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The interconnection between orthodontic treatment and Temporomandibular Disorder, in particular to orthopedic instability

PhD thesis

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List of Abbreviations

TMJ - Temporomandibular Joint

TMD - Temporomandibular Disorder

TM - Temporomandibular

DC/TMDs - Diagnostic Criteria for Temporomandibular Disorders

DDwR - Disc Dislocation with Reduction

DDwoR – Disc Dislocation without Reduction

CBCT - Cone Beam Computed Tomography

IL-1 - Interleukin-1

TNF-α - Tumor Necrosis Factor-alpha

MMP - Matrix Metalloproteinase

MRI – Magnetic Resonance Imaging

CR - Centric Relation

MI - Maximal Intercuspation

OB - Overbite

OJ – Overjet

SNB angle - Sella –Nasion-B point angle

ADA - American Dental Association

CPI - Condylar Position Indicator

SIP - sphingosine-1-phosphate

AOB – Anterior Open Bite

TAD – Temporary Anchorage Device

ARR - Apical Root Resorption

S1P - sphingosine-1-phosphate

MP – Muscle Pain

ANB angle – A point –Nasion point – B point angle

bMS - buccal Miniscrew

pMS - palatal Miniscrew

bMP - buccal Miniplate

TPA - Transpalatal Arch

DI - Dental Implant

ANOVA – Analysis Of Variance

CIl – Confidence Interval lower

CIu – Confidence Interval upper

1 Introduction

1.1 The interconnections between temporomandibular joint (TMJ) health and orthodontics

In Temporomandibular Disorder (TMD), however, has multifactorial origin (1), malocclusional aspects and the role of orthodontics became particularly in focus and a very popular field of study at the end of the eighties. The reason for that was, that more and more patients who had previously undergone some type of orthodontic procedure started to sue their doctors, claiming that they had developed Temporomandibular symptoms as a result of the orthodontic treatments (2). As a consequence, numerous organizations of the field urged the scientific study of the topic, especially in the form of offering great amounts of funds for studies and research. As a result, multiple prevalence studies were published at the beginning of the '90s, abridged in a comprehensive study by McNamara, Seligman, and Okeson in 1995 (3). The conclusions of this article were the following:

- TMD can be developed by healthy individuals,
- The number of these symptoms grows with age (especially in adolescence, and they are not necessarily caused by orthodontics),
- Orthodontic procedures in adolescence neither increases, nor decreases the likelihood of TMD,
- Extraction orthodontics does not go together with the occurrence of TMD, there is no specific method of orthodontics that carries a higher risk than others concerning TMD development,
- Although a reasonable goal of orthodontics is orthopedic stability, not reaching it does not necessarily lead to TMD,
- Therefore, there is no scientifically verified preventive therapy for TMD and in case of more serious symptoms they can be proven by simpler forms of treatment.

Despite the fact that these results were published a long time ago, some scientifically unverified correlations between TMD and orthodontics are still persisting (4, 5). It is interesting that the hypothesis of upper premolar extraction and anterior teeth retraction leading to TMD has greatly contributed to orthodontic trends shifting to the direction of avoiding extraction in the USA from the beginning of the nineties (6).

To our present knowledge, orthodontics causing TMD is not scientifically verified (2, 6-8). McNamara's conclusions published in 1995 still apply (3), moreover, they gained affirmation by a 20-year cohort study published in 2009 (9), according to which orthodontics is neither a causative nor a preventive factor in the development of TMD, moreover, patients with orthodontic anamnesis do not have a higher risk at developing or aggravating TMD.

Looking at the literature, it might seem controversial that if no scientific studies have been able to verify interrelations between orthodontics and the health or its deterioration of TMJ, then why would the theory of the two being strongly interrelated still stand? The answer is complex, among other things leading back to the multifactorial nature of TMD. One of the most commonly cited etiological factors of TMD is occlusion (2), whereas orthodontics can be defined as the controlled alteration of occlusion.

Above all this, we know from epidemiological data that TMJ-related symptoms and sound effects can be represented in childhood, typically more often occurring in adolescence and young adulthood, which - supposing the patient is being under orthodontic treatment - might give the impression that their development had been treatment-related.

With the development of orthodontic techniques, the circle of potential patients is growing, the more esthetical applications, longer kept teeth, and the improvement of the quality of prosthetic rehabilitation has increased the ratio of adult treatment. With the extension of the age group of patients, the number of clients with TMJ problems has been increasing, too.

Since orthodontic treatment can be a long procedure for many years when the attention of patients turns to their teeth, their chewing, and feelings of discomfort in the head-neck area, there is a higher probability of their growing awareness of TMJ symptoms, and connecting these to orthodontics.

The factors previously mentioned can all be possible reasons for seeing interrelations where there are parallel phenomena, but they carry an inverse risk too, so it is vital to keep in mind that literature does not exclude interrelations between orthodontics and TMD. The nature of these interrelations has not been detected by literature, further big-scale, and well-planned studies would be necessary to decide on the matter.

Orthodontists are obliged to take into consideration gnathological aspects, especially since they provide treatment of the formal and functional specialties of the younger generations, and with proper prudence, they can achieve greater stability and can potentially decrease the likelihood of developing problems in the temporomandibular (TM) region (2, 10, 11).

1.2 Characteristics of Temporomandibular Disorder

To understand pathological situations and progression we briefly describe the anatomy of the TMJ: The anatomical structures forming the temporomandibular joint include the bony surface of the glenoid fossa, anterior to this the articular eminence, the condylar head and the articular disc. Lateral to the condyle is the bilaminar zone, known as the retro-discal tissue, and the joint capsule strengthened with ligaments. The articular disc is biconcave shaped. The articular disc is connected to the condylar head by the discal collateral ligaments, lateral and medial. While opening the mouth, the condyle moves forward to the top of the articular eminence. In healthy joints, the position of the articular disc is easily moved with opening and closing movements, not only the ligaments, but due to the biconcave morphology of the disc and the force of the elevator muscles.

The elasticity of the ligaments is limited, once elongated, they do not return to their original length. As a result of ligament elongation superior lateral pterygoid muscle hypertonicity may induce alteration of the articular disc position. As the disc is pulled anteriorly, the posterior band of the disk may become thinner, and the articular disc loses the self-positioning ability and becomes displaced (12-14).

The term TMD refers to a group of pathologic conditions that affect the TMJ, masticatory muscles, and all the associated tissues.

TMD is characterized by several signs and symptoms:

1. Spastic headache, 2. Facial muscle pain, 3. Muscle tiredness, 4. Limited mandibular movement, 5. TMJ pain, 6. TM sound effect (clicking, popping, crepitus), 7. Lockjaw, 8. Pain synchronized with movement, 9. Parafunction (clenching, bruxism), 10. Occlusal

wear medium-expressed, localized or generalized. TMD is the most common reason for non-dental pain in the orofacial region, which can be accompanied by otalgia, headache, neuralgia, toothache and tinnitus.

Anatomy of the dysfunctional TMJ: Internal Derangement is the anatomical definition of phases describing the TM disc displacement. Diagnostic criteria were precisely described by Schiffmann et al. in 2014. in The Diagnostic Criteria for TMDs (DC/TMDs) which is widely accepted among the clinicians.(15)

There are four clinical stages of disc displacement:

I – Disc Displacement with Reduction (DDwR)

II - Disc Displacement with Reduction with intermittent locking

III- Disc Displacement without Reduction (DDwoR) with limited opening

IV - Disc Displacement without Reduction without limited opening

I. DDwR is the most common type of internal derangements. The articular disc is positioned anteriorly to the condyle. and while opening, the condyle moves across the posterior part of the disk. While closing, the disk slips back (reduces) anteriorly due to hyperactivity of superior lateral pterygoid muscle, altered disc morphology and ligaments elongation. This type is characterized by reciprocal clicking. Despite the displacement, the jaw retains a full range of motion, the mandible shows deviation to the affected side and at the end of opening it centers again. If pain is present, it is usually the muscles. If this condition is left untreated, it can progress to more severe stages.

II. DDwR with intermittent locking. In this stage, disc displacement with reduction is accompanied by intermittent locking episodes. It is a transitional phase between stage I. and stage III. Patients experience occasional instances where the disc does not return to its normal position during jaw movement, leading to temporary locking of the jaw (lockjaw). These locking episodes are usually brief, and the patient can eventually reopen the mouth after some effort. During these episodes, there may be an increase in discomfort, pain, and anxiety, as the jaw's mobility becomes temporarily restricted. The intermittent nature of the locking differentiates this stage from the earlier DDwR, where locking is absent.

III. DDwoR with limited opening represents a more severe stage. The articular disc is positioned anteriorly to the condyle constantly, without returning by opening. Opening is limited, because the destructed disc acts as a mechanical blockage which inhibits the condyle to move on the articular eminence, when opening the mouth. The mandible deflects to the affected side and does not center at the end of opening. This persistent displacement leads to significant limitations in mouth opening, often restricting it to 20-30 millimeters or less. Patients in this stage typically have pain and difficulty in eating. Clinically, this condition is often referred to as "closed lock".

IV. DDwoR without limited opening, occurs when the disc remains displaced and does not return, but the jaw has adapted to this condition. There is no significant limitation in mouth opening. Over time, the structures within the TMJ may undergo adaptive changes that make possible a near-normal range of motion. Although the range of motion is improved, patients may still feel discomfort or pain, and other signs of TMJ dysfunction may persist. This stage suggests a chronic condition where the condyle has adapted to the displaced disc, but the disorder remains (12, 16, 17).

1.3 Radiological signs of TMD

Condylar Morphological Characteristics in TMD Patients Based on CBCT Images

Variations in condylar morphology, often observed in TMD patients, can be effectively analyzed using CBCT. CBCT provides high-resolution imaging, allowing detailed visualization of the condylar structure and even assessment of therapeutic interventions such as occlusal stabilization splint therapy. Patients with TMD frequently exhibit alterations in condylar position, condylar morphology, including flattening, erosion, and osteophyte formation. These changes indicate degenerative joint disease. The molecular background of inflammation within the TMJ plays a crucial role in condylar deformations. Chronic inflammation within the TMJ leads to the release of pro-inflammatory cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α). These cytokines stimulate the production of enzymes like matrix metalloproteinases (MMPs) that degrade the extracellular matrix, including the cartilage and subchondral bone. This degradation results in the erosion of subchondral bone as the protective cartilage layer is worn away. This inflammatory milieu not only contributes to pain and dysfunction but also accelerates the degenerative changes, including condylar flattening as well (18, 19).

Hu et al. used CBCT to perform a morphometric assessment of TMJs in symptomatic subjects compared to controls, revealing significant degenerative changes in the TMD group, including reduced condylar height and increased prevalence of osteophytes (20).

Li and Zhang in their study involving 714 symptomatic and asymptomatic TMJs identified more pronounced degenerative changes, such as subchondral sclerosis and joint space narrowing, in symptomatic joints (21).

Shokri et al. conducted a comparative assessment of condylar position in TMD patients and asymptomatic patients using CBCT, finding significant positional differences that further underline the utility of CBCT in TMD evaluation (22).

In conclusion, CBCT is a valuable tool for assessing condylar morphological characteristics in TMD patients, providing detailed insights into degenerative changes and the impact of therapeutic interventions such as occlusal stabilization splint therapy.

Comparative Analysis with Other Imaging Modalities

While CBCT provides detailed imaging of the bony structures of the TMJ, it is often complemented by other modalities such as magnetic resonance imaging (MRI) for comprehensive evaluation. Fan et al. examined 353 patients with disc displacement and stated, that combined use of CBCT and MRI in assessing condylar erosion and TMJ disc displacements, providing a holistic view of joint pathology (23).

Chen and Li found after the examination of 744 condyles with both CBCT and MRI, that disc displacement did not necessarily lead to condylar bone changes, but 92.7% TMJs with condylar bone abnormalities had disc displacement (24).

Innovations in imaging techniques, such as dynamic 3D CBCT-MRI image fusion combined with an optical positioning tracking system, recording mandibular movements of the TMJs, have provided novel insights into the complex movements and interactions within the joint. This approach has enhanced the understanding of how morphological changes correlate with functional impairments in TMD patients (25).

Condylar Flattening

Condylar flattening is a frequent morphological change observed in patients with TMD. Several studies have elucidated the mechanisms contributing to this phenomenon (26). The mechanism resulting in osteoarthritic changes is the abnormal loading and mechanical stress distribution within the TMJ. In TMD patients, Centric Relation – Maximal intercuspation (CR-MI) discrepancy, parafunctional habits such as bruxism lead to uneven stress distribution. This altered mechanical environment promotes osteoarthritic changes in the TMJ like bone resorption in areas of high stress and compensatory bone formation in other areas, resulting in a flattened condylar surface (26, 27). Osteoarthritis is also characterized by the progressive degradation of the articular cartilage, subchondral bone changes, and synovial inflammation (18, 28).

Subchondral erosion

Subchondral erosion is a significant pathological feature observed in patients with TMD. This condition is characterized by the breakdown and loss of subchondral bone, which can lead to pain, dysfunction.

Mechanical stress and abnormal loading of the TMJ is playing a crucial role in subchondral erosion. In TMD patients, occlusal imbalances, CR-MI discrepancy, bruxism, and other parafunctional habits can cause uneven distribution of forces across the joint. This uneven stress accelerates bone remodeling processes, leading to bone resorption in areas subjected to excessive pressure. Over time, this can result in the erosion of the subchondral bone, weakening the structural integrity of the joint (29).

Condylar position

Condylar position in the fossa is a crucial aspect in the diagnosis and understanding of TMD. The condyle's position within the glenoid fossa can significantly influence the biomechanics and functionality of the TMJ, and deviations from the norm can be indicative of TMD as precisely described in the chapter about orthopedic instability.

In patients with TMD, condylar displacement or misalignment within the fossa is frequently observed. Several studies utilizing CBCT detect positional abnormalities.

Shokri et al. conducted a comparative assessment of condylar position in TMD patients and asymptomatic individuals using CBCT. Their study found that TMD patients often exhibited a more posterior condylar position in the fossa compared to asymptomatic controls, suggesting that posterior displacement may be associated with TMD symptoms. (22) Derwich et al. also highlighted the morphological and positional changes of the condyle in TMD patients using CBCT imaging. Their findings indicated that TMD patients showed significant variations in condylar position, with many presenting with a posterior and inferior displacement. These positional changes can lead to altered joint mechanics, contributing to the pain and dysfunction characteristic of TMD (28).

The relationship between condylar position and disc displacement is also significant. Fan et al. investigated the correlation between different types of disc displacements and condylar positioning in TMD patients. They found that posterior condylar positioning was often associated with anterior disc displacement, a common feature in TMD (27).

In summary, the position of the condyle in the fossa is a critical factor in the pathology of TMD. Deviations from the normal position, particularly posterior displacement, are commonly observed in TMD patients and are associated with disc displacement and joint dysfunction.

1.4 Interrelations between occlusion and TMD, functionally stable and unstable occlusion

Occlusion can influence the dynamic functional relationship between the mandible and the glenoid fossa in two ways. On the first hand, the chewing proportion affects the orthodontic stability, and on the second hand, the acute changes due to occlusion affect the joint function.

Orthopedic stability refers to a condition where the stable MI position of the teeth aligns with a musculoskeletally stable condyle position in the fossa. In this scenario, functional forces do not damage the joints. Conversely, orthopedic instability occurs when MI cannot be achieved in the CR defined as the most anterior superior position of the condyle. Often due to early contact of even a single tooth—resulting in a condyle position paired with unstable occlusion. In this case, the two jaws only make contact at certain points and therefore, MI can be achieved by moving/shifting the mandible. However, this adjustment can compromise the optimal CR of the condyle, potentially leading to further detrimental effects. The stability of the occlusion is the foundation of functional movements (chewing, swallowing, speaking), therefore achieving it is priority (30).

Knowledge of the ideal functional occlusion for orthodontics is indispensable because by moving teeth, we have an opportunity to create correct incisor and canine guidance. This way, orthodontic treatment can be regarded as a kind of occlusion therapy, which is all the therapies that aim at changing the occlusion. Apropos of this we are able to improve the function of the chewing apparatus and the functional position of the TMJ. There are two forms of occlusal therapy: it can be reversible if the occlusal surface and with that the condyle position are temporarily altered; or it can be irreversible, when occlusal conditions are permanently altered, and the original condition cannot be reconstructed. Irreversible therapy includes occlusal surface grinding, fixed prosthetic procedures, and orthodontic therapy. This type of therapy is only valid when TMD is certainly caused by malocclusion.(11) The following gnathological viewpoints need to be taken into consideration during the course of therapy:

1. Incisor guidance: Incisor periodontium has more sensitive tactile innervation than the latral zone. Incisors are to disocclude the denture in case of mandible protrusion, protecting the joint; this is called incisor guidance. This function is missing in the case of decreased overbite (OB) or increased overjet (OJ) (31-35).

Reaching adequate OB with intermaxillary mechanics can be achieved by front teeth extrusion, or molar intrusion, and the consequent autorotation of the mandible. A large OJ can be corrected by sagittal positioning of incisors. Excessive palatal tipping of the incisors can also be problematic since it limits the free sagittal protrusion of the mandible. This can be seen in the case of Angle II/2 patients and in other cases, where after the orthodontically indicated premolar extraction, the incisors were only tipped towards the palatal, and root torque was either missing or insufficient. The steep palatal surface of the proclined upper incisors limits the physiological movement of the mandible. The mandibular retroposition resulting from this is a quite common phenomenon (36, 37).

2. Canine guidance helps disocclude the mandible during lateral movements. This function may be compromised if the canine is ectopically positioned due to crowding or

improper sagittal alignment. Canine guidance can be restored through alignment methods such as premolar extraction or distalisation, but sometimes effective bracket positioning or corrective bending can achieve the proper canine position (34).

3. Hyperbalance contacts are often seen in the presence of lateral crossbite or due to the infraocclusal position of palatal cusps of the molar teeth (also called hanging molar cusps). Crossbite can be addressed by the various treatment methods, such as dental or skeletal expansion. Hanging molar cusps can be corrected by restoring proper molar inclination, which can be achieved by orthodontic intrusion to any orthodontic anchorage.

In order to realize these, it is essential to evaluate occlusion not only in the static conditions but during different dynamic protrusion and laterotrusion movement (36, 38, 39).

1.5 Importance of condyle position in orthodontic diagnosis

Many clinicians advocate that the ideal occlusion should be related to an ideal condyle-disk-fossa relationship, what they refer to as centric relation (CR) (40). TMD patients often show shift between maximal intercuspation (MI) and CR (40, 41). Moreover the degree of CR-MI discrepancy has been shown to strongly correlate with the severity of the symptoms and signs of TMD and therefore, it was proposed to be a contributory factor to the development of TMD (42). Dawson Crawford and Roth precisely explain how CR-MI discrepancy may lead to the development of TMD (43-45). They declared that if CR interference exists during jaw closure, the inferior lateral pterygoid muscle is non-physiologically contracted in order to achieve MI. The contraction of the muscle distracts the condyle out of CR position resulting in hyperactivation of the elevator muscles. Imbalance between the elevator and depressor muscles can lead to consequent masticatory muscle spasm and pain (43, 44). As stated by Okeson; positional stability of the joint is determined by the muscles that pull across the joint and prevent separation of the articular surfaces. The muscles' directional forces determine the optimum, orthopedically stable joint position (46). The continuous existence of occlusal interferences can contribute to chronic muscle hyperactivity, articular disc derangement and disc displacement which causes TMJ clicking and further progression will result in intracapsular disorders (43-45).

Apart from the fact, that one of the bases of orthodontic correction is the harmonization of teeth position and TMJ function, the viewpoint, that stable CR position should be used as a starting point of treatment instead of habitual MI has not spread in the general orthodontic practice (30, 44, 47-63).

Dental malocclusion represents a specific contact position that does not always lead to joint problems. However, malocclusion can be a potential etiological factor when combined with orthopedic instability (as previously discussed). The presence and measurement of orthopedic instability can only be realized after defining the stable condyle position. The concept of orthopedically stable malocclusion can only be introduced proceeding from the stable condyle position. This covers all the non-ideal bite positions, which are realized in the presence of the central stable position of the condyle (30). Contrary to this, we can talk about orthopedically unstable malocclusion if the bite position forces the mandible joint condyles to move out of their central stable position. This excursion is called the CR-MI shift. Numerous studies argue that the central relational position of the condyle does not range with the MI position determined by the occlusion (40, 47-50, 53-55, 58, 60-62, 64-75).

In practice, if the orthopedic discrepancy, or the CR-MI shift at the condyle level, is small (1-3 mm), it is less likely to lead to TMD. The likelihood of TMD largely depends on the individual's ability to adapt to such discrepancies. If condylar discrepancy reaches the 3-4 mm threshold, the likelihood of TMD occurrence increases (30). The situation gets more complicated when based only on clinical examination and anamnesis (age, Angle classification, direction of growth, etc.), therefore the measurement and direction of CR-MI discrepancy needs to be defined with the help of different examinations (47, 48).

Intraoral diagnosis is not reliable because of the defensive mechanisms (44, 55, 70-74, 76, 77) and at an intraoral level, the shift does not represent the shift on the condyle level. (40, 44, 47, 48, 53-55, 62, 65-69). Regarding radiological imaging techniques, the American Dental Association (ADA) found that making conventional two-dimensional X-ray is contraindicated in the definition of the condyle position (47, 78) (79-89).

Given the above, it is essential to rely on instrumental methods for accurately defining the CR (as detailed later).

The CR-MI difference and its significance in orthodontic-orthognathic planning can be represented with the Cordray study (90, 91). Cordray analyzed the CR-MI differences on the level of occlusion and condyle position in 596 deprogrammed (short deprogramming 5-10 minutes), asymptomatic patients and 596 deprogrammed (short deprogramming 5-10 minutes), patients with symptoms, and made comparisons about them.

During the model analysis the following parameters were examined:

Early occlusal contacts

Horizontal differences: OJ, Angle classification

Vertical differences: OB

Transversal differences: Dental midline

The three-dimensional position of the condyle was defined with a CPI (Condylar Position Indicator) (55), and these were correlated with the sex and the age of the subjects. The following were considered symptoms: 1. Spastic headache, 2. Facial muscle pain, 3. Muscle tiredness, 4. Limited mandibular movement, 5. TMJ pain, 6. TM sound effect (clicking, popping, crepitus), 7. Lockjaw, 8. Pain synchronized with movement, 9. Parafunction (clenching, bruxism), 10. Occlusal wear medium-expressed, localized or generalized.

The key to CR definition was the deprogrammed muscle, and the hardened front wax bite, with the help of which the condyle is navigated into the anterosuperior position of the fossa. The last phase of the rotation movement was carried out in the articulator, this way the occlusion next to the CR joint position becomes visible.

There are several consequences to be drawn from the Cordray study. The CR definition and sample articulation after deprogrammed muscles did not only show a 57.5% difference in the symptom-free group and 96.9% difference in the group with symptoms compared to the condyle position defined in the MI, but significant changes were seen on the occlusal level, according to early occlusal contact, increased OJ, decreased OB, Angle classification, and midline differences. What has clearly been confirmed is that a 1 mm condyle dislocation significantly changes occlusal relations and therefore the treatment plan, too (40, 44, 47, 48, 50, 53-55, 57, 58, 60-62, 65-69, 92).

The differences between CR and MI position greatly influence the treatment plan. An Angle class I occlusion in MI might become Angle class II in a CR position. OB can demonstrate significant differences, so a normal rate in MI position can show a weak or explicit open bite in the CR position. This will necessarily alter our treatment plan concerning the design of the anchorage, considering extraction or orthognathic surgery. For these reasons we need to reconsider if the lateral cephalograms images are suitable for forming accurate diagnoses. If we look at the occurrence of the 2 mm CR-MI condylar differences in the Cordray study, it is 52% in symptom-free patients and 96% in the case of patients with symptoms. When we look at the occurrence of a bigger, 3 mm CR-MI condylar difference, it affects 22.9% of symptom-free patients and 39.7% of patients with symptoms (90, 91).

Williamson, Shildkraut and Wood also found significant differences in 21 cases of the 24 measured cephalometric data. Obviously, this is due to the altered mandible position (57, 58, 92). Since we talk about major differences between CR and MI, the question emerges whether it would be worth making the lateral cephalogram in a CR position. If we follow this path, we will see that there are definite differences between the CR and MI lateral ceph's concerning the following parameters:

Increasing ANB angle in CR. Class I in MI changes into Class II in CR.

Decreasing Sella –Nasion-B point angle (SNB angle) and chin prominence in CR.

Increasing divergence of the maxillary plane-mandibular plane angle and decrease of facial axis in CR.

Increased OJ and decreased OB in CR.

In accordance with numerous other studies (40, 44, 47, 48, 53-55, 57, 58, 61, 65-68, 93, 94). Cordrays study has also shown that the frequency, the measure, and the direction of CR-MI difference do not correlate with sex, age, Angle classification, ANB angle, vertical growth form, and it has very weak correlations with occlusal characteristics. Other studies, however, show positive correlation between occlusal factors and TMJ dysfunctions (64, 95-109). It is unfortunate, that the mechanism of the development is not known, a number of studies have shown that the nature of malocclusion does not provide information about the direction and measurement of condylar dislocation (40, 44, 47, 48, 53-55, 57, 58, 60, 61, 65-68, 93, 94).

Transversal, intraorally noticeable shifts are described by many authors as possible etiological factors (30, 101, 105, 109), which shows that it goes together with asymmetric CR-MI dislocation on the condylar level. This explains the observation that the lateral crossbite is considered a possible etiological factor of TMD. We can conclude that the asymmetric component of the condylar dislocation is a more important factor than the measurement of the CR-MI dislocation (107). As far as TMD is concerned, the most critical transversal condylar dislocation is 0.5 mm or more, which is most often represented in muscle hyperactivity incoordination (30, 47, 94, 107, 108, 110).

It is important to emphasize that especially in the case of patients with symptoms a short (5-10 minutes before CR detection) deprogramming is not reliable regarding the condyle's central relation. In such cases adequate deprogramming can be achieved by occlusal splint therapy, usually a 6-12 months process (111), but treatment time can be reduced and efficiency improved by 24/7 full time splint wear (112).

Once we have reached a stable CR condyle position and the patient is symptom-free, or symptoms are acceptable by the patient and do not show improvement (112), orthodontic treatment can start. It is very important to maintain the CR position during the orthodontic treatment, to prevent return of the symptoms. Since the teeth are being moved, this maintenance cannot be implemented simply by splint usage, but bonded bite blocks are usually used on the most posterior teeth.

1.6 Age and gender distribution of TMD

Several studies have examined the age and gender distribution in TMD. Women tend to be more frequently affected than men, particularly in the 20-40 age group. Studies show that women experience TMD symptoms more intensely, especially during reproductive years, suggesting a possible relationship with hormonal factors. A large-scale study involving 3362 TMD patients found that women are 1.5 to 2 times more likely to develop TMD compared to men, with a peak prevalence in the 16-35 age range (113). A meta-analysis of Zieliński et al. showed that the worldwide incidence of TMDs was 34%. The age group 18-60 years was the most exposed to TMDs. They observed that for each continent, the female group was 9% to 56% larger than the male group (114). This gender disparity in TMD prevalence may be influenced by biological, hormonal, and psychosocial factors, but further research is required to understand details.

1.7 Occlusal stabilization splints as treatment of TMD

Over the years, the most preferably and commonly used therapy for treating patients with TMD with orthopedic instability has been the occlusal stabilization splint (115). Occlusal stabilization splint therapy is a non-invasive treatment for TMD. Due to its design, it can reposition the condyle to CR and switch off the neuromuscular adaptation to MI by relaxing the muscles and achieve orthopedic stability. The splint redistributes occlusal forces, reducing abnormal loading on the TMJ, muscle tension, and alleviating pain (19).

Therefore, in orthodontic patients reporting TMD due to orthopedic instability these stabilization splints are recommended prior to orthodontic therapy. Williamson reported 89,4% success of 160 randomly sampled TMD patients treated by full time occlusal stabilization splint (112).

During the splint wear, condyle is passively seated in the fossa, resulting in altered dental occlusion; usually first contact on the most posterior teeth and Anterior Open Bite (AOB) will develop (116, 117). Its effectiveness has been evaluated through changes in condylar morphology observed via CBCT. As mentioned before 2D tomograms are not recommended by the ADA for the diagnosis of TMJ dysfunctions (47, 78-89).

Retrospective CBCT analysis' evaluating the outcome of occlusal splint therapy in patients with TMD found significant improvements in post-treatment condylar morphology with reduced joint effusion and improved joint space symmetry (118, 119).

1.8 Orthodontic molar intrusion as a treatment method after splint therapy

As mentioned, condyle is passively seated in the fossa, occlusion alters resulting in first contact on the most posterior teeth and AOB (116, 117).

Before the era of temporary anchorage devices (TADs), possible therapeutic solutions for AOB were camouflage treatment by extruding the anterior teeth (120, 121), extraction, surgical maxillary impaction (122) and intrusion of posterior teeth by either intermaxillary or extraoral appliances. Although conservative noninvasive molar intrusion might be an appealing solution for AOB treatment, its predictability is still poor, due to different tissue reactions and bite force. High quality comparative studies between conventional and TAD-based treatments are still missing (123). Each molar intrusion technique had specific biomechanical considerations and potential side effects, but skeletal anchors definitely changed the thinking about this treatment method. Shellhart was the first who used dental implants for intruding molars (124). In 1996, Melsen and Fiorelli demonstrated that a significant amount of true orthodontic molar intrusion can be achieved which can largely facilitate the prosthetic reconstruction of partially edentulous patients (125). To achieve bite closure with skeletally anchored molar intrusion in AOB patients, the intrusion of upper molars is preferred.

The effect of molar intrusion, however a dental movement, has a skeletal effect on the craniofacial system, through the autorotation of the mandible (126). The amount of the autorotation based on the systematic review of Alsafadi et al., may have also clinically significant impact on the facial appearance. Of the 42, 12 studies were selected. Low level of scientific evidence was identified after risk of bias assessment. None of them were relevant randomized controlled trials. Out of the 12 selected studies, five studies used miniplates and seven studies used miniscrews. Mandibular counterclockwise rotation was found to be between 2.3° and 3.9° in six studies, while it was less than 2° in the remaining studies (127).

Interestingly molar intrusion acts not only through autorotation of the mandible, but as some kind of compensational tendency through front tooth extrusion as well, even without touching the incisors (128).

Many techniques have been introduced for skeletally anchored posterior teeth intrusion. In the following chapter we give a short overview about the conventional and advanced techniques which have introduced over the last decades, about side effects, and about the literature overviewing long term stability of molar intrusion.

1.8.1 Overview of molar intrusion techniques

Molar intrusion using intermaxillary appliances

Intermaxillary appliances using bite force and some kind of elastic appliance for molar intrusion might be theoretically effective for intruding posterior teeth.

Gurton et al. (129) used an intermaxillary appliance without skeletal anchorage in young growing 10y+- 7 months patients and achieved The mean intrusion of maxillary and mandibular molars was1.04 to 1.86 mm of intrusion. They detected incisors extrusion of 0.54 mm, and OB increased by 4.00 mm. The mandibular plane angle was decreased by 1.57 degrees.

Cinsar et al. used “rapid molar intruder” in their controlled trial in growing individuals, detected significant changes in ANB angle and lower facial height, and concluded that this type of treatment can be a safe and noncompliant alternative for early intervention of skeletal open bite correction (130).

Molar intrusion with bite blocks

Bite blocks may also be an effective way for molar intrusion. These appliances may alter occlusal forces and load on the selected teeth promoting molar intrusion while allowing anterior teeth to erupt. Withayanukonkij et al. reported successful outcomes using clear aligners with integrated bite blocks and squeezing exercise. Consistent occlusal force application through bite blocks effectively managed the vertical dimension without severe side effects like root resorption or periodontal damage, however the amount of molar intrusion was significantly less than the skeletal anchorage group (131).

Sankey et al. in their controlled trial examined hyperdivergent patients. The bonded palatal expander functioned as a posterior bite-block and was fixed in place throughout treatment. 79% of the patients presented poor masticatory muscle force received high-pull chincup 12 to 14 hours per day. Treatment significantly improved condylar growth and resulted in true mandibular autorotation 2.7 times greater than control values. Treatment also led to increased OB and decreased OJ (132).

Molar intrusion with interradicular and palatal miniscrews

The biomechanical advantage of miniscrews is their stable anchorage point, allowing precise force application directly to molars. Interradicular and palatal miniscrews offer precise molar intrusion, and because of the easy chairside insertion, still a popular technique. In a recent study of Liu et al. compared various techniques, finding miniscrews provided effective, stable molar intrusion with minimal relapse (133).

Foot et al. provided full distal segment intrusion in AOB cases with help of 2 interradicular miniscrews with an intrusive force of 500g. They found a mean molar intrusion of 2.9±0.8 mm with an OB increase of 3.0±1.5 mm. The intrusion resulted in 2.6°±1.3° ($P<.001$) clockwise occlusal plane rotation and a 1.2°±1.3° autorotation of the mandible. Incisors uprighted and elongated significantly (134).

Buschang et al. presented that palatally placed miniscrews can be used in adolescent high angle patients for molar intrusion, and their appliance design pointed out, that transversal control of the lateral teeth is a crucial factor to avoid side effects of palatal or buccal tip of the teeth (135).

To avoid transversal side effects like buccal or palatal tipping of the lateral teeth Paccini et al. used both palatal and buccal interradicular miniscrews for intruding supererupted molars. He found that molar intrusion is manageable with two interradicular screws per side (136).

Molar intrusion with zygomatic plates

Zygomatic plates provide stable anchorage for molar intrusion. It's extraalveolar insertion allows freer tooth movement due to the decreased risk of touching roots related to interradicular anchorage. This technique uses mostly modified surgical plates fixed by two or three screws in the zygomatic buttress. Disadvantage of this technique is the need for surgical exposure by inserting and removing the plate even though the failure rate is much lower than the transmucosally insertable orthodontic miniscrews (137, 138).

Erverdi et al. were the first who studied miniplate assisted molar intrusion. Force was applied bilaterally with Ni-Ti coil springs between the miniplate and the first molar. Their results showed that, with the help of miniplate anchorage, maxillary posterior teeth intruded effectively. As compared with an osteotomy, this surgical procedure eased treatment and reduced treatment time (139).

Tuncer et al. combined zygomatic plate anchored molar intrusion with corticotomy. This technique is supposed to reduce treatment time (140).

Although many techniques have been introduced for skeletally anchored posterior teeth intrusion (135, 141-146), in most of these articles, intrusion mechanics, force magnitudes and treatment details are precisely described, but only few articles, mostly case reports are dealing with the real condyle position (147-151).

1.8.2 Side effects of molar intrusion

It can be stated that apart from general failures like inaccurate planning of the biomechanical system or failure of the skeletal anchorage, Apical Root Resorption (ARR) is the only not easily predictable side effect of molar intrusion.

A number of variations of techniques and their impacts on ARR have been explored in recent research. Since advanced imaging techniques have appeared in daily routine, AAR and its characteristics can be easily detected by CBCT imaging compared to conventional panoramic x-ray (152).

The study by Liu et al. quantified molar intrusion associated ARR in miniscrew-assisted molar intrusion versus traditional segmental archwire intrusion techniques. Their findings indicated that miniscrew assisted molar intrusion was more effective 3.67 ± 1.13 mm versus 2.38 ± 0.74 mm in the segmental archwire group, and miniscrew group showed more AAR in the palatal root related to the segmental archwire approach (133).

Withayanukonkij et al. in their randomized controlled trial concluded similar results. After 6 months of treatment, significant root resorption of 0.21-0.24 mm appeared in the clear aligner group without skeletal anchorage and 0.38-0.47 mm in the skeletal anchored group. Maxillary molars were intruded 0.68 and 1.49 mm respectively (131).

In the development of a model to predict root resorption during intrusive orthodontic treatments, Zhou et al. provided insights into the mechanical and biological factors influencing ARR. Their model emphasized the role of force magnitude and direction in the resorptive process, suggesting that optimized force application could reduce the risk of ARR (153).

The molecular mechanisms underlying ARR were explored by Wang et al., who investigated the role of sphingosine-1-phosphate (S1P) signaling in stress-induced root resorption during molar intrusion. Their research identified that excessive orthodontic force could upregulate S1P signaling pathways, leading to enhanced osteoclastic activity and subsequent root resorption (154).

Also, variable force magnitudes can enhance side effect and ARR during maxillary buccal segment intrusion according to Akl et al. Their clinical trial demonstrated that higher force magnitudes were associated with greater ARR, reinforcing the importance of force calibration in minimizing resorptive outcomes (155).

Bellini-Pereira et al. conducted a systematic review and meta-analysis to evaluate root resorption following orthodontic intrusion. Their comprehensive review underscored the prevalence of ARR across various techniques and highlighted the need for careful planning to reduce resorptive incidents (156).

Overall, the literature suggests that while molar intrusion is effective for correcting AOB and overeruption of molars, it carries a risk of ARR that varies with individual genetic predisposition, with the method and magnitude of force applied, and with the amount of intrusion performed. Understanding these dynamics is crucial for optimizing treatment protocols to minimize adverse outcomes.

1.8.3 Stability of molar intrusion

Stability of molar intrusion is a highly critical factor in orthodontic treatment success. Regarding the stability of this type of tooth movement many studies and reviews had been performed. Gonzáles Espinosa et al. found that the stability of skeletally anchored molar intrusion is similar to that reported to surgical approaches, since 10 to 30% of relapse appears in both treatment methods. Evidence level however was found between very low and low (157). Chang et al. reported about similar results according to AOB (158). Contrarily Malara et al. concluded in their systematic review that due to the diversity of techniques used by different authors, it is not possible to state conclusively whether the skeletal anchored molar intrusion treatment of AOB provides long-term results that are comparable to orthognathic surgery procedures (159).

Beak et al. in their 5 years follow up study found that on average by 2.39 mm intruded maxillary first molars reerupted by 0.45 mm at the 3-year follow-up, for a relapse rate of 22.88%. 80% of the total relapse of the intruded maxillary first molars occurred during the first year of retention. Incisal OB significantly relapsed during the first year of retention as well, but did not exhibit significant recurrence between the 1-year and 3-year follow-ups (160).

Marzouk and Kassem examined the soft tissue changes and relapse 4 years post-treatment of 26 patient undergoing molar intrusion with zygomatic miniplates, and they found that total relapse rate ranged from 20.2% to 31.1% and that the changes in the first year post-treatment accounted for approximately 70% of the total relapse (126, 161). Deng et al. found long term stability of full upper arch intrusion in hyperdivergent patients AOB regarding the maxillary-mandibular plane angle (162).

In conclusion, we can state that long term follow-up studies show acceptable relapse rate after skeletally anchored molar intrusion, however high quality prospective randomized trials are still missing.

2 Objectives

The conservative treatment of TMD can be unstable, as prolonged use of occlusal splints might lead to occlusal changes, primarily AOB can develop.

Our hypothesis were the followings:

1. On the mounted models MI position of the lower arch differs from Centric „de jour" position and the difference increases with full time occlusal splint wear.

2. There is a difference between MI and post-splint CR mandibular position measured on the lateral cephalograms.

3. 24/7 wear of hard acrylic occlusal stabilization splint effectively manages TMD signs and symptoms.

4. Occlusal changes due to stabilization splint wear can be effectively treated by skeletally anchored molar intrusion.

5. The improvement of TMD can be detected as bone morphological changes on pre-treatment – post-treatment CBCT images.

Therefore, we evaluated the diagnostic records of orthodontic patients reporting previous TMD and had undergone splint therapy and a subsequent orthodontic treatment. Occlusal characteristics, cephalometric analysis and condylar morphology were assessed at different time points: pre-treatment, post-splint - in progress, and post-treatment.

3 Methods

In our retrospective study 47 orthodontic patient's diagnostic records were collected (18 males, 29 females, mean age: 35.3 years). They had TMD, treated at a private praxis of Martin-Goenaga, San Sebastián, Spain; between 2008–2018. *(Table 1.)*

Table 1. Age and gender distribution of the 47 patients

	Gender	
	Male	**Female**
Number of subjects	18	29
Mean age (years)	35.42	35.27
Age range (years)		
10–20	0	2
21–30	8	8
31–40	6	12
41–50	2	3
51–60	0	3
61–70	2	1

<u>Initial findings</u>

All the patients were diagnosed with orthopedic instability (CR-MI discrepancy) and had complaint of Muscle Pain (MP) (masseter, temporal, medial pterygoid and/or suboccipital), 31 subjects had DDwR (13 unilateral, 18 bilateral) and 16 patients had DDwoR. 9 of 16 subjects with DDwoR had DDwR in the other joint and therefore, were treated with full-coverage hard acrylic occlusal splints.

<u>Inclusion and exclusion criteria of patients</u>

29 patients were excluded due to one of the following reasons: missing diagnostic records (n=6), no use of skeletal anchors (n=6), lack of proper compliance in full-time splint wear (n=14) and because of moving to another location (n=3).

Therefore, from the original 47 patients, only 18 patients were included in the study.

Of the 18 patient's records were made in 3 time points:

T0: Initial records

T1: In CR after 3-12 months of full-time splint wear with a stable joint position

T2: In CR after molar intrusion

Type of records were:

1. Model analysis in MI and on CR registered models

2. Cephalometric measurements
3. TMJ position and morphology on CBCT images

Method of CR registrations

All CR registrations were performed with the dual wax bite method described by Cordray (10). The registrations were taken in two steps using a special, hard, blue bite registration wax sheet (Almore Bite Registration Sheet Wax-Almore Mfg. Company, USA). The anterior section consisted of a 4-layer softened wax and covered the front area (canine-canine) both on the lower and the upper arch. The posterior segment has two layers and it is extended to the first molar and the second premolar. It is important to ensure that the two waxes do not touch, and do not extend buccally beyond the dental arch to prevent the deformation from the buccal muscles.

The procedure is as follows:

1. The patient is seated in a dental chair tilted at a 45° angle.
2. a. Short deprogramming of the muscles before bite registrations: The patient was instructed to bite on a wooden spatula with pulsating forces, 5-second clench is followed by 5-second relaxation. This deprogramming lasted 5-10 minutes, and the wax bite was obtained immediately afterwards *(Figure 1.)*.

b. Long deprogramming of the patient musculature by 24/7 occlusal splint wear

3. The first four layers of the wax were softened and placed on the front teeth. The patient was asked to slowly close on the arc of mandibular closure without protrusion. The closing was manipulated so that the chin was gently guided by the thumb, placing the index finger onto the angulus. The closing was stopped when there was only a 2-3 mm gap between the posterior-most teeth. To remove the wax without distortion, patients were instructed to hold this position until the wax is cooled with air and hardened. Following the removal of the wax, it was placed in ice water. The patient had not closed his/her mouth until the full completion of the registration, for this time some cotton pad was placed between the jaws *(Figure 2.)*.
4. Next, for the posterior segment, the two wax layers were softened and placed in the mouth along with the previously cooled hard anterior wax block. The patient was then asked to gently bite onto the front block. This hard front block helped guide the mandible into CR, allowing the condyle to seat into the optimal anterior position. After removing

the posterior wax from the mouth, it was cooled and hardened the same manner as previously described for the anterior wax *(Figure 3.).*

5. Based on the wax bite and facebow registration, the models were mounted, and a clear autorotational movement with the thickness of the posterior wax (1-2 mm) was performed in the articulator. At the end of this movement, the two dental arches contacted, creating an occlusion near the stable condyle positions referred to as "centric de jour" (daily centric, followed by short deprogramming only). This indicated that the condyle had not yet reached the perfect CR. Every time this occlusion differs from the habitual occlusion, it suggests the presence of orthopedic instability. *(Figure 4.)*

Figure 1. Short deprograming with wooden spatule

Figure 2. Anterior wax bite leaving 1-2 mm space in the molar region

Figure 3. Front hardened and distal soft wax in the mouth

Figure 4. MI position and Centric „de jour” position of the lower jaw

Model Analysis

Panadent articulators (IML GmbH, Germany) were used for all mounting processes. OJ and OB were evaluated on the pre-and post-treatment articulator mounted models in four positions by using a Pittsburgh digital caliper (Harbor Freight Tools, Calabasas, CA, USA):

T0MI: Initially in MI and T0CR: in centric „de jour”

T1: In CR after 3-12 months of full-time splint wear with a stable joint position

T2: In CR after molar intrusion

Changes in OJ and OB were then calculated between the mounted positions (T0MI vs. T0CR, T0MI vs. T1, T1 vs. T2). The criteria of stable CR position were the following: no signs and symptoms of TMD (muscle tenderness, pain, locked joint), no change regarding the contact points on the splint for at least 3 appointments (12 weeks) and easy manipulation of the mandible by the clinician.

Cephalometric Measurements

Initial pre-splint (T0), post-splint (T1) and final post-treatment (T2) lateral cephalograms of the subjects were evaluated. T0 cephs were taken in MI position. For T1 cephs, wax bites were prepared (Beauty Pink Wax X, Miltex, York, PA, USA) based on the stable CR position achieved via splint wear. Wax bites were constructed in the CR mounted articulator with first contact on the most posterior teeth. Post-intrusion T2 cephs were captured in MI position which was equivalent (CR-MI discrepancy less than 0.5 mm) with CR as checked on the mounted casts. As described in *Table 2.*, A-point – Nasion – B-point (ANB) angle, vertical jaw relationship (Mandibular plane–Palatal plane angle) and Facial axis angle by Ricketts were evaluated on the lateral cephalograms.

Table 2 . Definitions of cephalometric measurements used in this study

Measurement	Definition
ANB angle	A point–Nasion–B point angle
Palatal plane–Mandibular plane angle	Angle between Posterior nasal spine–Anterior nasal spine and Gonion-Menton
Facial Axis angle by Ricketts	Angle between Nasion-Basion and the facial axis (Pterygomaxillare-Gnathion)

All tracings and superimpositions were performed digitally. Lateral cephs were superimposed by using cranial base and skull contours. Landmarks necessary for above mentioned measurements were marked and differences between T0 vs. T1 and T1 vs. T2 were evaluated.

<u>Condylar morphological and positional evaluation using bilateral CBCT scans of TMJ</u>

Pre-and post-treatment full face CBCT (NewTom 5G XL, Verona, Italy) was performed to examine several factors and to assess condylar position, detect any existing signs of internal derangement and monitor condylar morphological changes following the orthodontic treatment. Exposure settings for full face CBCT were: Kilovoltage Peak: between 90-110 with automatic adjustment, milliamperage varied in the range of 1-5 milliamper, exposure time ranged from 3.6 to 5.4 seconds and voxel side was set for 0.2 mm. CBCT data of all patients were evaluated in sagittal and coronal sections by two examiners blinded for the clinical diagnosis (neither knowing if the CBCTs were taken pre-or post-treatment). In case of disagreement a third examiner was asked in order to reach a final agreement. The most frequent osseous changes were examined in the CBCT images of the right and left TMJ areas.

1. Flattening of the articular surface- loss of an even convexity of the joint (*Figure 5. a*)

2. Surface erosion (decreased density of the cortical and adjacent bone) and/or condylar surface irregularity (loss of continuity of condylar cortex) (*Figure 5. b*)

3. Absence of condylar anterosuperior position and/or apparent irregular TMJ joint space (*Figure 5. c)*

4. Sclerosis (increased density of cortical bone extending into the bone marrow) *(Figure 5. d)*

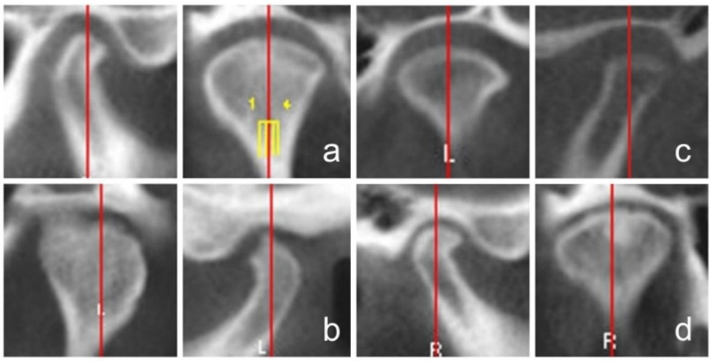


Figure 5. Representative CBCT images of the most frequent osseous changes of TMJ; flattening (a), surface erosion associated with surface irregularity (b), irregular TMJ joint space (c), sclerosis (d).

Mechanics used for molar intrusion

After achieving orthopedic stability and the elimination of TMD symptoms, post-splint AOB was treated by a non-surgical orthodontic approach. Molars were intruded by skeletal anchorage using three different techniques:

1. Buccal miniscrews combined with palatal miniscrews (n=8) *(Figure 6. a)*

2. Buccal miniplates combined with palatal miniscrews *(Figure 6. b)* or transpalatal arch (TPA) (n=8) *(Figure 6. c-d)*

3. Bilateral dental implants in the molar region (n=2) *(Figure 6. e-h)*

To avoid incisor extrusion, intrusion was started sectional in the distal segment using 0.022 bracket slot systems with 0.017x0.025 NiTi wires during intrusion. Since premolars and 2nd molars are intruding indirectly by the buccal wire, prevention of buccal tipping of these teeth is mandatory. In all patients, tip and torque of every intruded and neighboring teeth were controlled by palatal mechanics, torque bendings and bracket placements. The premolar brackets were flipped and bonded more occlusally, 2nd molar hanging cusps were intruded and controlled to a hook welded additionally to the omega loop of the TPA. On the palatal side either TPA or palatal miniscrews were used to prevent further tipping. Occlusal bite blocks were placed on lower molars to enhance intrusion. To maintain CR position of the condyle continuous adaptation or build up and control of bite blocks were necessary.

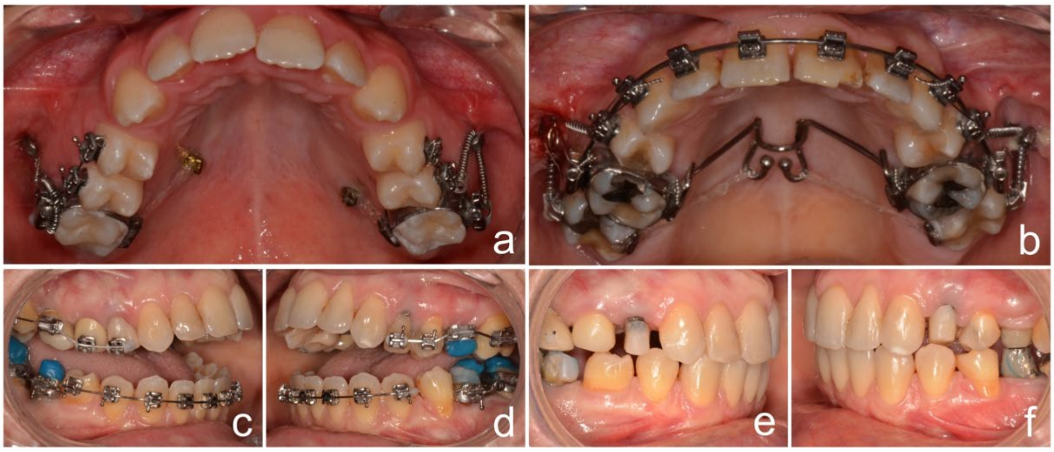


Figure 6. Skeletally anchored molar intrusion. Buccal miniplates combined palatal miniscrews (**a**) or with transpalatal bar (**b**) or bilateral molar dental implants (**c**–**f**) were used for orthodontic molar intrusion following occlusal splint therapy.

To prevent reeruption of the intruded teeth, following intrusion the molars were ligature tied to the TADs for at least additional 3 months. The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices and was approved by the Clinical Research Ethics Committee of the University Hospital Sta. Universitario Mª del Rosel, Areas II and VIII of Health of the Murcian Health Service (El ID: EO 19/52. Intrusion molar ortodoncia).

Statistical Analysis

All statistical analyses were performed using R Core Team (2018), R: A Language and Environment for Statistical Computing statistical software. Tracings of all lateral cephalograms were done by one examiner. To measure intraexaminer reliability, repeated tracings of all cephalograms and model measurements were done after 2 weeks. To determine the repeatability of measurements, mixed-effects model was used. In every examined variable, repetition had no significant effects on measure outcomes, supporting good intraexaminer reliability. To evaluate changes in OJ, OB and cephalometric parameters during the treatment multiple comparison correction was performed by repeated measures ANOVA followed by Tukey post hoc test. To verify differences in frequencies of pre-and post-treatment joint derangements McNemar's chi-square test was used with continuity correlation. Namely after the blinded examination, the pre- and post-treatment samples were re-paired again and as far as, there was no retrogression among the subjects, only those samples were included in the statistical analysis where pre-treatment symptoms were detected. Statistically significant differences between groups were defined at p values <0.05.

4 Results

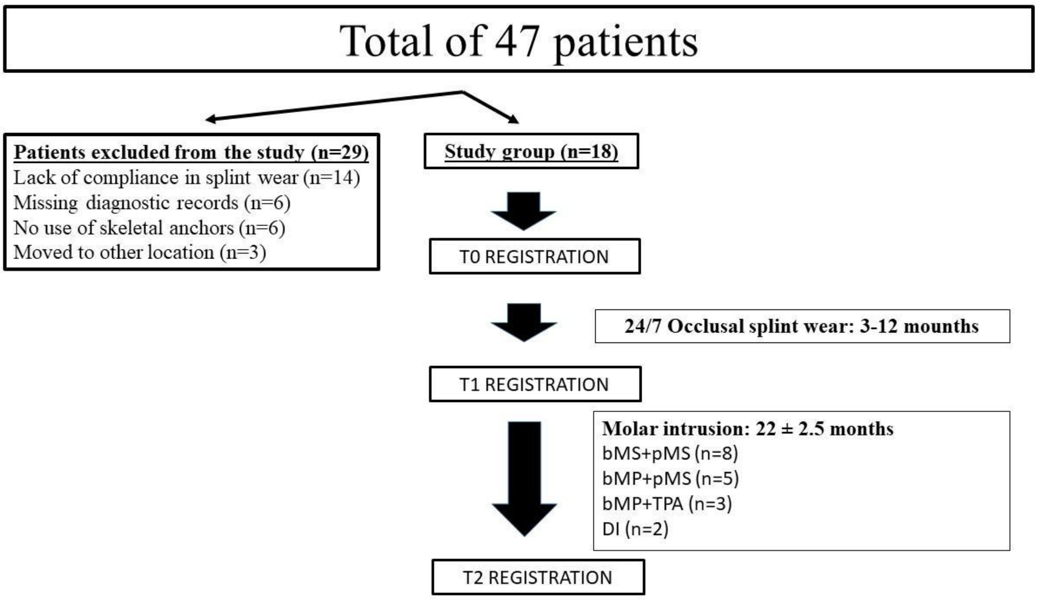
Table 3. summarizes the age and gender distribution of the total 47 subjects collected in a private praxis of Martin-Goenaga, San Sebastián, Spain between 2008–2018.

Table 3. Age and gender distribution of the subjects

	Gender	
	Male	**Female**
Number of subjects	18	29
Mean age (years)	35.42	35.27
Age range (years)		
10–20	0	2
21–30	8	8
31–40	6	12
41–50	2	3
51–60	0	3
61–70	2	1

Table 4. represents the inclusion and the treatment process of the patients.

Table 4. Process of inclusion and the treatment



According to the inclusion/exclusion criteria the examined patients' age and gender distribution were the following: 2 males (age of 18 and 19 years) and 16 females (mean age 28,7y) *(Table 5.)*.

Table 5. Age and gender distribution of the included subjects

	Gender	
	Male	**Female**
Number of subjects	2	16
Mean age (years)	18 and 19y	28,4y
Age range (years)		
10–20	2	6
21–30	0	4
31–40	0	4
41–50	0	1
51–60	0	0
61–70	0	1

Of the total 36 joints, 6 joints had neither MP nor disc dislocation, 4 joints MP only, 5 joints had DDwR without MP, 13 joints had DDwR with MP and 8 joints had DDwoR. The chief complaints and initial diagnostic findings of the included patients are summarized in *Table 6.*

Table 6. Chief complaints and diagnostic findings related to the TMJ of the included patients

	Gender	**Age**	**Left**	**Right**
subject 1	male	18	MP, DDwoR	MP
subject 2	male	19	NONE	MP, DDwoR
subject 3	female	17	MP, DDwR	NONE
subject 4	female	27	MP, DDwR	MP
subject 5	female	13	MP	MP, DDwR
subject 5	female	23	MP, DDwR	DDwR
subject 7	female	34	NONE	MP, DDwR
subject 8	female	18	MP, DDwoR	NONE
subject 9	female	13	MP DDwR	MP, DDwR
subject 10	female	34	MP, DDwoR	MP
subject 11	female	26	DDwR	MP, DDwoR
subject 12	female	16	NONE	MP, DDwR
subject 13	female	40	DDwR	MP, DDwR
subject 14	female	44	MP, DDwR	MP, DDwoR
subject 15	female	19	MP, DDwR	DDwR
subject 16	female	39	NONE	MP, DDwR
subject 17	female	23	MP, DDwoR	MP, DDwR
subject18	female	69	DDwR	MP, DDwoR

Table 7. represents the means, the lower (CI.l) and upper (CI.u) limits of 95% confidence interval of the changes between $T0^{MI}$ vs. $T0^{CR}$, $T0^{MI}$ vs. T1 and T1 vs. T2 mountings for OJ and OB and *Table 8*. the changes between T0 vs. T1 and T1 vs. T2 lateral cephs for the selected cephalometric variables, respectively.

Table 7. Changes in OJ and OB (* $p < 0.05$).

		Mean	**CI.l**	**CI.u**	***p* Value**
OB	$T0^{MI}$ vs. $T0^{CR}$	−1.3333 mm	−2.2082 mm	−0.4585 mm	0.0005 *
	$T0^{MI}$ vs. T1	−3.1389 mm	−4.0137 mm	−2.2641 mm	0.0000 *
	T1 vs. T2	4.0278 mm	3.1529 mm	4.9026 mm	0.0000 *
OJ	$T0^{MI}$ vs. $T0^{CR}$	1.2222 mm	0.3367 mm	2.1078 mm	0.0022 *
	$T0^{MI}$ vs. T1	2.5833 mm	1.6978 mm	3.4689 mm	0.0000 *
	T1 vs. T2	−2.0556 mm	−2.9411 mm	−1.1700 mm	0.0000 *

Table 8. Changes in Mandibular plane–Palatal plane angle, Facial axis angle by Ricketts and ANB angle (* $p < 0.05$).

		Mean	**CI.l**	**CI.u**	***P* Value**
Mandibular plane–Palatal plane angle	T0 vs. T1	2.5778°	1.776°	3.3800°	0.0000 *
	T1 vs. T2	−2.8333°	−3.635°	−2.0311°	0.0000 *
Facial axis angle by Ricketts	T0 vs. T1	−1.6667°	−2.684°	−0.649°	0.0004 *
	T1 vs. T2	2.3333°	1.316°	3.351°	0.0000 *
ANB angle	T0 vs. T1	1.4722°	0.8474°	2.0971°	0.0000 *
	T1 vs. T2	−1.6667°	−2.2915°	−1.0418°	0.0000 *

When comparing screening mountings to models in MI ($T0^{MI}$ vs. $T0^{CR}$) significant differences were found in horizontal and vertical overlap of the incisors. OB decreased by 1.33 ± 0.73 mm ($p = 0.0005$) while OJ increased by 1.22 ± 0.69 mm ($p = 0.0022$). Following full time acrylic splint wear (T0 vs. T1), there was a significant average increase by 2.58° ± 0.93° ($p = 0.0000$) in lower facial height (palatal plane-mandibular plane angle) and a significant decrease in facial axis angle by 1.67° ± 1.54° ($p = 0.0004$), which in turn had a sagittal effect as the ANB angle increased significantly by 1.47° ± 0.70° ($p = 0.0000$). Consequently, both OB and OJ showed a significant change on post-splint mountings when compared to centric occluded models ($T0^{MI}$ vs. T1); OB had an average decrease of 3.14 ± 1.65 mm (p = 0.0000) and OJ an average increase of 2.58 ± 1.51 mm (p = 0.0000).

Regarding molar intrusion its average amount measured on the level of the first molars was 1.95±0.58 mm. The average treatment time was 22 ± 2.5 months. In every examined variable, molar intrusion (T1 vs. T2) resulted in statistically significant changes as well. After intrusion of the molars, the mandible exhibited counterclockwise rotation, which was confirmed by decreased lower facial height and increased OB (4.03 ± 1.88 mm (p = 0.0000)), decreases in ANB and OJ. The palatal plane-mandibular plane angle decreased by 2.83° ± 1.78° (p = 0.0000), the ANB angle by 1.67° ± 1.12° (p = 0.0000) and the OJ by 2.06 ± 2.13 mm (p = 0.0000). The mean change in facial axis angle was + 2.33° ± 2.08° (p = 0.0000).

Figure 7.a shows representative superimpositions of T0 vs. T1 and *Figure 7.b* superimpositions of T1 vs. T2 lateral cephalograms, respectively.

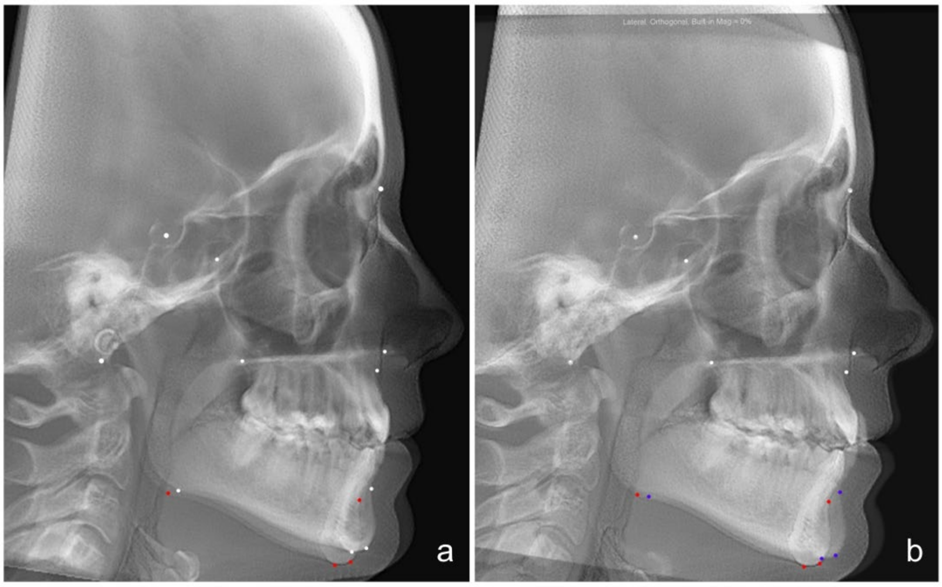


Figure 7. Representative superimpositions of pre-splint (T1) vs. post-splint (T2) (a) and post-splint (T2) vs. post-intrusion (T3) (b) lateral cephalograms.

Following splint wear (a), there was a significant increase in lower facial height and significant decrease in facial axis angle, which in turn increased ANB angle. After intrusion (b), the mandible exhibited counterclockwise rotation, which was confirmed by decreased lower facial height, increased OB and facial axis angle and decreases in ANB. When comparing pre -and post-treatment CBCT images of TMJ, the frequency of derangement was found to be different on the left and right sides. *Table 9*. summarizes the pre-and post-treatment frequencies of TMJ alterations. On the right side, flattening before the treatment was seen in 61.11% and 72.22% on the left side, which showed a significant improvement to 27.78% on the right and 38.89% on the left side following intrusion (post-treatment). Assessment of the CBCT findings of surface erosion and irregular condylar surface showed 72.22% on the right and 55.56% on the left side which significantly decreased to 22.22% on both post-treatment sides. Irregular TMJ space and/or absence of anterosuperior position of the condyle was 66.67% on the right and 61.11% on the left side, which significantly improved, as only 16.67% of the patients showed still non-ideal post-treatment condylar position. No pre-and post-treatment differences were found in sclerosis, as the frequency remained 22.22% of the right and 11.11% of the left TMJ.

Table 9. Frequency of osseous changes before and after therapy (* $p < 0.05$).

Morphological Signs	Pre-treatment Right	Post-treatment Right	*P* Value	Pre-treatment Left	Post-treatment Left	*p* Value
Flattening	61.11%	27.78%	0.0412 *	72.22%	38.89%	0.0412 *
Surface erosion, surface irregularities	72.22%	22.22%	0.0077 *	55.56%	22.22%	0.0412 *
Irregular TMJ space	66.67%	16.67%	0.0077 *	61.11%	16.67%	0.0133 *
Sclerosis	22.22%	22.22%	1	11.11%	11.11%	1

5 Discussion

Treatment of orthodontic patients with TMD due to orthopedic instability has always been challenging especially as one of the desired outcomes of the orthodontic therapy is the achievement of an orthopedic stability with an ideal harmony between occlusal functions and TMJ (40). Many case studies are available demonstrating TMD patients treated with stabilization splint and/or molar intrusion (144, 145, 163-165). But, so far, a series of larger number of TMD orthodontic subjects, treated by stabilization splint followed by molar intrusion, with the main focus on TMJ health and CR-MI harmony have not been examined so extensively and studies have not been published yet. The aim of our study was to investigate and demonstrate that TMD patients with an orthopedic instability can be effectively treated by the occlusal splint therapy followed by skeletally anchored molar intrusion.

TMD is by far a complex disease and the nature of it is not completely understood (166, 167). Most common signs and symptoms are masticatory muscle pain, TMJ sounds, limited movements (jaw opening capacity and deviations in mandibular movements), which tend to fluctuate with temporary remissions (168, 169). It has been generally accepted that TMD has a multifactorial origin (163). There is still a debate, whether occlusion plays a role in the etiology of TMD, nevertheless, completely rejecting the role of it may be inappropriate (40, 170). It has been reported that TMD is closely associated with some types of malocclusions, such as open bite, deep bite and posterior cross bite (165). Disharmony between CR-MI has been suggested to be a causative factor as well (41, 44) and it has been showed that the degree of CR-MI discrepancy has a strong positive correlation with the severity of TMD signs and symptoms (42, 44) and by achieving harmony between CR-MI during the orthodontic treatment decreases the risk of TMD. According to this, the mandible should seat ideally into MI during closure without condylar deflection from CR position caused by occlusal interferences. Therefore, CR-MI harmony should be one of the major goals of orthodontic treatment. In most of the published literature that have failed to prove an existing relationship between occlusion and TMD, several inadequacies are present, such as no instrumentation was used. Most of the studies used only questionnaires, clinical examinations and only dental cast (171, 172). In a review, McNamara, Seligman and Okeson have also found relative low association between TMD and occlusal factors, although in the studies they reviewed, the occlusions were evaluated only intraorally and by using chin-point evaluation (3). No attempt has been made to examine the condylar position and the possible effect on the stability of the TMJ by means of articulator models or precise determination of condyle with 3D imaging. To assess both condylar and occlusal relationships, articulator mounted models are recommended (173-175). The effectiveness (44, 47, 48, 50, 55, 60, 61, 68, 75, 176) and the reproducibility (40, 47, 55, 60, 61, 68, 94). This CR defining method has been confirmed by numerous studies. In our study, all diagnostic cast were mounted into articulators at different stages of the treatment; initially in MI ($T0^{MI}$), in centric "de jour" ($T0^{CR}$), after splint wear in CR (T1) and following molar intrusion in CR (T2), therefore we could monitor condyle position. We found significant CR-MI disharmony between the screening mountings and the initial records. The discrepancy was even more expressed when we compared the initial models with the post-splint ones, where following deprogramming the neuromuscular avoidance patterns were not present making the condylar seating accurate. These results agree with He et al., who investigated the relationship between CR-MI discrepancy and TMD have found that CR-MI shift is strongly correlated with the signs and symptoms of TMD (42). For TMD treatment, various methods have been used, including physio- and relaxation therapy, pharmacological interventions, arthroscopic surgery, behavioral and educational counseling and occlusal splints as well (12, 177). Pharmacologic therapies mainly aim to reduce pain and inflammation. There is growing interest for the use of polyphenols, however their beneficial effects on modulation of oxidative stress and inflammation remain highly limited due to their low bioavailability and biotransformation (178). A recent network meta-analysis of randomized controlled trials showed that hard stabilization splints in conjunction with counselling therapy can produce maximum benefit for TMD patients, furthermore, hard stabilization splint is far superior in patients with myogenous TMD (179). Recently, randomized clinical trials have indicated that stabilization splints are superior to other treatments for TMD due to orthopedic instability (169, 177). These splints are made of hard acrylic material, which can eliminate occlusal interferences, reduce abnormal muscle activity and therefore provide good neuromuscular balance. Splint therapy has been shown to be effective in changing the occlusal pattern of the teeth and improving the function of the masticatory system (12, 170, 180). All patients included in the present study received full coverage acrylic splint therapy prior to the orthodontic treatment, to eliminate the signs and symptoms. Patients were instructed to full-time splint wear, as strong association between wearing time and effectiveness had been previously reported (179). Following the splint wear altered occlusal relationship; AOB develops, which should be corrected. Molar intrusion is one of the most valid treatment approaches used for open bite corrections (127). It has a similar effect to surgery in that the maxillary impaction autorotates the mandible in counter-clockwise direction (up- and forwards) and as an indirect consequence the incisor relationships will improve as well. Compared to orthognathic surgery, application of TADs requires no compliance, has low risk and morbidity, is less expensive and invasive and more acceptable by patients. Several studies investigated the biological processes involved in molar intrusion (181, 182). In animal studies, alveolar bone and nasal/sinus floor remodeling without pulp vitality loss and clinically significant root resorption have been found to occur during and following molar intrusion (181, 182). Furthermore, micro-CT studies of human teeth has also confirmed that root resorption following molar intrusion is clinically insignificant (141). Moreover, Akan et al. (145) demonstrated that molar intrusion has no negative effect on TMJ and masticatory system. According to these, in all subjects, TADs were used in order to correct AOB developed after splint wear. In our study, after intruding molars, mandibular counterclockwise rotation occurred toward closing the bite, which in turn induced up-and forward displacement of the B point as well as reduction in the ANB, mandibular plane angle and anterior facial height. The average mandibular rotation seen in our patients was 2.8°, which is similar to others (135, 141, 144-146). Regarding the dental changes, following molar intrusion we found an average increase in OB, which is similar change observed by others as well (144, 183, 184).

So far, numerous imagining techniques have been used to evaluate morphological changes of the TMJ. Panoramic radiographs have 2D limitations and low sensitivity due to structural distortion and superimposition of the zygomatic process (185). For visualization of disc-condyle relationship Magnetic Resonance Imagining (MRI) technique has been used as the gold standard diagnostic method (186). CT can be used to detect bony changes, however, besides its high diagnostic efficacy, CBCT has several advantages over it, such as; lower radiation dose, better accessibility, lower cost (187). In this study we used CBCT to evaluate the pre-and post-treatment (following intrusion) condylar morphology. Among the 18 patients with orthopedic instability, flattening, surface erosion and surface irregularities were the most frequent pre-treatment bony changes. This agrees with Shahidi et al., who found flattening in 73.3% of TMJ related symptomatic cases (188). When comparing pre-treatment and post-treatment joints, except the sclerosis, significant improvements were seen following treatment in the three examined variables on both sides; approximately 50% of the condylar surfaces regained their convexity, cortical bone continuity and condylar position improved by about 40%. In a previous study, flattening was found to show positive correlation with TMD (189). Those studies, where no correlation has been found between TMD and morphological changes, the high prevalence of bony changes in asymptomatic patients was explained by the adaptive and compensatory potential of the TMJ (190). Furthermore, a systematic review pointed out a potential sample selection bias among the papers comparing morphological changes between TMD and non-TMD patients; namely, in most studies patients included in those studies were referred to TMD and facial pain services, meaning that only asymptomatic and not the healthy control group could have been assured (191). In summary, our results highlighted that occlusal splint therapy followed by orthodontic molar intrusion has a positive impact on bony changes of the TMJ.

The limitations of the study were:

1. Relatively small sample size. Orthodontic treatment after stabilization splint is not a general practice yet. Few TMD patients are seeking TMD specialist first, and not thinking about orthodontic treatment. In our study we examined the skeletally anchored molar intrusion only. TMD patients treated with molar intrusion can be managed if mostly vertical changes are present and we need about 2-3 mm of molar intrusion. In patients with larger AOB, excessive amount of transversal discrepancies, or larger sagittal discrepancies need to be treated surgically. Smaller vertical discrepancies do not need skeletal anchorage, usually bite blocks on the posterior teeth is sufficient. The number of these excluded patients only was 12. We did not register the number of surgically treated patients.

2. Large drop out of the treated TMD patients. Of the 47 patients treated with TMD 14 were excluded because of improper use of occlusal stabilization splint. TMD patients are

quite a special group of patients. Many were treated orthodontically or by other TMD specialists, which make them tired in longer treatments. This may count as a significant psychological factor in patient compliance.

3. Using different types of skeletal anchors for intruding molars: To find the proper mechanics for molar intrusion, is highly dependent of the anatomical situations like: missing tooth in the molar region, where dental implant is planned as a part of the prosthodontic rehabilitation, anatomy of the infrazygomatic crest, amount of interradicular bone or height of the attached gingiva. If exact mechanics is planned the same type of tooth movement can be achieved, however, special attention has to be drawn to avoid side effects.

6 Conclusions

The results of this study showed that full time occlusal splint therapy followed by skeletally anchored molar intrusion is an effective therapeutic method to treat orthopedic instability resulting in TMD. Condyle can be fixed in the centric position, which results not only in muscle relaxation and reduction of soft tissue inflammation, but can often improve hard tissue conditions, like condylar pathologies. As a result of these improvements signs and symptoms of TMD can be efficiently reduced or even fully eliminated. Occlusal changes and bite opening resulting from condylar repositioning however should be treated to prevent relapse of TMD. Skeletal anchors like miniscrews and miniplates are adequate tools to perform bodily tooth movements, like molar intrusion and consequent mandibular autorotation, with no, or minor morbidity. Paying adequate attention to the CR of the condyle, relapse of TMD can be avoided and CR-MI harmony can be achieved.

7 Summary

We evaluated diagnostic records of 18 patients who reported previous TMD and had undergone splint therapy. Post-splint AOB was treated with skeletally anchored molar intrusion. We observed that occlusal splint wear due to condylar seating resulted in mandibular distorotation, while orthodontic molar intrusion restored these conditions (AOB) by autorotation of the mandible. All these effects could be visualized on mounted models and lateral cephalograms. Morphological changes in the condyle were analyzed with pre- and post-treatment CBCT images. Surface erosion and irregular condylar surfaces reduced significantly on both sides. Irregular TMJ space improved significantly. However, no differences in sclerosis were observed.

Occlusal splint therapy followed by orthodontic molar intrusion effectively restored CR-MI harmony, making it a proper method for orthodontic treatment of TMD patients.

Highlights:

1. In our examined study group there was a significant difference between MI and Centric „de jour" mandibular position, which difference increased after full time occlusal splint wear. For this reason, interdisciplinary monitoring of CR position by mounting models helps the effective treatment.

2. In our examined study group there was a significant difference between MI and post-splint CR mandibular position measured on the lateral cephs. For this reason, analyzing post-splint lateral cephs makes orthodontic diagnosis more accurate.

3. In the treated population 24/7 wear of hard acrylic occlusal stabilization splint effectively managed TMD signs and symptoms, resulting in occlusal changes and AOB.

4. Occlusal changes due to stabilization splint wear could be effectively treated by skeletally anchored molar intrusion.

5. The improvement of TMD could be detected as bone morphological changes on pre-treatment – post-treatment CBCT images.

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