure 1). TMD pain and TMJ sounds appeared to be highly associated ($\chi^2(1) = 176.6$; $P < 0.001$).

Table 1: Descriptive statistics of the predictor variables.

Independent variable	
Age (years)	14.5 (±1.6)
Gender	
Male	1,974 (50.1%)
Female	1,966 (49.9%)
Sleep bruxism	
No	2,874 (82.0%)
Yes	633 (18.0%)
Awake bruxism	
No	3,334 (90.0%)
Yes	372 (10.0%)
Chewing gum	
No	261 (6.2%)
Yes	3,943 (93.8%)
Biting nails	
No	2,105 (50.0%)
Yes	2,104 (50.0%)
Biting pens and pencils	
No	2,397 (56.9%)
Yes	1,819 (43.1%)
Biting lips and/or cheeks	
No	1,793 (42.6%)
Yes	2,414 (57.4%)
Smoking cigarettes	
No	3,658 (86.7%)
Yes	559 (13.3%)
Alcohol consumption	
No	2,166 (51.4%)
Yes	2,046 (48.6%)
Being stressed	
No	1,680 (39.9%)
Yes	2,534 (60.1%)
Feeling sad	
No	2,183 (51.8%)
Yes	2,030 (48.2%)
School type	
Lower levels	2,386 (56.3%)
Highest level	1,849 (43.7%)
Ethnic background	
Native Dutch	3,368 (82.0%)
Nonnative Dutch	740 (18.0%)

The dichotomized categorical variables are presented as absolute numbers (ratio); age is presented as mean value (±standard deviation).

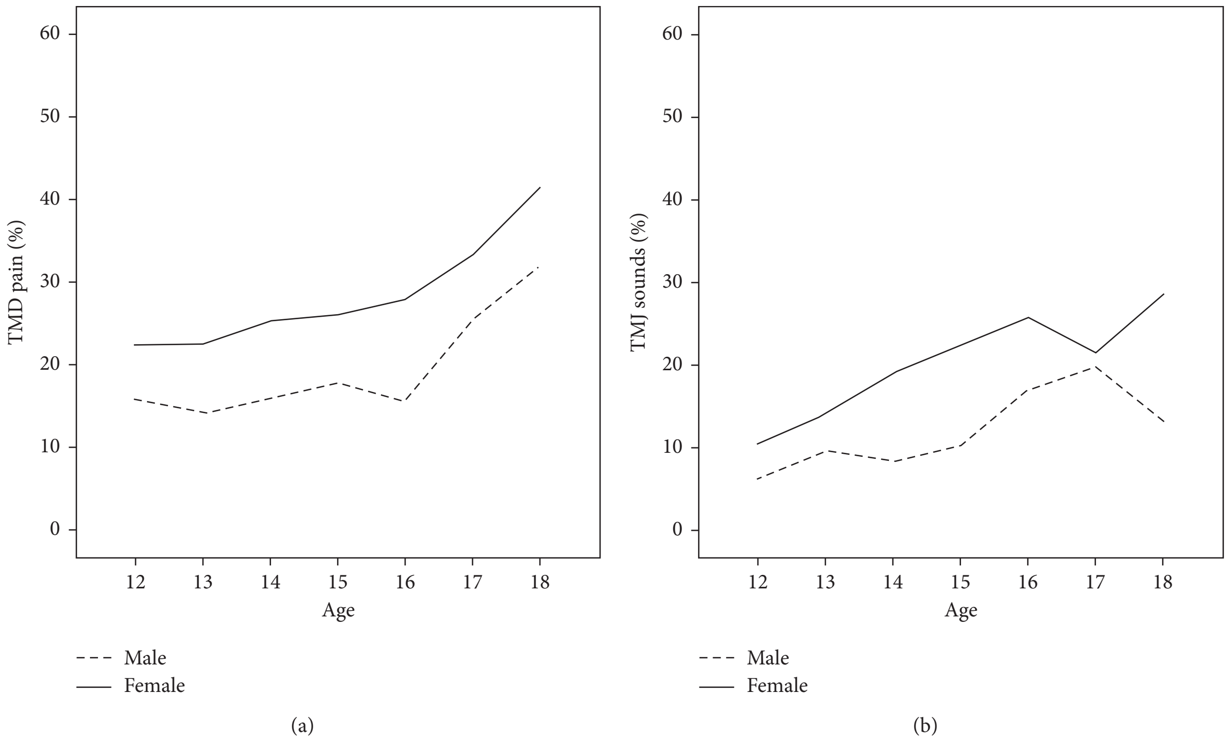

Figure 1: Age- and gender-specific prevalence of TMD pain (a) and TMJ sounds (b) among Dutch adolescents.

Table 2: Single and multiple logistic regression models for the prediction of TMD pain among Dutch adolescents.

	Single regression				P-to-Exit	Multiple regression ($n = 3,131$)		
	n	P value	OR	95% CI		P value	OR	95% CI
Biological items								
Female gender	1,964	<0.001	1.66	1.42–1.94		0.008	1.29	1.07–1.55
Age (years)	4,106	<0.001	1.12	1.06–1.17		<0.001	1.11	1.05–1.17
Smoking cigarettes (positive)	559	<0.001	1.60	1.31–1.95	0.467	—	—	—
Drinking alcohol (positive)	2,044	<0.001	1.49	1.29–1.73	0.097	—	—	—
Sleep bruxism (positive)	631	<0.001	1.76	1.45–2.14		<0.001	1.60	1.29–1.98
Awake bruxism (positive)	372	<0.001	1.93	1.53–2.44	0.262	—	—	—
Chewing gum (positive)	3,938	n.s.	1.00	0.74–1.36				
Biting nails (positive)	2,100	n.s.	0.95	0.82–1.10				
Biting pencils (positive)	1,816	<0.001	1.34	1.16–1.55	0.435	—	—	—
Biting lips and/or cheeks (positive)	2,409	<0.001	1.69	1.45–1.97		0.003	1.33	1.10–1.61
Psychological items								
Being stressed (positive)	1,679	<0.001	2.33	1.97–2.74		<0.001	1.60	1.28–1.99
Feeling sad (positive)	2,025	<0.001	2.14	1.84–2.48		<0.001	1.55	1.27–1.88
Social items								
Non-Dutch ethnicity	738	n.s.	0.97	0.80–1.18				
Highest educational level	1,848	n.s.	1.03	0.88–1.19				

Associations are expressed as odds ratio (OR) and 95% confidence interval (CI). For each removed predictor variable, the P-to-Exit is reported; n.s. = not significant. Significance levels are 0.05 and 0.01, respectively.

In order to find out which biological, psychological, or social factors had the strongest association with the presence of pain-related TMDs, logistic regression analyses were performed. In the first step, all variables were entered consecutively in a single regression model in order to determine their unadjusted association with the TMD pain. Regarding the included 5-point ordinal variables, inspection of the regression coefficients of the dummy variables revealed that perfect linearity of their effect on the presence of TMD pain was present only for the predictor "biting lips and/or cheeks." All ordinal variables were therefore dichotomized (no = 0; all other categories = 1). Table 2 shows the results of the single and multiple regression models. Except for the biological items gum chewing and nail biting and the social items ethnic background and educational level, all variables had a significant association with TMD pain in the single regression model. According to the multiple regression model, the following variables appeared

Table 3: Single and multiple logistic regression models for the prediction of TMJ sounds among Dutch adolescents.

	Single regression				P-to-Exit	Multiple regression ($n = 3,337$)		
	n	P value	OR	95% CI		P value	OR	95% CI
Biological items								
Female gender	1,959	<0.001	1.81	1.51–2.16		<0.001	1.77	1.45–2.16
Age (years)	4,090	<0.001	1.19	1.13–1.26		<0.001	1.21	1.14–1.29
Smoking cigarettes (positive)	557	<0.001	1.55	1.23–1.94	0.156	—	—	—
Drinking alcohol (positive)	2,040	<0.001	1.53	1.29–1.82	0.406	—	—	—
Sleep bruxism (positive)	633	<0.001	1.62	1.30–2.02	0.045	—	—	—
Awake bruxism (positive)	369	<0.001	1.98	1.53–2.56	0.262	<0.001	1.79	1.36–2.36
Chewing gum (positive)	3,922	0.046	1.50	1.01–2.22	0.011	—	—	—
Biting nails (positive)	2,093	n.s.	1.14	0.96–1.34				
Biting pencils (positive)	1,811	n.s.	1.34	0.96–1.35	0.435	—	—	—
Biting lips and/or cheeks (positive)	2,406	<0.001	1.66	1.39–1.98		<0.001	1.46	1.19–1.80
Psychological items								
Being stressed (positive)	1,668	<0.001	1.81	1.50–2.17	0.042	—	—	—
Feeling sad (positive)	2,019	0.001	1.31	1.12–1.56	0.123	—	—	—
Social items								
Non-Dutch ethnicity	732	n.s.	0.81	0.64–1.02				
Highest educational level	1,846	n.s.	0.86	0.73–1.02				

Associations are expressed as odds ratio (OR) and 95% confidence interval (CI). For each removed predictor variable, the P-to-Exit is reported; n.s. = not significant. Significance levels are 0.05 and 0.01, respectively.

to be the strongest predictors of TMD pain: female gender, increasing age, sleep bruxism, biting on lips and/or cheeks, stress, and feeling blue. There were no signs of multicollinearity among the predictor variables in the final model.

Table 3 shows the results of the regression analyses with the presence of self-reported TMJ sounds as an outcome variable. Again, most biological items were associated with joint sounds in the single regression model. In addition, feeling stressed and feeling sad had a significant association with TMJ sounds. The multiple regression model revealed that female gender, increasing age, awake bruxism, and biting on lips and/or cheeks were the strongest predictors of TMJ sounds.

4. Discussion

The present questionnaire study aimed to assess the prevalence rates of two categories of temporomandibular disorders (TMDs), namely, pain-related manifestations of TMDs and TMJ sounds, in a large group of Dutch adolescents aged between 12 and 18 years. In addition, we examined which biological, psychological, or social risk indicators were associated with them and if both categories of TMDs yielded similar risk indicators. The results demonstrated that self-reported TMD pain is relatively common among 12- to 18-year-old Dutch adolescents, with an overall prevalence of about 20%. Besides the fact that the occurrence of TMD pain was highly associated with that of TMJ sounds, this pain was correlated to female gender, increasing age, reports of sleep bruxism, biting on lips and/or cheeks, stress, and feeling sad. The overall prevalence of TMJ sounds was about 15%; female gender, increasing age, awake bruxism, and biting on lips and/or cheeks were the best predictors. Except for the psychological factors that appeared to be associated with TMD pain only, pain-related TMDs and TMJ sounds shared similar biological risk indicators.

4.1. Prevalence of TMD Pain. It is generally acknowledged that depending on the study, the prevalence of TMD pain in children and adolescents varies widely [27]. In 2007, a large-scale study was published that focused on TMD pain among adolescents aged 12–19 years [13]. Of the 28,899 adolescents that participated, 4.2% reported TMD pain during their annual routine examination in Public Dental Service (PDS) clinics. In another Swedish study, seven percent of the 862 adolescents from a public dental clinic were diagnosed with TMD pain [28]. This rate was also found in a recent study on Norwegian adolescents [29]. The most likely explanations for the fact that the present study yielded a higher prevalence rate (namely, 21.6%) are differences in diagnostic criteria and the method of data collection. In the present study, orofacial pain had to be present within the last month, whereas in the study by Nilsson, a time span of one week was used. In the studies by List et al. and Ostensjo et al., a clinical pain diagnosis according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) was set, which may have resulted in a lower prevalence. On the other hand, when these clinical criteria were applied in two Brazilian studies performed on young adolescents, it was concluded that about 25% of the schoolchildren could be diagnosed with painful TMDs [20, 30]. As long as no uniform diagnostic criteria are available to obtain a reliable diagnosis of TMDs in the young population, studies on this topic will continue to present a multitude of different results. Future studies must therefore aim to develop a standardized assessment tool for the young population. Unfortunately, the recently published Diagnostic Criteria for TMD (DC/TMD) [2] have not yet been validated for usage among children and adolescents.

4.2. Risk Indicators for Pain-Related TMDs. Regarding the role of biological risk indicators on pain-related forms of TMDs, we demonstrated that the prevalence of TMD pain increases with increasing age in the period of adolescence. This is in line with several other studies (e.g., [11, 13, 31, 32]) and coincides with the suggestion that pubertal development increases the probability of self-reported TMD pain [12, 31]. Moreover, girls had higher rates of TMD pain at all ages studied compared to boys (namely, 26.1% and 17.6%, resp.), which corroborates with most studies on this topic (e.g., [12, 13, 28, 33]). Even though it is likely that sex differences exist in basic pain mechanisms and in associated psychosocial factors, the mechanisms underlying this difference are still not well understood [34]. Another biological factor that is frequently suggested to be associated with TMD pain in adolescents is overloading of the masticatory system due to oral habits (e.g., [20, 35]). As a result, it was not surprising that the final regression model included sleep bruxism and the adverse oral habit "biting on lips and/or cheeks."

Based on the present findings, it appeared that the two included psychological factors (namely, being stressed and feeling sad) contributed significantly to the presence of TMD pain among adolescents. Again, this is not surprising as both factors are frequently mentioned in relation to this pain (e.g., [31, 36–38]). The same neurotransmitters, especially serotonin and norepinephrine, are involved in both pain and mood regulation [39]. An increase of cortisol secretion in people with high psychological load has also been shown to be related with chronic pain development [40]. However, caution has to be paid to this assumption, as causal links have not been clearly defined. Do these factors increase the risk of TMD pain or are they the result of this pain because such persons have become more stressed and less cheerful by their pain condition?

Finally, the social factors ethnic background and educational level were not associated with the presence of TMD pain. The negative findings in this study might show that differences in ethnicity and educational level in Dutch adolescents do not necessarily represent different social environments in relation to the report of pain. Out of a vast range of social factors that have been considered to influence an individual's pain behaviour, parent emotions, behaviours, and health seem to play an important role in a child's pain experience [41]. This topic might be an interesting avenue for future research.

4.3. Prevalence of TMJ Sounds. The overall prevalence of self-reported TMJ sounds was 15.5%, which is in line with approximately 14% as reported in a recent meta-analysis on the prevalence of TMJ sounds (click or crepitation) in children and adolescents [42]. Unfortunately, the authors of that systematic review did not differentiate between boys and girls. The gender-specific prevalence rates that we found in the present study (19.3% for girls and 11.7% for boys) seem to corroborate with those presented in earlier studies [12, 43]. On the other hand, even though a lower overall prevalence was found in a study of Feteih (8.7% of the participants reported joint sounds), they still observed a higher prevalence in girls [44]. It is generally acknowledged that differences in methodology lead to considerable variation in prevalence of TMJ sounds [42]. However, it can still be concluded that TMJ sounds are a commonly reported sign of TMDs in the adolescent population.

4.4. Risk Indicators for TMJ Sounds. As for TMD pain, four biological factors appeared to be associated with TMJ sounds. Consistent with other studies on the young population, the prevalence of TMJ sounds increased considerably with age [14, 15, 45], especially during adolescence. Until now, there is no explanation for this trend. It has been suggested that increasing age leads to a temporary space insufficiency within the TMJ [14]. During the period of adolescence, the articular eminence gets its more prominent anatomical shape [46], which can cause a lack of space within the TMJ complex [14]. As a result, this insufficient space forces the disc to be pushed from its normal position on top of the condyle to the anterior or anterolateral side during the closing movement of the mouth. The disc only resumes its normal position during the opening movement, during which TMJ sounds are produced [47, 48]. As for TMD pain, female gender was found to be associated with TMJ sounds. However, conflicting evidence exists regarding this association [14, 15, 49]. As the current study utilized self-reported data, the finding that prevalence rates are higher among girls might also be due to the fact that female adolescents report physical symptoms more often than their male counterparts [50–52]. Finally, the associations found in this study between daytime clenching and/or grinding and TMJ sounds and between biting on lips and/or cheeks and TMJ sounds corroborate with other studies [53–55]. A possible explanation for these associations is that adverse oral activities cause compression of the articular disc as was shown in a finite element model study [56]. The occurring stresses may facilitate the disc to be dislodged off the head of the condyle to the anterior or anterolateral side, thus creating clicking sounds upon condyle translation movements [18, 47].

4.5. Methodology. This study has several limitations. First of all, pain-related TMDs and TMJ sounds were obtained by a questionnaire with no objective confirmation of signs and symptoms, thus being at risk of recall bias. However, high validity can exist between self-reported pain questions and the outcome of a clinical examination in adolescents [13]. Likewise, in a longitudinal study on signs and symptoms of TMDs in Finnish adolescents by Könönen and Nystrom, reported and clinically examined TMJ clicking sounds correlated significantly with each other [45]. Second, for an indication of TMJ sounds, all pupils had to note if they experienced any clicking or popping sound when opening or closing the mouth. The presence of crepitation was, however, not asked for. Even though crepitation has a much lower occurrence in the adolescent population, if present at all [15, 42], other results might have been obtained in case this type of TMJ sound was included. Third, the present study was conducted in an adolescent population composed of nonpatients. However, to fulfill the objective of determining associations with biological, psychological, and social risk indicators, different results might have been obtained in case a group of symptomatic patients was included. Therefore, further studies should be performed with representative samples of patients with TMD pain and TMJ sounds as well. The fourth aspect that should be mentioned is that, with increasing age, larger cognitive capacity, and better recall, older adolescents might remember and therefore report any physical symptoms better than younger ones [50]. This might have influenced the obtained results with respect to prevalence and associations.

5. Conclusions

This study indicates that both pain-related manifestations of TMDs and TMJ sounds are a common finding in the adolescent population. Both categories share similar biological risk indicators, whereas psychological factors were only associated with pain-related TMDs.

Data Availability

All relevant data are within the paper. On request, the data sets generated and/or analyzed during the current study are available from the corresponding author.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Clinical Study

Evaluation of C-Reactive Protein Level in Patients with Pain Form of Temporomandibular Joint Dysfunction

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Temporomandibular joint dysfunction is a functional disorder concerned with the abnormal functioning of the muscles of the stomatognathic system and temporomandibular joints involved in the dynamic movements of the jaw and surrounding structures. The aim of the study was to compare the level of C-reactive protein in patients with pain and painless forms of temporomandibular joint dysfunction. *Materials and methods*. The study group consisted of 72 patients who reported to the prosthetic treatment because of temporomandibular joint dysfunction. The study group included 36 patients with pain form of dysfunction, and the control group included 36 patients with painless form of disorder. Each patient underwent specialized examination of functional disorders in order to diagnose the type of dysfunction and was commissioned to carry out a study of the blood test concerned with evaluation of the C-reactive protein (CRP) level in the same analytical laboratory. The results of the investigation were subjected to statistical analysis. The research obtained approval from the Ethics Committee of the Jagiellonian University (KBET/125/L/2013). Level of Evidence for primary research was established as type V. *Results*. The mean values of C-reactive protein levels in both groups were in the normal range and did not differ statistically significantly, which indicates the fact that the pain form of the temporomandibular joint disorders is not associated with inflammation of the soft tissues of the joint. *Conclusion*. Painful form of the temporomandibular joint dysfunctions is not connected with the inflammation of joints.

1. Introduction

Temporomandibular joint dysfunction includes dysfunction of the masticatory muscles of the stomatognathic system and temporomandibular joints and the surrounding structures. They are often associated with abnormal conditions of occlusion. Functional disorders do not include all disorders associated with musculoskeletal organs including inflammatory, degenerative arthritis, and cancer lesions of the muscles (multiple sclerosis, tetany, and dermatomyositis). They are often the result of muscles undergoing prolonged and excessive work and nonphysiological loads occurring in the stomatognathic system [1–4].

The pain form of the disease is manifested by spontaneous pain in the preaural region, accompanied by pain or tenderness of the masseter muscle. Pain that appears during palpation examination of temporomandibular joints is frequently not related to inflammation of the soft tissue around the temporomandibular joints, as it is claimed by several authors [1, 3, 5–9]. The cause of this problem is a long-term overload of the soft tissue causally associated with excessive muscle tension, that sometimes even persists for years [1–4, 6, 9].

C-reactive protein (CPR) was first isolated in the blood serum in 1930 by Tillet and Francis in a bacteriological laboratory in the Rockefeller Institute in New York. Long years of research on the protein allowed for its assessment in a clinical setting. CRP is synthesized primarily by hepatocytes and the Kupffer and Browicz cells and is a cyclic pentamer with a molecular mass of 120 kDa. Its expression was also found in monocytes and lymphocytes. Each of the subunits of the protein is composed of 206 amino acids noncovalently linked together [10–12]. Each amino acid has a single disulfide bridge formed by cysteines at positions 37 and 78. Among the modifying agents of CRP concentration are cytokines and interleukins 1 and 6. The mechanism of stimulation of the biosynthesis of CRP is still not fully understood. CRP is present in healthy individuals in an amount of 0–5 mg/l. There is no evidence of differences of this marker that depends on gender. Currently, it is recognized as an important marker of ongoing inflammation and cancer reaction in the body and one of the major proteins of the acute phase. Its concentration may be increased even thousand-fold within 48 hours of the onset of inflammation. CRP is used as one of the markers of choice in monitoring the acute phase response because the markers increase to a relatively high concentration compared to basal concentration [13–16].

Marking of C-reactive protein concentration is based on the immune reaction of monovalent antibodies against CRP using the methods of radial immunodiffusion, immunoelectrophoresis, immunonephelometry, radioimmunoassay, and enzyme immunoassay. In recent years, the methods are immunoblotting, ELISA assays, and techniques of modern molecular biology [12, 14].

The aim of the study was to evaluate the level of C-reactive protein in patients treated for the pain form of temporomandibular joint dysfunction.

2. Materials and Methods

The study enrolled a group of 72 patients, aged 21 to 48 years, of both sexes, who reported to the prosthodontic treatment in the Consulting Room of Temporomandibular Joint Dysfunction at the Dental Institute at the Jagiellonian University in Cracow, between January 2015 and February 2017, due to the pain and painless forms of the temporomandibular joint dysfunction, and acoustic symptoms, accompanied by excessive tension of the masticatory muscles. Symptoms persisted from 3 to 12 months prior to the beginning of the treatment. All patients were subjected to a specialist functional examination of the masticatory organ using typical procedures: information of spontaneous and provoked ailments, muscles and temporomandibular jaw palpation, functional manipulation, assessment of ranges of mandibular movements, joints' sounds, and dental rating. Patients were consecutively and alternately assigned to the study and control groups, 36 patients in each. The study group consisted of pain form of temporomandibular joint dysfunction and the control group included painless form of this dysfunction.

During the study, we analyzed information concerned with general health and present complaints, and a functional examination of the stomatognathic system was conducted, with particular regard to the nature and intensity of the perceived pain and discomfort of temporomandibular joints and masticatory muscles, which occurred prior to treatment and radiation of pain, the type of sound symptoms (clicks), volume, and the phase of the movement of lowering and lifting the jaw, during which there were tension-type headache and back pain (Table 1). Examination was conducted once.

Functional assessment of the masticatory apparatus and muscles consists of a medical interview and a physical examination. Another important element of a medical interview was to evaluate the patient's posture, facial expression, and the general well-being after the patient enters the surgery. Through a medical interview, detailed information about the current general health condition was revealed (including information about chronic and hereditary diseases); the examining physician obtained information about the patient's surgical treatment and head trauma history within the last 6–8 months and the current medications being taken on daily basis. In this context, particular attention was given to muscle and joint conditions, with a focus on multiple sclerosis, osteoporosis, fibromyalgia, trigeminal neuralgia, hormonal disorders, and autoimmune diseases.

Physical examination started with a facial symmetry test; the oral cavity was examined for the dental and periodontal status and the condition of oral mucosa. If the patient had any missing teeth, the number and location of existing natural teeth in the occlusion support zones were investigated. Dental classification (according to Eichner index or Galasińska–Landsberger classification) was recorded in the patient's medical file. Dental prosthetic restorations, if present, were examined in terms of their clinical value.

A clinical examination of temporomandibular joint consists of palpation and auscultation; palpation was performed simultaneously on both sides of the face by exerting a force of around 400 g per square centimeter. Auscultation was performed with the aid of a double-tube stethoscope. The individual palpation force was measured using an electronic kitchen scale [1, 3, 17, 18].

Factors of inclusion in the study were pain form of temporomandibular joint dysfunction, the required age range, and a good general state of health (particularly with regard to cardiac and metabolic disorders). Good general state of the patients' health means that patients did not suffer from the medical conditions that could have an influence on the level of CRP.

Factors for exclusion from the research included the will (consent) of the patient, the presence of general diseases, traumas, or local inflammations.

All respondents were directed to one external medical analysis laboratory to determine the level of C-reactive protein in the blood serum. For this purpose, the immunoturbidimetric assay was performed for the in vitro quantitative determination of CRP in human serum and plasma using Roche/Hitachi cobas c systems. It was also assumed that the correct level of this marker in patients who show no evidence of inflammation taking account of the above method is 0 to 5 mg/l [12, 14]. All patients underwent ultrasound examination of the temporomandibular joints.

In case of the measure giving the constant results, statistical analysis was based on the traditional methods of calculation: mean values, standard deviation, minimal values, maximal values, standard error of the mean, variance analysis for dependent variables, and post hoc Tukey test for dependent variables being the statistical significance measure.

To compare the dependencies between the results obtained in consecutive clinical tests, the nonparametric

Table 1: A summary of symptoms obtained during functional examination of stomatognathic system conducted in both groups.

Symptoms of temporomandibular joint disorders			Group I		Group II	
			W	M	W	M
Intrinsic pain	Single TMJ	Acute	14	6	0	0
		Dull	6	3	0	0
	Bilaterally	Acute	8	5	0	0
		Dull	1	2	0	0
Mastication pain or/pain presence during lower jaw movements			28	14	0	0
Pain of the TMJs triggered by palpation			20	13	0	0
Pain associated with lower jaw movements			28	17	0	0
Masticatory muscle pain			20	5	0	0
Radiation of pain			8	5	0	0
Sounds, snaps in TMJs	Single TMJ	R	9	1	8	3
		L	2	2	3	1
	Bilaterally	R	4	2	2	3
		L	4	2	2	3
Subjective feeling of increased tension in muscles			22	7	24	6
Constricted opening of the lower jaw			4	1	3	0
Constricted lateral mandibular movements			2	1	3	1
Mandibular deviation during opening			15	5	16	2
Difficulty in chewing			15	14	14	2
Occlusion parafunctions			20	8	21	5
"Closed ear" symptom on the affected TMJ side			2	2	4	2
Sudden hearing impairment			1	0	2	1
Tinnitus			2	0	1	1

Friedman test, Kendall's W, and Wilcoxon signed-rank test (comparing two related samples) were used. For statistical studies, special computer software STATISTICA 2010 was used. A p value less than 0.05 was accepted as statistically significant. The research obtained approval from the Ethics Committee of the Jagiellonian University (KBET/125/L/2013). Clinical Trial Gov. Identifier was registered as well: NCT03065608.

Level of Evidence for primary research was established as type V.

3. Results and Discussion

The study involved 72 patients, ranging from 21 to 48 years, divided into two groups of 36 people. Group I included 24 women and 12 men (mean age 29), and group II control included 27 women and 8 men (mean age 31). Analysis of the results of clinical examinations conducted in both groups show a homogeneous clinical material (sound symptoms in the temporomandibular joint, range of motion of the jaw, abnormal range and symmetry of movement of the jaw, and difficulty in chewing foods) with the exception of pain, which is a factor differentiating patients between group I and II. The results of the clinical examination (symptoms indicating the occurrence of functional disorders) are summarized in Table 1.

In group I, the mean level of CRP was 2.54, the extreme values were 5.9–0.14, median was 2.15, and the standard deviation was 1.54. In group II, the average value of C-reactive protein was 2.69 (peak of 5.2–0.7), median was 2.4, and the standard deviation was 1.87. Average values of amounts of CRP did not significantly differ statistically, since $p > 0.05$. The results of the statistical calculations are graphically depicted in Figures 1 and 2.

None of the examined patients had signs of inflammation in the temporomandibular joints in ultrasound examination (pleural joint).

The authors of many publications [10–16, 19] emphasize the high utility of this marker in the diagnosis and confirmation of the presence of inflammation in the body, which also reflects a severity of current inflammation process. The level of this protein is increased between 6 and 8 hours after the pathogen in the body was found. The normalization of CRP is a valuable indicator of the patient's recovery. One should pay attention to general medical conditions concomitant to dysfunction because, for example, heart problems associated with the occurrence of continuous inflammation of the vascular endothelium will result in increase of CRP level and it will be due to the current associated medical main condition [19].

In the dental treatment specificity, the elevated level of CRP has been found in many diseases, such as periodontal disease, gangrenous pulp, fungal diseases of prosthetic base, or posttraumatic conditions—fractures of the jaws [12, 15]. While the states of inflammation of the temporomandibular joints are rare, and even more, they are not accompanied by temporomandibular joint dysfunction. They take the form of inflammation of the joint capsule (synovitis), the synovial membrane lining the inner surfaces of the bag, capsule ligaments (capsulitis), the retrodiscal tissues, and the area behind the articular disk (retrodiscitis) and inflammation associated with destructive changes in the bone (osteoarthritis). In each of these forms, the main causes of the inflammation for most parts are macrotrauma and mechanical damage. In contrast to functional disorders, when the pain associated with the movements of the mandible is dominant, inflammation is associated with continuous pain [1, 2, 20, 21].

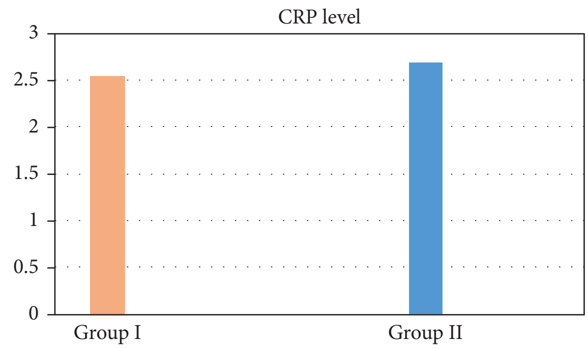

Figure 1: Average C-reactive protein values, obtained in both groups, presented graphically.

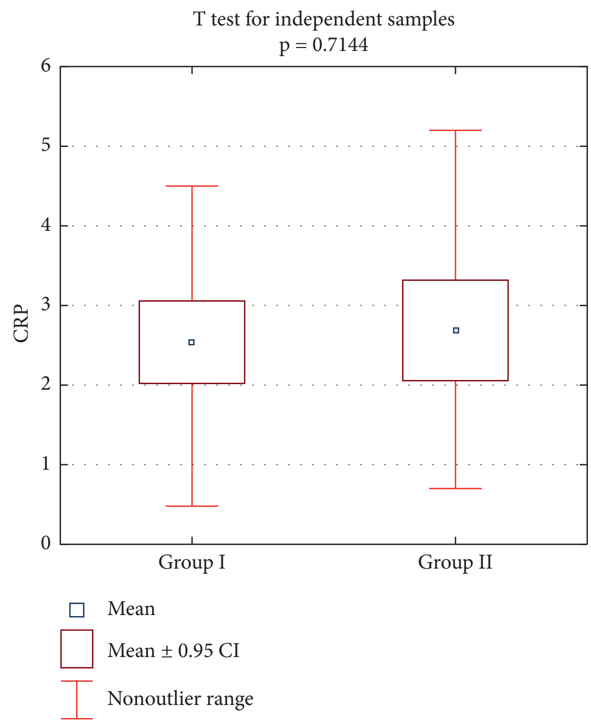

Figure 2: Average C-reactive protein values, obtained in both groups, presented in statistical evaluation.

CRP levels in our own study of both groups are in the normal range, and therefore this indicates that the pain form of temporomandibular joint dysfunction of subjects is not associated with the occurrence of the state of the inflammation in the soft tissues and bones of the temporomandibular joints. The presence of pain in the palpable test is often interpreted as an evidence of inflammation of tissues, but it is not confirmed in the clinical and laboratory tests.

Pain in any joint structure is called arthralgia. It would seem that pain is originated from the articular surfaces when the joints are overloaded by the work of muscles. It is impossible because of lack of the innervation of the articular surfaces, so arthralgia can originate only from nociceptors located in the soft tissue of the temporomandibular joints, like disc and capsular ligaments, and retrodiscal tissue [1–3, 16, 21, 22]. The temporomandibular articulation is unique in the body in that the two joints must always move simultaneously. Two distinct movements, rotation and translation, occur in the joint during mandibular opening and closing. Normal movements of the mandible depend on proper function of the temporomandibular joints. If the dysfunction is connected with muscles and joints prolonged overload, it will result as disruption of normal condyle-disc complex spatial relationship. In such a clinical form of dysfunction mainly the retrodiscal ligament is destroyed, and it is responsible for the occurrence of pain. The disc is then dislocated, mostly anteriorly. Meyer [23] describing the rules for the temporomandibular joint examination technique emphasizes that tenderness elicited by the palpation of the joint is invariably associated with joint inflammation.

In general, diseases such as arthritis and temporomandibular joint dysfunction can occur with elevated CRP because of general disease, as indicated by Lin et al. [24]. Nordahl et al. [16] described the progression of radiographic changes of the temporomandibular joint with reference to plasma levels of interleukin-1beta (IL-1beta), C-reactive protein (CRP), and disease duration. They point at the correlation of these factors with the severity of pathological changes. Progression of the overall grade of radiographic changes in the joints occurs in the group of the patients with chronic inflammatory joint disease. Increased levels of CRP are associated with progression of joints' bone loss.

Analyzing the available literature, it can be assumed that the use of studies evaluating CRP levels can be very helpful in diagnosing or excluding the inflammatory component of the temporomandibular joints. Kostrzewa-Janicka et al. indicate that more information could be obtained from synovial fluid of joints, like cytokines and their receptors, which are involved in the pathogenesis of temporomandibular joints. However, it is very difficult to aspirate the proper amount of synovial fluid from such a small joint, although recent advances in arthroscopic surgery allowed the direct examination of these joints [18]. These authors point out that in the case of joint diseases not related to functional disorders, the concentration of neuropeptides, cytokines, leukotrienes, prostaglandins, and catabolic products, identified in the joint's fluid, are correlated with joint pain and presence of surface lesions observed within the joint [18].

The above test results show the importance of information on the general principles of the treatment of pain form of temporomandibular joint dysfunction that the administration of antibiotics in case of pain on the palpation test of the temporomandibular joints may be wrong. Such a clinical situation requires careful verification and use of additional tests to plan an appropriate treatment [1, 2].

This provides valuable information for proper diagnosis and correct treatment in temporomandibular joint dysfunction with the use of occlusal splints and occlusal correction of the teeth contacts and supporting numerous treatments in physiotherapy, such as laser biostimulation, sonophoresis, physiotherapy, and manual therapy. Intraoral splints are commonly used in dental treatment for a variety of conditions. Such splints alter the condyle-disc-fossa relationship, probably by changing the loading status of joints and discs. The antibiotics are not necessary for such a kind of treatment [22].

Despite the etiological factor associated with the psychosocial sphere, this provides valuable information for proper diagnosis, and correct treatment of temporomandibular joint dysfunction is primarily occlusal splint, correction of occlusal contact, and numerous supporting physiotherapy treatments, such as biostimulation laser, sonophoresis, and manual techniques [1, 2, 5, 25–28].

4. Conclusion

Pain form of the temporomandibular joint dysfunctions is not connected with inflammation of the temporomandibular joints.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Research Article

Dentists' Awareness of Physical Therapy in the Treatment of Temporomandibular Disorders: A Preliminary Study

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Background. Physical therapy (PT) has been shown to be one of the most effective conservative treatments for temporomandibular disorders (TMD). Not all dentists are aware of the importance of the collaboration with physical therapists in the treatment of TMD pain. *Objectives*. To determine the awareness of dentists in Florida about the importance of PT for TMD pain and to create awareness related to collaborations. *Methods*. An online questionnaire was used. A contact list of dentists was obtained from the Florida Dental Association. The overall awareness and information on patient referral were presented per dentist specialty. *Results*. A total of 256 dentists completed the survey. Prior to the survey, 41% of the dentists reported not aware that PTs can treat TMD patients. Oral surgeons and orthodontists were more aware about PT compared to other specialties. After the survey, 81% of the dentists were more likely to refer their TMD patients to PT, and 80% were interested to know more about the benefits of collaborations. *Conclusion*. This study shows the lack of dentists' awareness in Florida about the benefits of PT for TMD treatment. This study increased the awareness of the surveyed dentists in Florida about the benefit from a multidisciplinary approach.

1. Introduction

The temporomandibular joint (TMJ) is part of the musculoskeletal system responsible for mandibular function which includes mastication, phonation, and deglutition [1]. Temporomandibular disorders (TMD) are defined as a musculoskeletal disorder affecting the TMJ, the masticatory muscles, and associated structures including dental occlusion and the cervical spine [2, 3]. TMD are the most common chronic orofacial pain condition, and it can significantly affect the patient's quality of life by diminishing the individual's ability to work and interact in social environment [3].

Approximately 10% of the population has pain in the TMJ [4], and 3.6%–7% of the population will seek treatment due to the severity of their symptoms [3, 5]. TMD signs and symptoms may include local pain in the TMJ and/or masticatory muscles, limited mouth movements, TMJ sounds, and headaches [5–7]. Cervical spine disorders were shown to be associated with TMD pain 70% of the time [7–11].

The different types of TMD are classified based on the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) [12]. TMD can be acute or chronic, simple or complex with persistent and associated cognitive, psychosocial, and behavioral factors [12]. A multidisciplinary approach is particularly important for successful treatment of chronic TMD cases [13]. Treatment of TMD pain may involve dentists, physical therapists (PTs), speech pathologists, physicians, and psychologists. An ideal treatment option would be the one that is least invasive and most cost-effective, while considering the TMD associated factors such as parafunctional habits, poor posture, widespread pain, poor sleep, and depression [3].

Physical therapy (PT) is one of the most effective conservative treatments for TMD pain [14]. PT is among other noninvasive therapies including behavioral therapy and occlusal appliances that were shown to improve patients with TMD [15]. The most important contribution by PTs is the identification of the musculoskeletal components that contribute to the symptoms of the patient [7]. Because the TMJs are part of the musculoskeletal system, PTs can treat TMJ-related pain with similar interventions as they would in most other body joints. PT includes a large number of modalities to treat TMD pain secondary to inflammation, masticatory muscle pain, TMJ hypo/hypermobility, disc displacement, bruxism, and fibrous adhesion [7]. Based on systematic reviews [16, 17], manual therapy, jaw exercises, and postural reeducation were shown to be effective to reduce pain and improve mobility/function in TMD patients.

More collaboration between dentists and PTs for the management of TMD pain is needed so as to improve the treatment outcomes of these patients. Not all dentists are aware of the importance of involving PTs in the treatment of TMD pain. The awareness of dentists from Florida about PT's role for TMD treatment is unknown. Therefore, the primary objective of this research was to determine the current level of awareness of dentists in Florida about the importance of PT and the collaboration with PTs in the treatment of TMD. The secondary objective was to increase the awareness level of dentists regarding the importance of PT and the benefits of the collaboration between dentists and PTs in TMD treatment to potentially increase collaborations between dentists and PTs in the treatment of TMD for best outcomes.

2. Materials and Methods

2.1. Study Design. This was a cross-sectional descriptive study approved by the Institutional Research Board from Florida International University (IRB-14-0205).

2.2. Participants. Dentists in Florida with an active dental license and members of the Florida Dental Association were contacted. A contact list of dentists was obtained from the Florida Dental Association. The dentists were contacted by an email, which included a statement of the study objectives and a link to the online survey. By completing and submitting the survey, the dentists were informed that they were consenting to participate in the study. The dentists were informed that no identifiable information will be published or released and that participation is voluntary. All data were confidentially analyzed. In addition, they were informed that they will receive no compensation for participating in the study. However, an educational brochure with information related to PT for treating TMD pain was available to them upon completion of the survey. A reminder email was sent 3 times every 2 weeks from the initial recruitment email.

2.3. Questionnaire. A questionnaire was created using Qualtrics online survey software (Qualtrics Labs Inc., Provo, Utah). The survey was revised by 2 dentists to gather feedback for improvements. Feedback was considered and changes to the survey were implemented. The questionnaire included a total of 24 questions: 7 related to demographics, 12 on TMD patient population and referrals, and 5 related to general knowledge (Appendix 1). The online survey was estimated to take approximately 5–10 minutes to complete.

2.4. Data Analysis. Descriptive statistics were calculated to analyze the responses. Data were presented as total number of participants (n) and frequency (%). Written information provided by some dentists was considered and presented. The overall knowledge related to PT among the respondents and information on patient referral were calculated and presented per dentist specialty.

3. Results

3.1. Participants' Demographics and Characteristics. From over 10,000 emails sent, a total of 256 dentists completed the survey (response rate of 2.5%). The mean age of the participants was 51 years with a range of 26 to 78 years, and 172 of the participants (67%) were male. Ninety-seven percent of the participants (243) had earned their professional doctoral degree, 2% [5] had earned an academic master's degree, and 0.4% [1] had earned an academic doctoral degree (PhD). Two hundred twelve participants (86%) reported practicing dentistry in a private practice setting, and most of the participants (41%) practiced for 21 to 35 years. Twenty-eight percent (65) were from South Florida District followed by West Cost District (24%) and Central Florida District (19%). The majority of the participants (73%) were general dentists followed by orthodontists (8%) and other specialties (18%), which included pediatric dentistry, TMJ and orofacial pain specialist, and neuromuscular dentistry. Table 1 shows detailed demographic and characteristics of participants.

Thirty-nine percent of the dentists (95) had never taken continuum education course on TMD. For those dentists reporting yes for taken courses on TMD, the courses included topics related to etiology and treatment of TMJ disorders; occlusion; bite plane therapy; TMD and occlusion; splint therapy, medication and restorative therapy; surgical and nonsurgical treatment; facial pain; myofascial pain and TMD; arthroscopic surgery, traumatic derangement; joint prosthetics and replacement; and occlusion and posture. Six dentists reported PT as part of the topic in the continuum education course taken.

3.2. TMD Patients' Information. More than half of the dentists surveyed (57%) estimated anywhere from 1 to 15% of their patients suffered from TMD symptoms. Only 2 dentists reported not having seen these type of patients, and 17 dentists (7%) reported that more than 55% of their patients have TMD. The most common characteristics of TMD evaluated and/or treated were parafunction habits (89%), muscle tightness/tender points (75%), occlusion alterations (75%), and headaches (69%). The least common characteristics were TMJ hypermobility (26%) and TMJ degeneration (38%). Other TMD characteristics evaluated and/or treated included condyle fracture, traumatic injury, neuropathic pain, and craniocervical issues. Only 7

Table 1: Participants' demographics and characteristics.

Variable	Value
Age, years (mean, standard deviation, and range)	51 ± 13 (26–78)
Gender, male/female (total number, percentage)	172 (67%)/84 (33%)
Highest level of education (total number, percentage)	
Professional doctorate	243 (97.5%)
Academic master	5 (2%)
PhD	1 (0.4%)
Areas of practice (total number, percentage)	
General dentist	178 (73%)
Orthodontists	20 (8%)
Endodontist	9 (4%)
Prosthodontics	5 (2%)
Periodontist	7 (3%)
Oral surgeon	7 (3%)
Other	18 (7%)
Years of practice (total number, percentage)	
0–5	36 (15%)
6–10	26 (11%)
11–15	21 (9%)
16–20	20 (8%)
21–25	32 (13%)
26–30	32 (13%)
31–35	37 (15%)
36–40	23 (9%)
41–45	13 (5%)
46–50	5 (2%)
51–55	1 (0.4%)
>56	1 (0.4%)
Continuum educational course in TMD	
Yes	150 (61%)
No	95 (39%)

dentists (3%) reported never evaluating a patient with a TMJ-related problem. Methods of TMD evaluation most often used by dentists included observing jaw movements during opening/closing (86%), evaluating for dental occlusion (84%), TMJ palpation (83%), and signs of parafunctional habits (81%). Other methods reported to evaluate TMD patients included neck range of motion, radiographs, photographs, MRI, diagnostic anesthesia, biopsychosocial measurements, and surface electromyography (sEMG). Most of the patients (55%) presented a chronic condition during the initial evaluation, as opposed to the acute (25%) and subacute conditions (20%).

When asking the dentists whether or not their TMD patients also presented with neck pain, poor posture, and/or cervicogenic headache, 13%, 34%, and 32% reported never

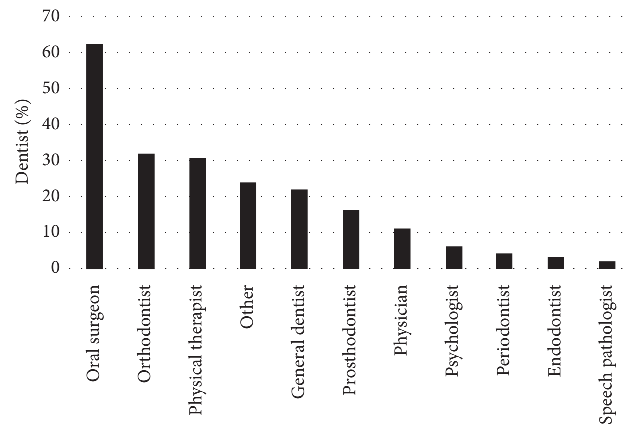

Figure 1: Health care providers TMD patients are referred to.

evaluating these conditions, respectively. From those who had evaluated, 76%, 58%, and 59% reported finding these conditions, respectively, present in their patients.

3.3. Treatment and Referral. The most frequent methods used to treat TMD patients (if patients are not referred) were the use of bite splints (90%), prescription medication (62%), followed by occlusion correction (58%). However, 69 dentists (30%) utilized other treatment methods including ice/heat, arthrocentesis, diet alteration, jaw and neck exercises, botox, trigger point injection, thermotherapy and cryotherapy, and soft tissue massage. Eighty-six percent (86%) reported referring TMD patients to other health care providers. Most of these dentists (70%) reported referring up to 25%. Thirteen percent (13%) reported referring 75–100% of their TMD patients. The health care providers to which TMD patients were most commonly referred were oral surgeons (62%), orthodontists (32%), and PTs (31%) (Figure 1). Other providers described included TMJ/orofacial pain specialist, chiropractor, massage therapist, gnathologist, neuromuscular dentist, endocrinologist, neurologist, osteopath, and ENT. Table 2 shows the distribution of TMD patient referral per dentist specialty. The specialty that refers the most the TMD patients to PTs was oral surgeons (80% of them) followed by orthodontists (55%).

The most common reasons for TMD patient referral to a PT included neck pain (43%), masticatory muscle tenderness (34%), and postural alterations (31%) (Figure 2). The most common reason for not referring a patient to PT was that they did not know about the benefits of PT to the patient (58% of them). Other reasons reported were "lack of knowledge of a PT that treats TMJ or contact information," "insurance payment," "no formal referral system set in place," and the belief that "PT is only a temporary fix" or "it is out of their skill set." In fact, 41% of all the dentists surveyed had no knowledge that PTs were capable of treating patients with TMD.

3.4. Physical Therapy Awareness. Prior to the survey, 41% of the dentists reported not aware that PTs can treat patients with TMD by, for example, reeducating jaw movements, and

Table 2: Health care providers TMD patients are referred to by dentist specialty (total number and percentage).

Patients referral to	General dentist	Orthodontist	Endodontist	Prosthodontist	Periodontist	Oral surgeon	Other
	Dentist specialty						
General dentist	26 17.81%	9 45.00%	4 44.44%	0 —	2 40.00%	1 20.00%	3 27.27%
Orthodontist	53 36.30%	0 —	2 22.22%	0 —	1 20.00%	4 **80.00%**	4 36.36%
Endodontist	3 2.05%	1 5.00%	0 —	0 —	1 20.00%	0 —	0 —
Prosthodontist	18 12.33%	2 10.00%	4 44.44%	2 50.00%	2 40.00%	2 40.00%	1 9.09%
Periodontist	6 4.11%	0 —	2 22.22%	0 —	0 —	0 —	0 —
Oral surgeon	100 **68.49%**	10 50.00%	3 33.33%	1 25.00%	3 **60.00%**	0 —	7 63.64%
Physical therapist	42 28.77%	11 **55.00%**	1 11.11%	1 25.00%	2 40.00%	4 **80.00%**	1 9.09%
Physician	15 10.27%	5 25.00%	0 —	1 25.00%	0 —	1 20.00%	0 —
Psychologist	6 4.11%	5 25.00%	0 —	1 25.00%	0 —	0 —	0 —
Speech pathologist	1 0.68%	1 5.00%	0 —	0 —	0 —	0 —	1 9.09%
Other	34 23.29%	6 30.00%	3 33.33%	1 25.00%	1 20.00%	0 —	4 36.36%

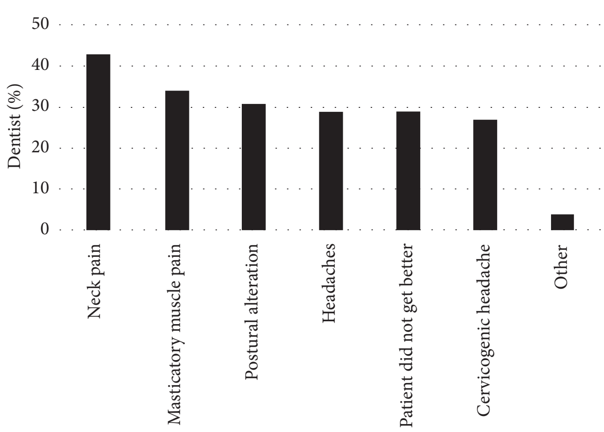

Figure 2: Conditions under which TMD patients are referred to physical therapy.

restoring masticatory muscles (Table 3). In addition, 32% of the dentists reported not aware that cervical spine may be involved with masticatory region pain. Oral surgeons and orthodontists were more aware about PT for TMD management compared to other specialties (Table 3).

After asking the dentists surveyed if they are more likely to refer any of their TMD patients to a PT after participating in the survey, 184 dentists (81%) are more likely to refer to a PT by answering yes or may be. Reasons for not being likely to refer or may be are as follows: “do not know how the process is to refer it,” “none have offered services,” “too specific of treatment for PT to be helpful,” “insurance issues,” “not allowed to refer,” “PT treatment only helps temporarily,” or “do not know where to refer in my area.” At the end of the survey, 80% of the dentists (180) were interested to know more about the benefits of the collaborations with PTs to treat TMD patients. The proportion of dentists’ interest on knowing more about the benefits of the collaborations with PTs to treat TMD patients is also shown in Table 4 by dentist specialty.

4. Discussion

This was the first study evaluating the awareness of dentists in Florida about the importance of the multidisciplinary approach with PT for the management of TMD pain using an online questionnaire. Information about TMD patients treated by dentists, TMD patient referral, and their interest to know more about PT for the management of TMD pain is described. However, the results of this study should be interpreted with caution because the response rate was very low, and therefore the generalizability of the findings is questionable. However, this preliminary study presents relevant information regarding the current level of awareness among the participants and can help further increase the level of collaboration between PTs and dentists in the treatment of TMD. From the 88 of surveyed dentists who had never referred a TMD patient to a PT, 65 of them (74%) were not aware of the benefits of PT in treating TMD patients. Perhaps, the referral to PTs would be greater if more dentists were aware of PT for TMD patients. In fact, after this survey, 81% of the dentists are more likely to refer a TMD patient to PT. Other studies should investigate if the referral is actually happening in Florida. According to a dentist author in his

Table 3: Dentists' awareness about physical therapy treatment for TMD by dentist specialty.

	Aware	Not aware
General dentist	96 (58%)	70 (42%)
Orthodontist	14 (70%)	6 (30%)
Endodontist	5 (56%)	4 (44%)
Prosthodontist	2 (40%)	3 (60%)
Periodontist	4 (57%)	3 (43%)
Oral surgeon	6 (100%)	0 (0%)
Other	8 (50%)	8 (50%)
Total	135 (59%)	94 (41%)

Table 4: Dentists' interest on the benefits of collaborations with physical therapists to treat TMD patients by dentist specialty.

	Yes	No
General dentist	133 (83%)	28 (17%)
Orthodontist	16 (80%)	4 (20%)
Endodontist	6 (67%)	3 (33%)
Prosthodontist	4 (80%)	1 (20%)
Periodontist	4 (57%)	3 (43%)
Oral surgeon	5 (83%)	1 (17%)
Other	11 (69%)	5 (31%)
Total	179 (80%)	45 (20%)

article with a PT colleague [2], 50% of all his patients are referred to PT. Based on the TMD patients' characteristics reported by the dentists in our survey, it appears that most of them could be referred to PT for further treatment.

Approximately 1/3 of dentists surveyed do not evaluate their TMD patients for poor head and neck posture and the presence of cervicogenic headaches. Also, 13% of dentists do not evaluate for the presence of neck pain. As previous researches show correlation between TMD pain and the presence of cervical spine disorders including neck pain and poor posture [7, 9–11], dentists should be aware of these disorders in their patients in order to possibly refer the patients to PTs for further treatment and collaboration. On the other hand, PTs should be also aware of any possible tooth-related pain or dental occlusion problems related to TMD during their evaluation in order to possibly refer the patient to the dentist. For example, if parafunction habits are common in patients with TMD, a dental splint may be fabricated by the dentist. At the same time, PTs can deprogram the masticatory muscles with soft tissue massage and intraoral mobilizations before the exercises. TMD patients will have better treatment outcomes if both dentists and PTs work together [2]. In a randomized control trial, patients who received a combination of dental splint therapy with PT had greater gains in mouth range of motion than splint therapy alone [18].

The health care providers to which TMD patients were most commonly referred to were oral surgeons (62%). Oral surgeons were the health care providers who refer the most the TMD patients to PTs. Table 4 shows that almost 70% of general dentists refer patients to oral surgeons. It seems that TMD patients are mostly referred to PT for postsurgery treatment. Studies indicate that PT has a positive effect in relieving pain and restoring TMJ function after surgery [19, 20]. However, if applicable, TMD patients should be referred to PT before a nonconservative treatment such as surgery is considered. In addition, in the cases where surgery is needed, PT should be considered as a presurgical treatment in order to prepare the patients for surgery. The benefits of the surgery may be increased if PT is done before surgery. Gladly, 55% of the orthodonticts refer TMD patients to PT.

A lack of dentists' awareness about the benefits of PT for the treatment of TMD patients leads to less patient referral and collaborations with PT. In fact, the most common reason for not referring a patient to a PT was the lack of awareness of PT benefits (58%). More awareness related to the relationship between cervical spine and orofacial symptoms is needed as 32% of the dentists were not aware. For instance, cervical spine postural reeducation is recommended for TMD patients in addition to manual therapy and jaw exercises [16]. PT is considered an integral part of TMD treatments [13]. Physical therapy, as well as behavioral therapy and occlusal appliances help to improve patients with TMD [15]. Therefore, according to the authors of this study, information on the role of PT on TMD treatment should be part of seminars and lectures in the curriculum of Dentistry Programs to inform them on the importance of interdisciplinary treatment of TMD patients.

From the dentists' awareness about the benefits of PT for the management of TMD patients prior to the survey (146 dentists), 62 (43%) are more likely to refer patients to PTs after participating in the survey. But 58% of them said may be or are not likely to refer (31% and 27%, resp.). Therefore, the fact that some dentists are aware about the benefits of PT does not mean that the referral is happening. One of the possible reasons for the low rate of referral of patients with TMD to PTs is the lack of available PTs with expertise in treating TMD because not all PTs are trained and confident about providing care to TMD patients. The number of PTs with specialized training and advanced education in the area of TMD such as PTs certified by the Physical Therapy Board of Craniofacial and Cervical Therapeutics (many of them members of American Academy of Orofacial Pain) represents a small fraction of the American Physical Therapy Association (APTA). Therefore, more education related to TMJ, TMD, and the multidisciplinary approach between dentists and PTs in the pain management of TMD patients should be also reinforced in all PT Programs. Interestingly, one comment received by a dentist was that there is a need to also educate the PTs regarding collaborations. A study with PTs about their knowledge to treat TMD patients should be conducted. Their capabilities to collaborate with dentists should be also measured. If more PTs are capable of treating these patients the likelihood of dentists to refer their patients may increase. Information related to should be part of the curriculum of all PT programs.

TMD can be complex because patients may present different conditions including arthralgia, myalgia, myofascial pain, disc displacement disorders, degenerative joint disease, and headache attributed to TMD among other classifications [12]. In addition, other associated factors may be present such as generalized pain, sleep disturbances, and depression. Therefore, diagnosis and treatment of these patients is challenging [12], and a multidisciplinary team is recommended to treat TMD. However, not all disciplines are necessarily needed for treating all cases of TMD. Patients' symptoms should be considered to decide which professionals need to be involved.

4.1. Study Limitations. From over 10,000 contacted dentists, only 2.4% of them responded to the survey. The authors believe that not all email addresses were updated in the list provided and that could have affected the amount of responses received. In order to maximize participation, the survey was made to be short (5–10 minutes to complete). In addition, a brochure with information about PT treatment was available upon participation. Other strategies to increase participation should be considered in future studies.

This study included dentists from the State of Florida only. Future studies should include larger sample (higher response rate) by not only including dentists from other states, but also including more dentists from the other specialties. The majority of the dentists who responded the survey were general dentists (73%). Results may not be generalizable when data were analyzed by specialty. Therefore, the results should be interpreted with caution; future studies with higher response rates and including different dental specialties are needed.

5. Conclusion

According to this survey, a large percentage of the dentists that completed the survey were not aware of the benefits of PT in treating TMD pain. This study helped to increase the awareness level of the surveyed dentists in Florida about the importance of physical therapy and the benefit from the multidisciplinary approach with PT to their patients. Most of the dentists surveyed (80%) were interested to know more about the benefits of the collaborations with PTs to treat TMD patients. This is important as the increased awareness of dentists about the importance of physical therapy and the interest to know more about the benefits may increase collaborations between dentists and PTs in the treatment of TMD patients in Florida. TMD patients are more likely to be benefited from those collaborations. Future studies should investigate if collaborations between dentists and PTs are increasing and if TMD patients treatment benefit from those collaborations.

Appendix

Survey

Questions related to demographic and work experience:
Do you agree to participate?
Yes, I consent to participate.

(1) Gender
   (a) Male
   (b) Female

(2) How old are you? Please enter in years.
   ____

(3) Highest level of Dentist degree completed
   (a) Bachelor's degree
   (b) Master's degree
   (c) Doctoral degree

(4) Do you currently practice?
   (a) Yes
   (a) No

(5) How many years have you been practicing?
   (a) 0–5
   (b) 6–10
   (c) 11–15
   (d) 16–20
   (e) 21–25
   (f) 26–30
   (g) 31–35
   (h) 36–40
   (i) 41–45
   (j) 46–50
   (k) 51–55
   (l) More than 55 years

(6) What is your Florida Association District in which you currently work?
   (a) Atlantic Coast District
   (b) Central Florida District
   (c) Northeast District
   (d) South Florida District
   (e) Northwest Florida District
   (f) West Coast District

(7) Which title best describes you?
   (a) General Dentist
   (b) Orthodontist
   (c) Endodontist
   (d) Prosthodontist
   (e) Periodontist
   (f) Oral Surgeon
   (g) Other: ______________________________

(8) Have you ever taken continuing education courses on temporomandibular disorders (TMD)?
   (a) Yes
   (b) No
   8.a. If yes, what topic(s) specifically?
   ____
   ____
   ______

Questions related to TMD patients population and referrals

(9) What percentage of your patients would you estimate to suffer from TMD symptoms (temporomandibular joint-TMJ or muscle pain, clicking, popping, headaches, etc.)?
   (a) 0%
   (b) 1–5%
   (c) 5–15%

(d) 15–25%
(e) 25–35%
(f) 35–45%
(g) 45–55%
(h) 55–75%
(i) 75–90%
(j) 90%–100%

(10) What type of TMD you have had evaluated and/or treated? (you may select more than one)

(a) TMJ disc displacement
(b) TMJ degeneration
(c) TMJ hypermobility
(d) TMJ hypomobility/mouth opening limitation
(e) Muscle tightness/tender points
(f) Occlusion alterations
(g) Parafunction habits (i.e., bruxism)
(h) Headaches
(i) Never evaluated or treated a patient with TMJ-related problem (If true, skip to question 15.)
(j) Other: Please add:

(11) From the options below, what do you normally include in the evaluation of these patients? (You may select more than one)

(a) TMJ palpation
(b) Masticatory muscles palpation
(c) Jaw movements during opening/close
(d) TMJ sounds
(e) Signs of parafunction habits
(f) Dental occlusion
(g) None of the above
(h) Other:

(12) What stage of the disorder have most of your patients with TMD presented with during evaluation?

(a) Acute
(b) Subacute
(c) Chronic

(13) Does any of the conditions below were present in your patients with TMD during evaluation?

	Yes	No	Never evaluated
Neck pain			
Poor posture			
Cervicogenic headache			

(14) When treating patients with TMD, what methods do you normally use? (you may select more than one)

(a) Bite splints/occlusal guards
(b) Occlusion correction/braces
(c) Prescription of medication
(d) If other treatment, please specify ___________

(15) Do you refer patients with TMD to other practitioners?

(a) Yes
(b) No (If true, skip to question 19)

(16) What percentage of these patients do you refer?

(a) 0–5%
(b) 5%–25%
(c) 25%–50%
(d) 50%–75%
(e) 75%–100%

(17) Which health care provider/specialty do you refer to specifically? (You may select more than one option).

(a) General Dentist
(b) Orthodontist
(c) Endodontist
(d) Prosthodontist
(e) Periodontist
(f) Oral Surgeon
(g) Physical Therapist
(h) Physician
(i) Psychologist
(j) Speech pathologist
(k) If other, please specify _________________

(18) If you had referred a patient with TMD to a physical therapist, what would be the reason(s) for the referral (patient symptoms/condition)? (You may select more than one option).

(a) Neck pain
(b) Postural alteration (e.g., forward head posture)
(c) Masticatory muscle tenderness
(d) Headaches
(e) Cervicogenic headache
(f) Patient did not get better after your treatment
(g) Other________
Never referred to physical therapy

(19) If you have never referred a patient with TMJ-related problem to a physical therapist, what is/are the reasons?

(a) No need of PT treatment
(b) Did not know about the benefit of physical therapy to the patient
(c) Other:

Questions related to general knowledge

(20) Prior to this survey, were you aware that physical therapist can treat patients with TMD by, for example, reeducating jaw movements and restoring masticatory muscle function?

(a) Yes
(b) No

(21) Prior to this survey, were you aware that cervical spine pain may be involved as a cause of masticatory region pain?

(a) Yes
(b) No

(22) Prior to this survey, were you aware that the evidence suggests that physical therapy can improve TMD symptoms with oral exercises, manual therapy, and postural reeducation?

(a) Yes
(b) No

(23) After participating in this survey, are you more likely to refer a patient with TMD to a physical therapist when needed?

(a) Yes
(b) May be
(c) No

29.a. If no, why?__________

(24) Would you be interested in learning more about the benefits of the collaborations with physical therapists to treat TMD patients?

(a) Yes
(b) No

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

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Clinical Study

The Efficiency of Anterior Repositioning Splints in the Management of Pain Related to Temporomandibular Joint Disc Displacement with Reduction

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Background and Objective. Intra-articular temporomandibular disorders are often related to pain in the area of the temporomandibular joint, ear, and temple. The aim of the study was to investigate the efficiency of anterior repositioning splints in decreasing pain related to temporomandibular joint disc displacement with reduction. *Methods*. The research material consisted of 112 patients, aged 24 to 45 years, of both genders, who reported for treatment at the Consulting Room of Temporomandibular Joint Dysfunctions at the Jagiellonian University in Cracow between 2014 and 2016 due to pain in the area of the temporomandibular joint(s) and noise(s) of temporomandibular joint(s) present during jaw movements with comorbid contracture of masticatory muscles. Subjects were examined according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) protocol and, after diagnosis of painful disc displacement with reduction and masticatory muscle contracture, they were assigned randomly to either the study or control groups (56 patients in each). In the study group, we used an anterior repositioning splint on the full lower arch for about 20 hours usage over a 4-month period. In the control group, a noninvasive therapy was applied using a biostimulation laser over 12 sessions performed every second day on the area of both temporomandibular joints with mouth open and while performing muscle self-exercises with a dominant protrusive position of the mandible. Pain intensity was evaluated using the Verbal Numerical Rating Scale (VNRS) immediately before the treatment and then after 4 and 16 weeks. The obtained data were analyzed using the Mann–Whitney U test ($p \leq 0.005$). *Results*. The VNRS values reported during the final examination for the study group were significantly lower than for the control group ($p = 0.0004$). *Conclusions*. The anterior repositioning splint is an efficient tool in decreasing pain related to disc displacement with reduction. This trial is registered with Clinicaltrials.gov NCT03057262.

1. Introduction

Intra-articular temporomandibular disorders present as various pathological conditions, often concerning derangements of the condyle-disc complex [1, 2]. They occur because the physiological relationship between the articular disc and the condyle head changes. According to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), we can distinguish four basic types of articular disc displacements: disc displacement with reduction, disc displacement with reduction with intermittent locking, disc displacement without reduction with limited opening, and disc displacement without reduction without limited opening [3].

Many studies confirm that disc displacement with reduction (DDwR) is the most prevalent derangement of the condyle-disc complex [4–6]. The DC/TMD defines DDwR as an intracapsular biomechanical disorder when, in closed mouth position, the disc is in an anterior position relative to the condylar head, and the disc reduces upon opening of the mouth (medial and lateral displacement of the disc may also be present; clicking, popping, or snapping noises may occur with disc reduction) [3]. DDwR could be the result of masticatory muscle contracture. Acoustic symptoms such as clicking, popping, and snapping are evidence of disc displacement with reduction. Clicking occurs when the condylar head of the mandible skips the rear edge of the displaced articular disc during mouth opening and/or closing. Afterwards, the disc does not return to the correct position in relation to the condyle when the mandible is again, upon closure, in the central position. Clicking may occur in the initial, middle, and final phase of the mandible opening movement. Different studies have reported that pain is a comorbid symptom of temporomandibular joint (TMJ) disc displacement [7, 8]. When the disc is anteriorly displaced, the ligaments of the rear disc are elongated, stretched, and damaged, and the bilaminar zone is compressed; and thus, pain can be generated. Sometimes acoustic symptoms are accompanied by pain located in the area of the temporomandibular joints and surrounding tissues, intensifying when the patient opens their mouth and chews food. Over the years, many studies have confirmed the efficacy of anterior repositioning splints (ARS) for the management of TMJ discs displacements, but the number of studies simultaneously evaluating the level of pain is limited [9, 10].

Therefore, the aim of the study was to investigate the efficiency of anterior repositioning splints in the alleviation of pain related to temporomandibular joint disc displacement with reduction.

2. Materials and Methods

This is a prospective outcome study which consisted of 112 subjects of both genders with unilateral or bilateral disc displacement(s) with reduction and pain in the area of TMJ. Patients were recruited from the Consulting Room of Temporomandibular Joint Dysfunction at the Jagiellonian University in Cracow during the years 2014–2016 and were included in the study if they met the following criteria: (1) unilateral or bilateral presence of clicking, popping, and/or snapping noise(s) detected with palpation during opening or closing or lateral or protrusive movements in TMJ(s); (2) in the previous 30 days, any TMJ noise(s) present with jaw movement or function; (3) unilateral or bilateral pain in the area of TMJ(s); (4) presence of masticatory muscle contracture during palpation; (5) full dentition or single tooth loss; (6) good general health; (7) positive mandible protrusion test; (8) no contraindications for laser therapy; and (9) patient consent to be involved in the study. Other patients representing TMJ intra-articular disorders who had undergone treatment during the years 2014–2016 were excluded because of partial tooth loss or edentulism, contraindications for laser therapy as well as absence of appropriate symptoms and/or consent to be involved in the study.

Clinical assessment of temporomandibular joints and masticatory muscles was performed by one experienced, self-trained examiner according to DC/TMD recommendations [3]. TMJ noise(s) had persisted for between 3 and 18 months prior to the beginning of the study among included subjects. All patients reported pain in the area of TMJ(s) and positive mandible protrusion test, resulting in the disappearing of the clicking, popping, and/or snapping during mouth opening or closing or lateral movements from protrusive incisal positioning of the mandible. This test was a clue to use the anterior repositioning splint. Patients were randomly assigned to the study group or control group (56 patients in each). Both groups were informed about prevention for disc(s) displacement with reduction. In the study group, we used a typical acrylic anterior repositioning splint fabricated in tete-a-tete (incisal) jaw position, covering the full lower teeth arch to recapture a displaced disc and decrease the level of pain. ARS was recommended for 20-hour use for four months. In the control group, we used a biostimulation laser (Terapus 2, Accuro, Poland), wavelength 808 nm, power 32 J, over 12 sessions (the duration of each session was 3 min 45 s), performed every other day, on the area of both temporomandibular joints (distance to the skin was 1 cm) with opened mouth and systematic performance of TMJ and masticatory muscle self-exercises twice a day for 5 minutes for 16 weeks, according to the TMJ self-mobilization described by Shaffer et al. [11].

Pain level was evaluated using the Verbal Numerical Rating Scale (VNRS). VNRS comprises assessment that is based on an 11-point numerical scale (0–10) in combination with a color-coded scale, in which an increase in the score is accompanied by an increase in color intensity indicated on the scale. Clinical examinations of TMJ noise(s) and pain level evaluations were performed immediately before the treatment (examination I) and then during follow-up visits after 4 weeks (examination II) and 16 weeks (examination III). At the beginning of the treatment, each ARS was adjusted, and upon follow-up visits, occlusion was checked using clinical observations and marking paper to prevent occlusal changes.

The study protocol was conducted in accordance with the Declaration of Helsinki and approved by the Local Bioethical Committee (no. 122.6120.43.2016). All patients provided written informed consent prior to participating in the study.

The obtained data were compared using the Mann–Whitney U test because of noncompliance with the normal distribution in the tested groups ($p \leq 0.005$).

3. Results

A total of 112 subjects were included in the study: 83 women and 29 men, aged 24–45 years (mean age: 31). The study group (SG) included 40 women and 16 men, and the control group (CG) contained 43 women and 13 men. The clinical

Table 1: The results of clinical findings collected during follow-up visits within the study group.

Parameters of pain occurring in the area of TMJ			Women Examination I	Women Examination II	Women Examination III	Men Examination I	Men Examination II	Men Examination III
Pain	Unilateral	Acute	24	6	1	8	4	1
		Mild	6	2	0	5	2	1
	Bilateral	Acute	2	0	2	1	0	0
		Mild	8	5	0	2	1	0
Pain that occurs during food chewing or jaw movements			28	11	1	14	10	1
Pain during palpation			20	16	1	13	16	0
Impaired movement of the mandible			38	3	1	24	11	3
Referral of pain within the head			29	12	0	15	7	2
Clicking in temporomandibular joint		Unilateral	28	24	4	11	5	0
		Bilateral	12	8	2	5	2	1

Table 2: The results of clinical findings collected during follow-up visits within the control group.

Parameters of pain occurring in the area of TMJ			Women Examination I	Women Examination II	Women Examination III	Men Examination I	Men Examination II	Men Examination III
Pain	Unilateral	Acute	12	6	1	7	5	3
		Mild	26	12	6	3	3	2
	Bilateral	Acute	3	1	1	1	0	0
		Mild	2	1	1	2	1	0
Pain that occurs during food chewing or jaw movements			26	19	5	11	10	1
Pain during palpation			22	16	10	12	16	0
Impaired movement of the mandible			21	23	11	10	9	4
Referral of pain within the head			22	12	6	9	6	5
Clicking in temporomandibular joint		Unilateral	32	4	9	10	6	4
		Bilateral	11	8	2	3	2	1

findings collected during follow-up visits in SG and CG and their specification are presented in Tables 1 and 2. SG participants of both genders most often complained of unilateral acute pain in the area of TMJ which corresponded to other clinical findings, for example, pain occurring during chewing or jaw movements, pain during palpation, impaired mandible movement, referral of pain within the head, and unilateral clicking in TMJ. The frequency of the above symptoms in SG decreased with the progress of the applied intervention. CG female participants most often complained of unilateral mild pain in the area of TMJ, and CG male participants most often complained of unilateral acute pain in the area of TMJ, which in both genders corresponded to other clinical findings, for example, pain occurring during chewing or jaw movements, pain during palpation, impaired mandible movement, referral of pain within the head, and unilateral clicking in TMJ. The frequency of the above symptoms in CG decreased with the progress of the applied interventions. There were no occlusal changes among participants during ARS therapy. Pain levels reported by patients during follow-up visits are presented in Figure 1. The mean value of VNRS obtained during examination I in SG was 5,589 points and in CG was 5,436. These results did not differ significantly ($p = 0.5015$), which indicates that groups

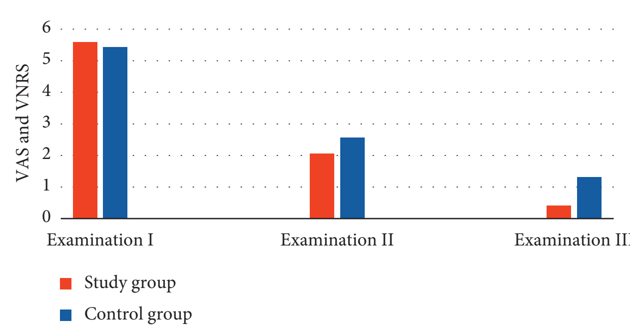

Figure 1: The values of VNRS reported in examinations I, II, and III.

are similar in terms of reported pain levels. The VNRS values collected during examination II are lower across the two groups in comparison to examination I (SG was 2,054, and CG was 2,571), and they differ significantly ($p = 0.00048$). The values collected during examination III are much lower across the two groups in comparison to examination I; namely, the mean value of reported VNRS for SG was 0.411, and for CG was 1.303. These mean values differ significantly ($p = 0.0004$). The statistical analysis is presented in Table 3,

Table 3: The results of statistical analysis concerning reported values of VNRS.

Group	Examination I	Examination II	Examination II
Study group			
$\bar{x} \pm s$	**5.589** ± 1.304	**2.054** ± 1.095	**0.410** ± 0.626
Min-max	3–8	0–4	0–2
Median	5	2	0
Control group			
$\bar{x} \pm s$	**5.436** ± 1.548	**2.571** ± 1.188	**1.303** ± 1.007
Min-max	2–9	0–5	0–4
Median	5	3	1
Mann–Whitney U test, $p \leq \mathbf{0.005}$	$p = \mathbf{0.5015}$	$p = \mathbf{0.00048}$	$p = \mathbf{0.00040}$

and it showed a significant decrease in reported VNRS values during follow-up visits. These analyzes indicate that anterior repositioning splints were an effective tool in pain relief in the group of patients with disc(s) displacement with reduction.

4. Discussion

Disc displacement with reduction is the most common derangements of the condyle-disc complex [12]. There are several forms of these derangements, but anterior and anterior-medial displacements are the most frequent [12–14]. Disc displacements may be partial or complete, depending on their extension. Trauma, anatomy of TMJ, bruxism, stress, masticatory muscle contracture, and abnormal dental occlusion may lead to elongation of the disc ligaments and indirectly to disc displacements and excessive load within temporomandibular joints and retrodiscal tissues [7, 15–19].

A serious limitation of this study was the use of only clinical findings without magnetic resonance imaging (MRI) for ruling in a diagnosis of DDwR, because the sensitivity of this method without imaging is 0.34 [3]. According to DC/TMD, imaging is the reference standard for this diagnosis to increase validity, but in Poland, it is not a standard procedure to refer a patient for MRI without serious medical indications; otherwise, he/she will be forced to cover the fee for any such imaging, because the national healthcare system will not cover these costs (the Polish private health insurance sector is underdeveloped). Therefore, we have to base diagnoses on clinical findings.

The use of ARS in the treatment of disc displacement plays an important role, due to TMJ tissue unloading including retrodiscal tissues and insertions of selected masticatory muscles to articular discs [10, 19, 20]. The occlusal splint therapy which was carried out by the authors with the use of ARS was dependent on the results of a positive mandible protrusion test, resulting in the disappearance of the noise(s) during mouth opening from the protrusive incisal position of the mandible. There is some dispute among researchers and clinicians concerning the efficiency of treatment with the use of repositioning splints, with some researchers reporting that occlusal splints are not useful in the treatment of all derangements of the condyle-disc complex. Badel et al. performed a study concerning the effectiveness of Michigan-type splints in displaced disc recapture [21]. The study showed that this splint is not an efficient tool in disc recapture in cases with disc displacement with or without reduction. Conti et al. proved that a positive result from a clinical procedure using an occlusal splint is related to the splint design [22]. Therefore, the practitioner has to correctly choose the design of the occlusal splint upon clinical manifestation of the temporomandibular disorders.

On the other hand, randomized clinical trials performed by Schiffman et al. and Haketa et al. showed that occlusal splint therapy could be an efficient method in displaced disc recapture and also pain level alleviation [23, 24]. In both clinical trials, the authors compared occlusal splint therapy with other treatment options, including conservative and surgical approaches, and concluded that all of these are efficient in the management of intra-articular TMJ disorders.

The assumption behind the control group design was to use noninvasive intervention with low risk of side effects to reduce TMJ(s) pain. Therefore, laser biostimulation combined with TMJ and masticatory muscle self-exercises was a suitable solution. The setup of 12 laser sessions, performed every other day on the area of both temporomandibular joints, is a standard and valid procedure in the Consulting Room of Temporomandibular Joint Dysfunction at the Jagiellonian University for TMJ(s) pain alleviation. Furthermore, regular performance of exercises by the patient provides long-term biomechanical stability to impaired TMJ(s) and masticatory muscle function. The combination of noninvasive techniques could be a sufficient solution to reduce pain among patients with temporomandibular disorders [20].

Invasive treatment such as arthroscopies, arthrocentesis, and other surgical techniques are still considered after failure of conservative management [20, 25]. Invasive procedures are always associated with risk, such as lesion of the articular structures and facial nerve or perforation of the mandibular fossa. However, a few authors suggest the implementation of arthrocentesis to both joints as a good solution for healing retrodiscal tissues [26, 27]. Pain relief in this group of patients is one of the main goals of treatment and the most common cause of patients reporting to the doctor. Evaluation of the efficacy of ARS for the treatment of DDwR showed a significant reduction of pain in the area of the temporomandibular joints. Mean VNRS values were much lower in SG treated with anterior repositioning splints than in CG. Therefore, we can assume that this treatment option is effective upon painful disc displacement with reduction. Management of pain related to TMJ disc displacement using ARS has been also positively evaluated by other authors [28–30].

5. Conclusion

Considering the limitation of the study, we can state that the anterior repositioning splint is an efficient tool in decreasing pain related to disc displacement with reduction.

Abbreviations

ARS:	Anterior repositioning splint
CG:	Control group
DC/TMD:	Diagnostic Criteria for Temporomandibular Disorders
DDwR:	Disc displacement with reduction
SG:	Study group
TMJ:	Temporomandibular joint
VNRS:	Verbal Numerical Rating Scale.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Malgorzata Pihut created research concept, performed occlusal splint therapy and laser therapy, collected and analyzed the data, and wrote the manuscript. Malgorzata Gorecka selected the references. Piotr Ceranowicz edited the manuscript. Mieszko Wieckiewicz analyzed the data, wrote and edited the manuscript, selected the references, and finally revised it before submission. All authors read and approved the final manuscript.

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Clinical Study

Functional Assessment of the Stomatognathic System, after the Treatment of Edentulous Patients, with Different Methods of Establishing the Centric Relation

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The study compares subjective experiences of patients, wearing complete dentures. Two different methods of determining a centric relation were performed: the traditional method using wax occlusal rims and the Gerber method, based on gothic arch tracings. The success rate of establishing a centric relation in both methods was evaluated (rentgenodiagnostics). The influence of the method used to obtain the centric relation on patients' stomatognathic system (condyle centralization, pain) was also evaluated. Better results were achieved in gothic arch tracing method. Before every prosthetic treatment of edentulous patients, a functional analysis of the TMJ is necessary. The lack of centric relation, in a long term adaptation patients, does not lead to TMD symptoms. This trial is registered with NCT03343015.

1. Introduction

In the field of intensive development of dental techniques, milling of finished blocks of cobalt-chromium or zirconia has almost entirely supplanted the manufacture of cast crowns and bridges. With removable dentures, the progress only applies to the cast metal framework. Methods of manufacturing complete dentures and methods of bite registration have not changed as far. In the case of partial removable dentures, we mostly register the adapted occlusion, while all the components of bite registration are only used in some cases of missing teeth. The determination of occlusion (often with the intention of increasing the vertical dimension) is finding everything from scratch, what in literature is the so-called "experience of the doctor" [1]. The matter is often complicated by the one-sided contraction of the masseter muscle that changes the rest position of the mandible, often making it impossible to determine the central relation [2]. In these cases, a preprosthetic treatment, with the goal of eliminating headaches, restoring balanced muscle tone, and establishing appropriate relations in the temporomandibular joints (TMJ), seems reasonable [3, 4].

In complicated occlusal situation, dentists often rely on the patients' subjective feelings. Occlusal splints are used mostly during night sleep. To properly evaluate the effect of the treatment, RTG images of the temporomandibular joints should be performed. First RTG of the TMD structures should be performed before prosthodontic treatment, with the mandible position, that patient is acustomed to. Second RTG should be performed after splint therapy, to compare condyles position in TMJ [5, 6].

Parafunctional activity with prolonged occlusal contacts increases masseter muscle hypertension. As a result of this hyperactivity a headache or neck pain appears, often misdiagnosed as migraine or tension type headache. Temporomandibular joint pain and muscle myalgia, which are a burden to the patient, are hard to submit to a repeated prosthetic treatment [7–9]. In the process of prosthetic treatment of edentulous patients, the most important task is establishing the proper intraarticular relation in TMJ. The

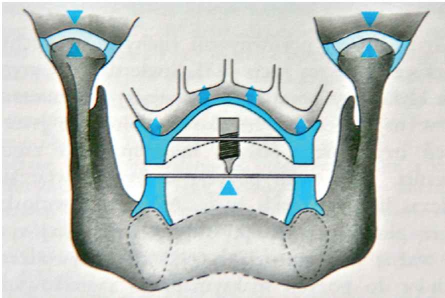

Figure 1: The scheme of gothic arch tracing method.

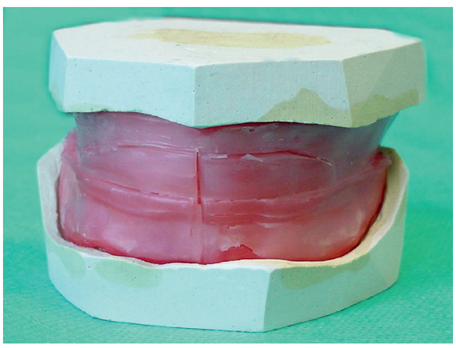

Figure 2: The scheme of wax occlusal rims method.

risk of an undesirable error can occur, even with novel computer-assisted technologies [10]. In addition, bruxism should be confirmed or excluded, because improperly reproduced occlusion in complete dentures may lead to iatrogenic side effects. In patients with a high level of stress, a muscular-related TMD is observed more often, as well as in women [11].

The following are the two basic definitions related to the physiological function of the masticatory system [12]:

(i) *Maxillo-mandibular (cranio-mandibular) relationship*: in this relationship, the condyles articulate with the thinnest avascular portion of their respective discs with the complex in the anteriosuperior position against the slopes of the articular eminences [13]. This position is independent of tooth contact. This position is clinically discernible when the mandible is directed superiorly and posteriorly. It is restricted to a purely rotary movement, about the transverse horizontal axis [14–16].

(ii) *Maximum intercuspidation*: the cusps of the teeth of both arches fully interpose themselves with the cusps of the teeth of the opposing arch, sometimes referred to as the best fit of the teeth in position 0 mm to about 1 mm anterior from the apex of the tracing, the so-called tracing arrow point. To determine the centric relation, you can use the method of gothic arch tracings (Figure 1). Determining the centric relation with wax occlusal rims is very controversial (Figure 2). However, the occlusal vertical dimension is questionable in both methods [17].

1.1. Aim of the Study. The aim of the study was to determine, in retrospective, which of the methods of bite registration gives a better guarantee to guide the mandibular condyle into a centric position, in the mandibular fossa. The study also evaluates the influence of each method on the function of the stomatognathic system.

2. Material and Methods

Edentulous patients were enrolled to the study in The Department of TMD Zabrze, Poland and in The Zahnarztpraxis in Germany, retrospectively, after the prosthodontic therapy. They were treated by two specialists, one in Poland and one in Germany. For the study, 72 patients, who were divided into two groups, were selected. 36 people were treated with the gothic arch tracing method (group I: 23 women with an average age of 58.4) and 36 people were treated with the wax occlusal rims method (group II, 18 women with an average age of 61.7). A precise distribution of age and gender is presented in Figures 1 and 2.

Inclusion criteria were

(1) temporomandibular disorder (TMD) according to RDC/TMD group I and group II,
(2) edentulous patient with complete dentures,
(3) patients agreement for taking part in the study.

Exclusion criteria were

(1) patients addicted to analgesics drug,
(2) neurological diseases with headache (migraine and cluster headache),
(3) trauma in the head and neck region in past 2 years.

During the control visit (1–1.5 years after establishing a centric relation), a detailed functional assessment of stomatognathic system was performed. In anamnesis, a very special attention was given to any symptoms of headaches in the head and neck region in the past. Examination of masticatory muscles was performed: masseter muscles, neck muscle, and muscle of the upper limb. Patients with pain and headaches in the past, before the prosthodontic therapy, were supposed to mark the intensity of this pain on Visual Analogue Scale (VAS: 0–10). Severe pain was marked as 10 points in VAS scale, and no pain was marked as 0 points. Anamnestic index (AI) and Dysfunction Index (DI) were measured, according to special forms. Anamnestic index (AI) according to Helkimo was marked as

(i) A0 (no dysfunctional symptoms),
(ii) A1 (medium dysfunctional symptoms),
(iii) A2 (severe dysfunctional symptoms).

Helkimo index in a modified version was used (Di), and the clinical assessment was performed as follows:

(1) Opening range: the distance between upper and lower central incisors during the opening movement was measured with the ruler:

0 points > 40 mm
1 point 30–39 mm
5 points < 30 mm

Table 1: Values of basal estimated descriptive parameters for both groups.

Group	Average values	SD standard deviation	Min	Quartile1	Median	Quartile3	Max	Test S–W
I	58.4	11.5	31.0	54.8	59.0	64.8	78.0	**<0.05**
II	61.7	11.9	35.0	58.3	64.0	68.5	78.0	>0.05

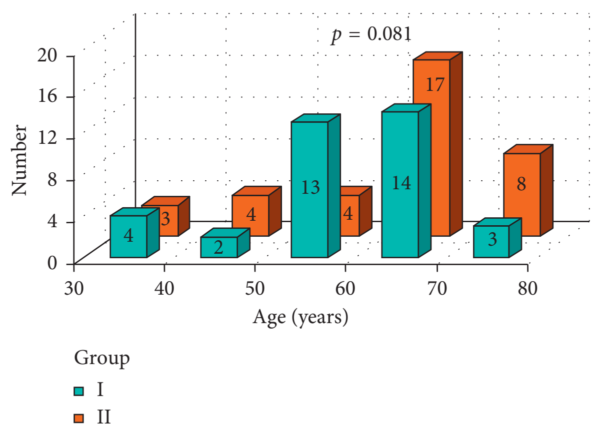

Figure 3: Age and result of Mann-Whitney test: comparison of both groups I and II.

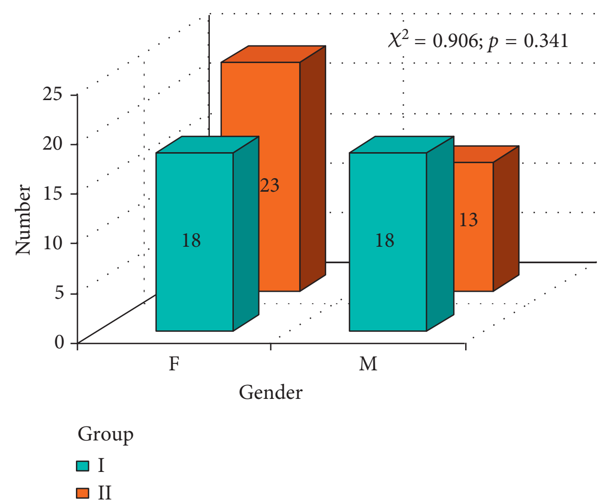

Figure 4: Gender and χ^2 test results, comparison of both groups I and II.

(2) Mandibular deviation during opening: deviation during opening movement was measured between maxillary and mandibular midline:

0 points < 2 mm
1 point 2–5 mm
5 points > 5 mm

(3) TMJ dysfunction observed as clicking, locking, and luxation:

0 points < 2 mm
1 point 2–5 mm
5 points > 5 mm

(4) TMJ pain during palpation:

0—no pain
1—palpable pain
5—palpebral reflex

(5) Muscle pain during bilateral palpation:

0—no pain
1—palpable pain
5—palpebral reflex

The total score of each patient ranged from 0 to 25 points, and patients were classified as follows:

0 points Di 0 = no dysfunction
1–4 points Di I = mild dysfunction
5–9 points Di II = moderate dysfunction
9–25 points Di III = severe dysfunction

Collected data were analyzed with Microsoft Excel. A statistical analysis was performed. Among analyzed data, only age parameter was expressed in quotient scale. Normal distribution was verified with Shapiro-Wilk test. Results were presented in Table 1. The rest of the parameters were expressed in ordinal scale (AI, DI, and VAS) or nominal scale (gender, condyles position in TMJ, and different pain types), and nonparametrical tests such as Mann-Whitney and Chi-squared tests with Yates correction were used.

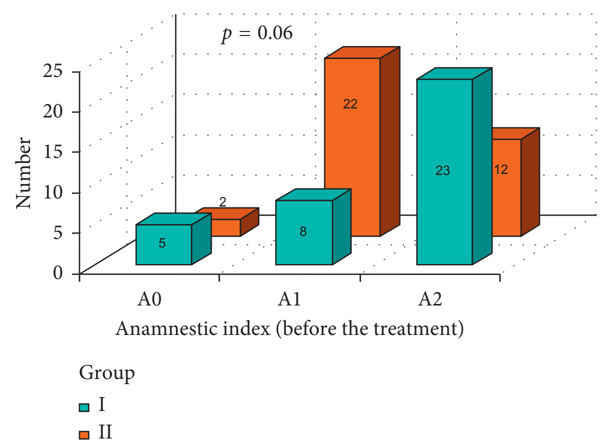

Figure 5: Anamnestic index (AI) in both groups before the prosthodontic treatment.

Designated p values were noted in figures and tables. Calculation was performed in Excel files. Student t-test was used for dependent variables ($p < 0.05$).

3. Results

In Table 1 basic age parameters of subjects in both groups were collected.

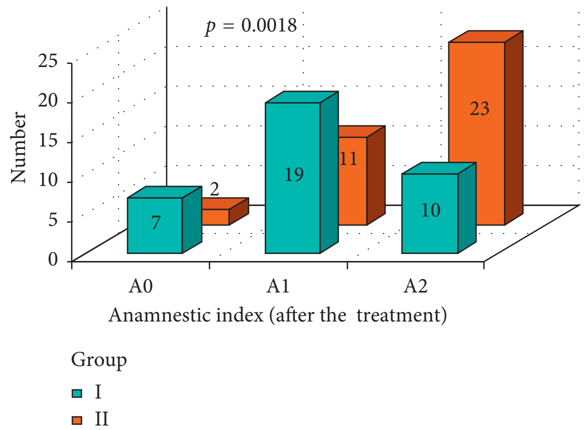

FIGURE 6: Anamnestic index (AI) in both groups I and II after the prosthodontic treatment.

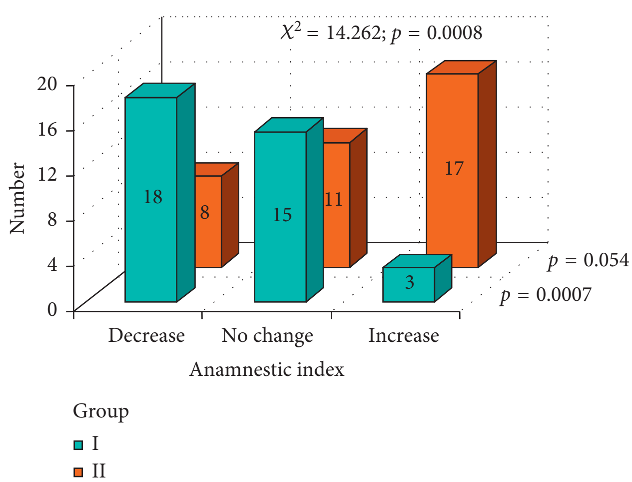

FIGURE 7: Changes in AI index after the prosthodontic therapy in both groups.

In Figure 3, age in both groups was presented and Mann-Whitney test resulted in no statistically important difference between group I and group II. The gender comparison of both groups I and II was tested with χ^2 test. There was no statistically important difference between group I and group II (Figure 4)

In Figures 5 and 6, a subjective patients' assessment of dysfunction symptoms anamnestic index (AI) was presented, in both groups, before and after the prosthodontic treatment. Mann-Whitney test resulted in no statistically significant difference between group I and group II before the treatment Figure 5. After the therapy, a statistically important difference was observed (Figure 6) with $p = 0.0018$. According to Figure 6, better results were achieved in group I.

In Figures 7–9, changes in AI parameter were present in both groups I and II. In group I, favorable changes of AI index were noted, with $p = 0.0007$. In group II, changes in AI index were not statistically significant ($p = 0.054$); however, we can observe an unfavorable tendency. A statistically significant difference between changes in AI values between group I and group II was marked with χ^2 test.

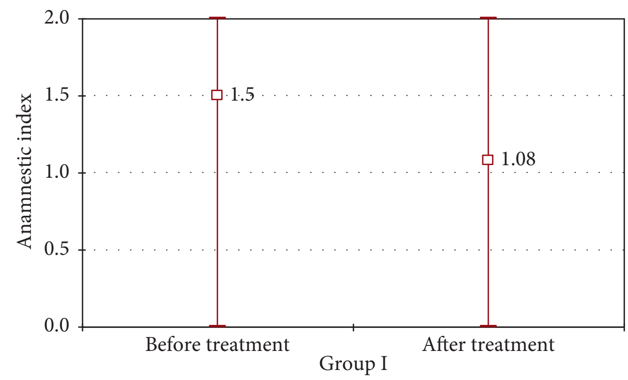

FIGURE 8: Average, minimal, and maximal values of AI index in group I before and after the prosthodontic therapy.

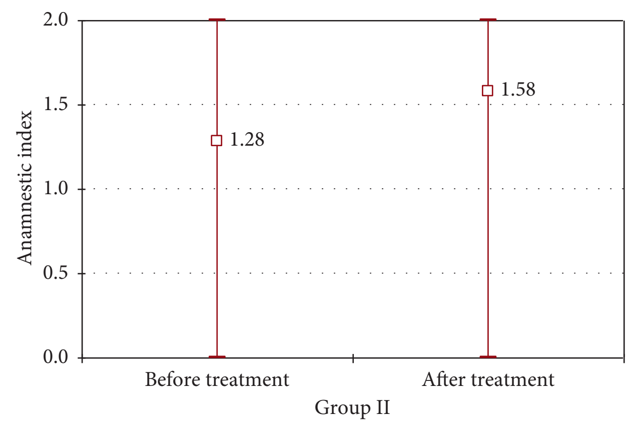

FIGURE 9: Average, minimal, and maximal values of AI index in group II before and after the prosthodontic therapy.

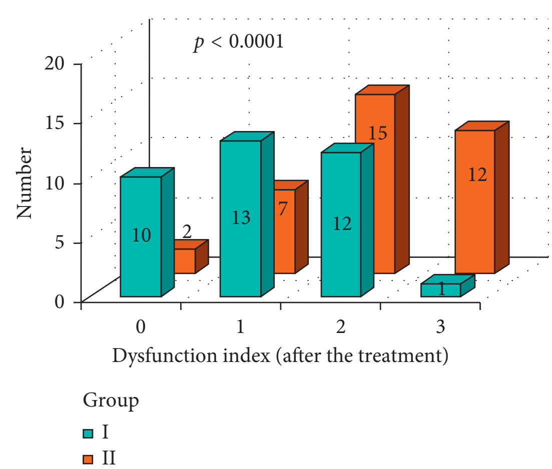

FIGURE 10: DI index values after the prosthetic therapy in group I and group II.

In Figures 10 and 11, dysfunction index (DI), established after the prosthodontic treatment, was presented in both groups I and II. A statistically significant difference between DI values between group I and group II was marked with χ^2 test ($p < 0.0001$). More favorable results were observed in group I.

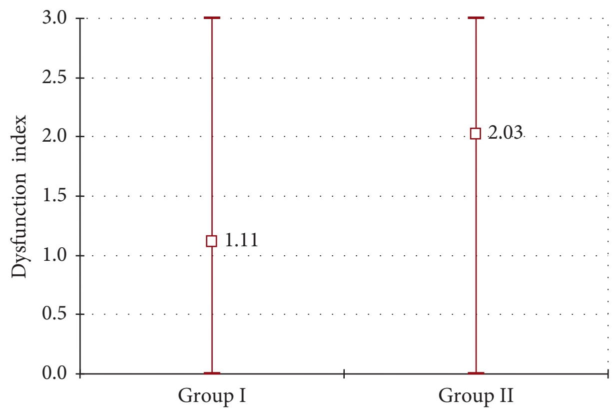

FIGURE 11: DI index average values and minimal and maximal values after the prosthetic therapy in group I and group II.

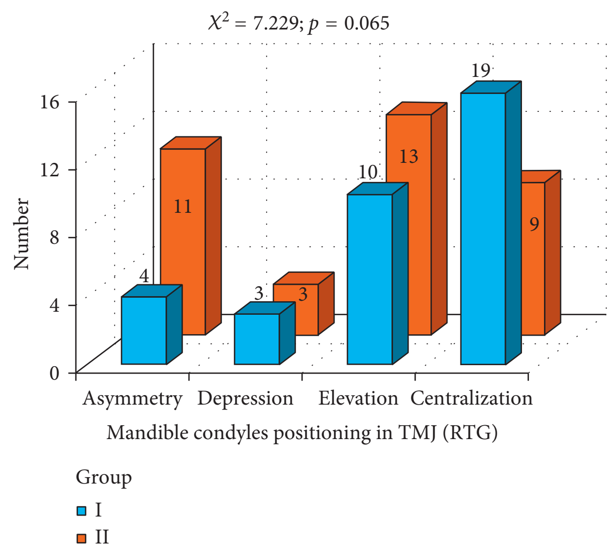

FIGURE 12: Evaluation of condyles centralization in group I and group II.

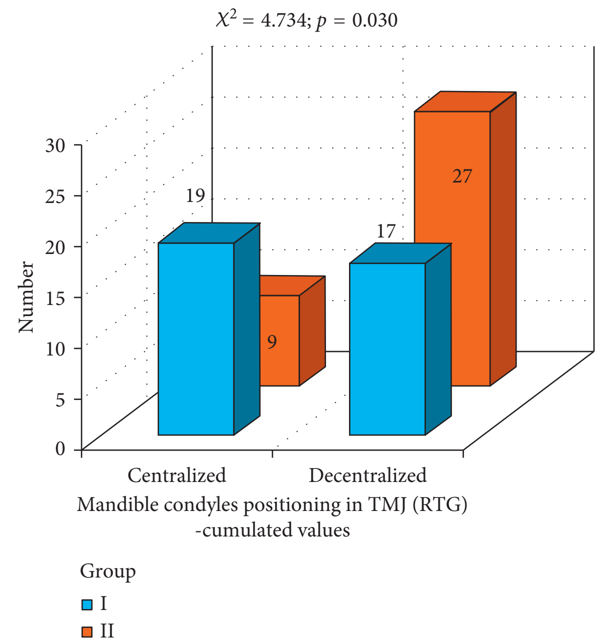

FIGURE 13: Evaluation of condyles centralization in group I and group II: condyles centralization and cumulated values for condyles decentralization.

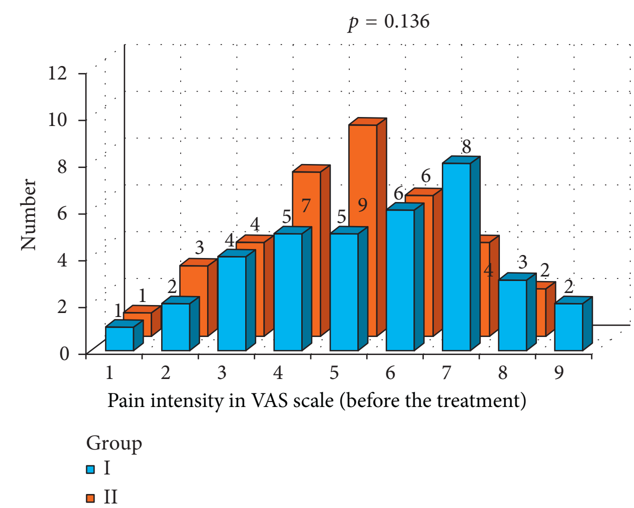

FIGURE 14: Pain intensity schedule in VAS scale before the prosthodontic treatment: group I and group II comparison.

Evaluation of condyle position in temporomandibular joints (RTG) in both groups is presented in Figure 12. Test χ^2 indicated the level of significance almost classical ($p = 0.065$). The amount of centralized condyles in temporomandibular joint suggests favorable situation in group I. Additional parameter was measured: positions of condyles in the temporomandibular joint (TMJ) that were not central were cumulated together in one group (Figure 13). Obtained results suggested statistically significant difference between group I and group II ($p = 0.030$). Better results in condyles centralization were achieved in group I.

Statistical analysis also included evaluation of pain intensity in VAS scale. In Figures 14 and 15, pain intensity schedules (in VAS scale before and after the prosthodontic therapy) for both groups are compared. Results were compared with Mann-Whitney test. Before the prosthodontic treatment, there were no statistically significant differences in pain intensity between group I and group II ($p = 0.136$) (Figure 14). After the prosthodontic treatment, a statistically significant difference in pain intensity was observed between group I and group II ($p = 0.0001$). Favorable analgesic effect was achieved in group I (Figure 15). Subjective pain experiences of patients in group I were recognized as lower VAS values and in group II were recognized as higher VAS values (Figure 15).

In Figure 16 the schedules of changes in pain intensity, as a result of prosthodontic therapy, in both groups are presented. In group I (the gothic arch tracing method), a statistically significant reduction in pain intensity (VAS) was observed ($p = 0.0041$). In group II (the wax rims method), a statistically significant increase in pain intensity (VAS) was marked ($p = 0.0001$). The χ^2 test indicates statistically

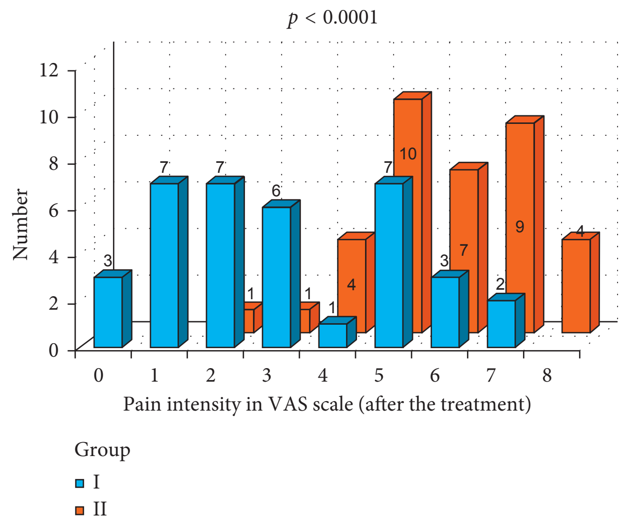

Figure 15: Pain intensity schedule in VAS scale after the prosthodontic treatment: group I and group II comparison.

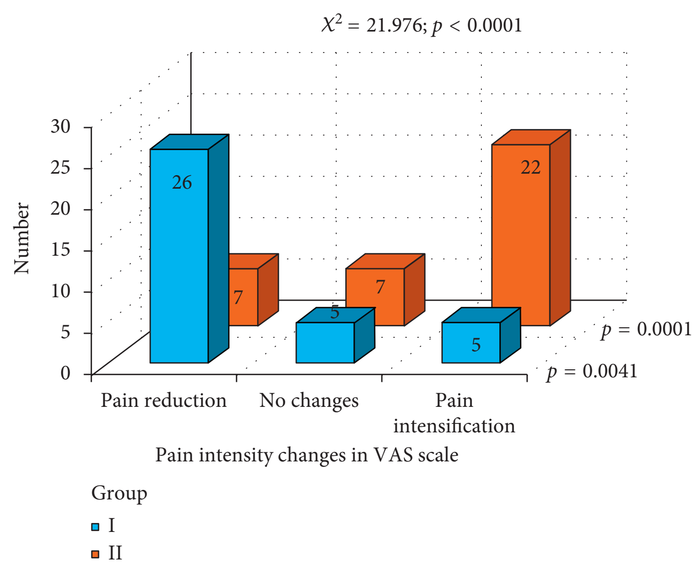

Figure 16: Pain intensity changes in both groups, as a result of the prosthodontic therapy.

significant difference in pain intensity changes between group I and group II, after the treatment ($p < 0.0001$).

On the basis of collected data, we can conclude that changes in pain intensity in VAS scale were observed in both groups: the gothic arch tracing method (group I) and wax occlusal rims method (group II). In most cases, the prosthodontic treatment resulted in reduction of subjective pain intensity experiences (VAS scale) in patients in both the groups. The efficacy of pain reduction was better in group I—the gothic arch tracing method. During the analysis of the condyle position in TMD, the centric position was found more often in group I—the gothic arch tracing method. Establishing the centric relation with the gothic arch tracing method leads to the most posterior position of the condyles. However, it is a very problematic issue to determine the proper occlusal vertical dimension in both groups.

4. Discussion

Several authors have found disturbances in centric relation (CR)-maximum intercuspation (MI)-non centric position of condyles in TMJ and as an important risk factor for TMD [14, 18, 19], and others have opposed this theory [20–22]. From the achieved results, one can conclude that the physiological occlusion should be established in the centric relation because only this approach guarantees a high effectiveness in eliminating factors that disturb the normal function of the stomatognathic system [16, 23]. To establish a proper centric relation, the method of gothic arch tracings should be used routinely because it ensures a better assessment of the centric relation of the condyles in the TMJ, comparing to the method of wax occlusal rims. However, the method of the gothic arch tracings does not guarantee the

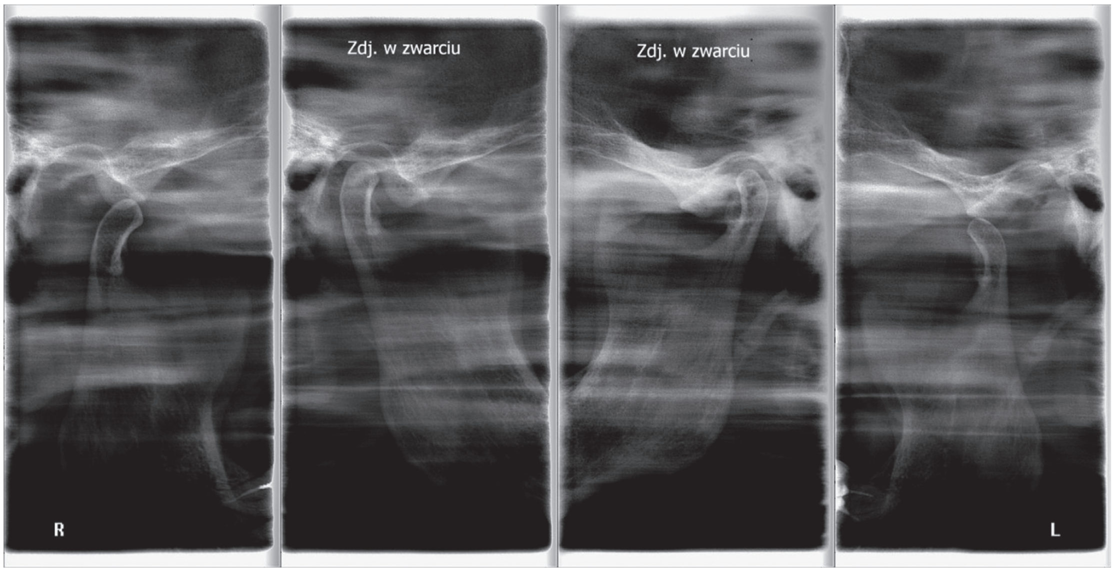

FIGURE 17: The radiographs of a nonconcentric condylar position: deficient vertical dimension (condylar position in occlusion—internal scans) and a muscle contracture in the right TMJ.

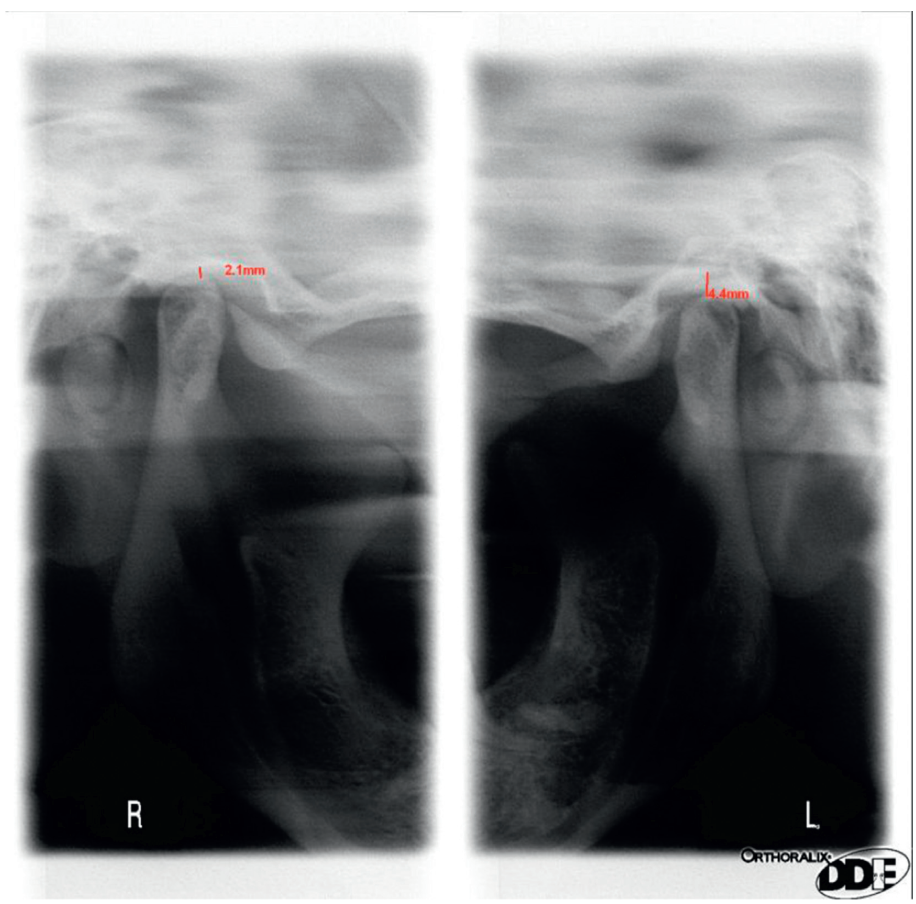

FIGURE 18: The radiographs of the TMJ and nonconcentric condylar position: in occlusion deficient vertical dimension in the right TMJ (no gap between condyle and fossa in the right TMJ, narrowed joint space).

correct occlusal vertical dimension. Radiographic evaluation of the TMJ (in centric relation and in maximal opening) is necessary for determining the proper occlusal vertical dimension in both methods (Figures 17–19). Authors strongly recommend this approach. Before every prosthetic treatment of edentulous patients, a functional evaluation of

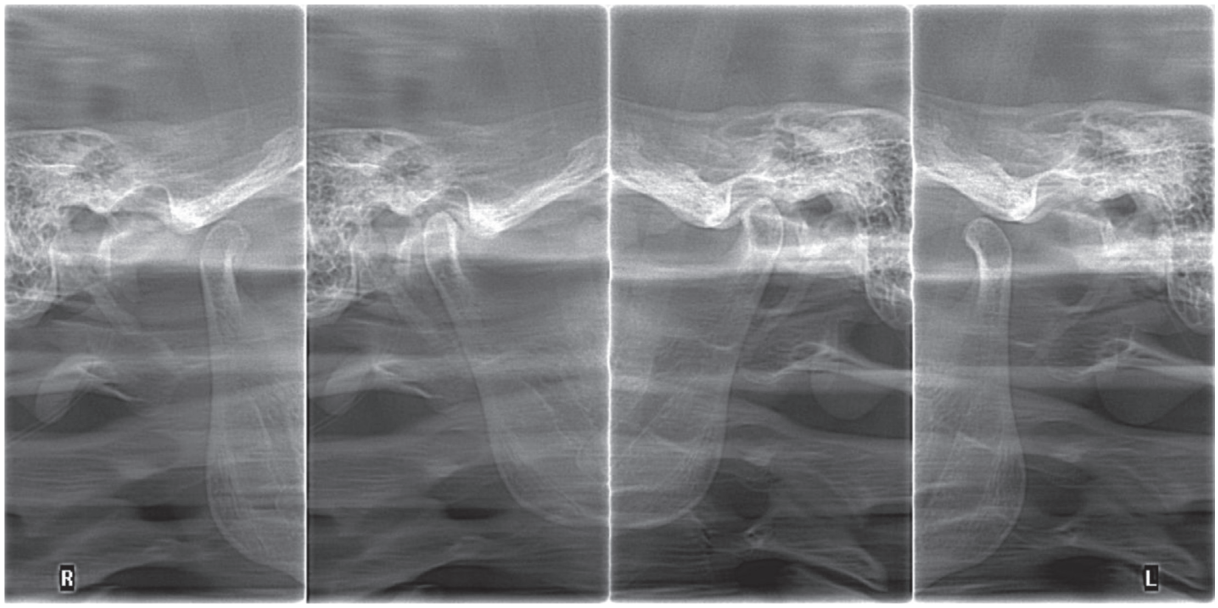

Figure 19: The radiographs of the TMJ with nonconcentric condylar position: an excessive left-sided occlusal vertical dimension (inferior condylar position in occlusion—internal scan, left TMJ).

the TMJ and the whole stomatognathic system is necessary. The lack of these evaluations is often followed by a symptomatic treatment of headaches in patients with TMD. The method of wax occlusal rims can even worsen the condition of the edentulous patients, with an undetected, disharmonic tension of the masseter muscles (Figures 17 and 18).

5. Conclusion

(1) The gothic arch tracing method guarantees a better assessment of the centric relation of the condyles in the temporomandibular joints, comparing with wax occlusal rims method.

(2) The wax occlusal rims method can worsen the condition of the edentulous patient with an under diagnosed, disharmonic tension of the masseter muscles.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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