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RESEARCH ARTICLE

EFFICIENCY OF INTRA-ARTICULAR INJECTIONS WITH HYALURONIC ACID IN PATIENTS WITH TEMPOROMANDIBULAR JOINT OSTEOARTHRITIS – A RETROSPECTIVE STUDY

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ABSTRACT

Background & Objective: According to the RDC/TMD classification of temporomandibular disorders (TMDs), one very often diagnosis is osteoarthritis of temporomandibular joint (TMJOA). TMJOA is a slowly progressive and degenerative disease affecting all TMJ structures, mainly the articular cartilage. Its etiology is trauma and joint overloading. TMJOA's management has been attempted with several treatments, but the most usual choice is intra-articular injections with hyaluronic acid. The aim of this study is to evaluate the efficiency of such injections at patients with TMJOA. **Methods:** Thirty five (35) patients, 9 men and 26 women, have been included in the study. They are divided into two age groups: seventeen (17) of age 40 – 59 years old and eighteen (18) of age over 60 years old. Their medical records have been gathered and examined, and a follow-up visit was scheduled for each of them for clinical examination and discussion over a structured questionnaire. **Results:** Regarding the pain, the average value of painful symptoms is 3,780 out of 5 before treatment, whereas after treatment the same average value is equal to 0,457. It seems that the number of patients that stopped complaining about TMJ sounds is higher after their treatment by 16 patients (10 out of 35 before treatment, 26 out of 35 after treatment). Finally, a reduction of mouth opening was pointed out in only 3 patients at the follow-up visit, much less that the initial number of 33 patients with reduced mouth opening before treatment. **Conclusion:** Intra-articular injections with hyaluronic acid appear to be of great value for patients with TMJOA. TMJOA is usually expressed with painful symptomatology, but the prevalence of asymptomatic patients is not very low. So, it is important to suspect TMJOA clinically and refer patients for radiological assessment.

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INTRODUCTION

Temporomandibular joints (TMJ) are two highly vascularised and innervated joints with anatomical and functional complexity, which operate concurrently (1, 2). Each of them consists of the glenoid fossa of the temporal bone, the condyle of the mandible and the articular disk, which separates each joint in two intra-articular spaces (1). However, TMJs have some unique characteristics that differentiate them from other joints (3). The differences are related to the loading forces, TMJs' operating movements and histological structure of TMJs' cartilages (3, 4). To specify, TMJs bear limited forces and their cartilage layers consist both type I and type II collagen in contrast to the other joint cartilages, and their movements are three-dimensional and complicated, including protrusion, retrusion, lateral excursion, and jaw opening and closing (3, 4, 5, 6). Temporomandibular disorders (TMDs) are a common dysfunction of TMJ attributed to muscular or intra-articular impairments (7). The classification of TMDs is based on the diagnostic criteria RDC/TMD, introduced and scientifically respected since 2014 (7, 8). So, TMDs may

be intra-articular or extra-articular, namely myalgia of one or more masticatory muscles, arthralgia of TMJ, articular disk displacement, or osteoarthritis of TMJ (7, 8, 9). The scientific community has not fully understood TMDs' etiology yet, although various theories have been proposed as possible factors leading to such disorders (10, 11). TMDs' etiology seems to be multifactorial with several predisposing, initiating and perpetuating factors, as TMJs' functionality and anatomy are complicated (2, 9, 11). Regardless of the etiology, TMDs affect patients' lives at a significant level by restricting fundamental maxillofacial functions, such as chewing and speaking. Patients' life quality is also affected due to the maxillofacial pain that usually accompanies TMDs (10). Intra-articular derangement of TMJs is observed in around 20% of the population (2). Osteoarthritis is the intra-articular TMD examined in this study. It is a degenerative TMJ disease with severe progressive impact on both hard and soft tissues of TMJs (1). Osteoarthritis of TMJ is considered a low-inflammatory arthropathy within the spectrum of facial pain syndromes (1, 8). There still appears to be a diagnostic and treatment challenge regarding this TMD, as its properties are unique and may vary from those of osteoarthritis of other joints (1). The aim of this study is to examine the effectiveness of intra-articular injections of hyaluronic acid in patients' TMJs with osteoarthritis.

MATERIALS AND METHODS

On the basis of the approval of Bioethics Committee of the School of Dentistry of Aristotle University of Thessaloniki, the research team proceeded in searching and gathering the medical records of patients considered as suitable, according to the inclusion and exclusion criteria of the approved scientific protocol. The records were archived at the Laboratory of Oral and Maxillofacial Surgery. Regarding the inclusion and exclusion criteria of the protocol, a patient was suitable for the study when diagnosed with painful osteoarthritis of one or both TMJs within the period 2021 – 2023 and treated with intra-articular injections of hyaluronic acid. Factors such as the gender, the age, the biometric characteristics, any comorbidities and the socio-cultural profile of the patients were not to reject a patient's inclusion in the study. So, overall, 35 medical records were collected and thoroughly examined, as described afterwards.

From each medical record, specific sections were examined. These sections were personal information (name, gender, year of birth and contact information) and medical notes in the spectrum of our study (TMD diagnosis, TMJ pain before treatment, TMJ noise before treatment and reduced mouth opening before treatment). The procedure was conducted under high confidentiality, in order to guarantee the anonymity of the patients included in the study. The personal data was stored at an electronic data base, which was accessible by only one of the researchers. The data was pseudonymised and anonymised, as ordered by the General Data Protection Regulation (GDPR, 2016). The collected and stored data is valuable to understand the patients' clinical condition before the treatment with intra-articular injection with hyaluronic acid. So, in order to compare their condition after the treatment with that one before, all patients whose medical records were included in the study were contacted and agreed to come for a follow-up visit at the Laboratory of Oral and Maxillofacial Surgery of School of Dentistry, Aristotle University of Thessaloniki. This follow-up visit did not include any clinical, radiological and other laboratory examinations, except the measurement of mouth opening, according to the bioethical approval. The time of the follow-up visit of each chosen patient was scheduled at least six (6) months after the last intra-articular TMJ injection, so that the clinical condition was not affected by hyaluronic acid's positive influence in the impaired TMJ. At the follow-up visit, the patients were asked to answer a structured questionnaire, which included subjective questions about their condition after the treatment (Table 1). The only clinical examination conducted at their follow-up visit was, as mentioned previously, the measurement of mouth opening, evaluated as reduced (< 35 mm) or accepted (> 35 mm).

Table 1. Questionnaire of follow-up visit

PAIN						
1. Do you feel any pain near the temporomandibular joint?	A. Yes			B. No		
2. Is the pain constant or not?	A. Constant			B. Not constant		
3. What triggers the pain?	A. Chewing	B. Wide mouth opening		C. Automatic pain		
4. How intense would you rate this pain today, on a scale of 0 to 5?	A. 0	B. 1	C. 2	D. 3	E. 4	F. 5
TMJ SOUNDS						
5. Do you hear noise regularly when you open or close your mouth?	A. Yes			B. No		
6. Is yes, when is this noise observed?	A. When opening mouth	B. when closing mouth	C. In every jaw movement			

RESULTS

Throughout the examination of the selected medical records, the following epidemiological observations were made regarding the sample of our study:

- Nine (9) patients are male, and twenty six (26) patients are female.
- All patients were over 40 years old at the beginning of their treatment.
- There seems to be an equivalent distribution of patients in two age groups: 17 patients are between 40 – 59 years old and 18 patients are over 60 years old. For that reason, we are going to examine the pain level, the mouth opening and the TMJ sounds before and after treatment for the two age groups separately and see if there is any statistically significant difference.

Findings related to the treatment protocol followed for the patients of our sample are:

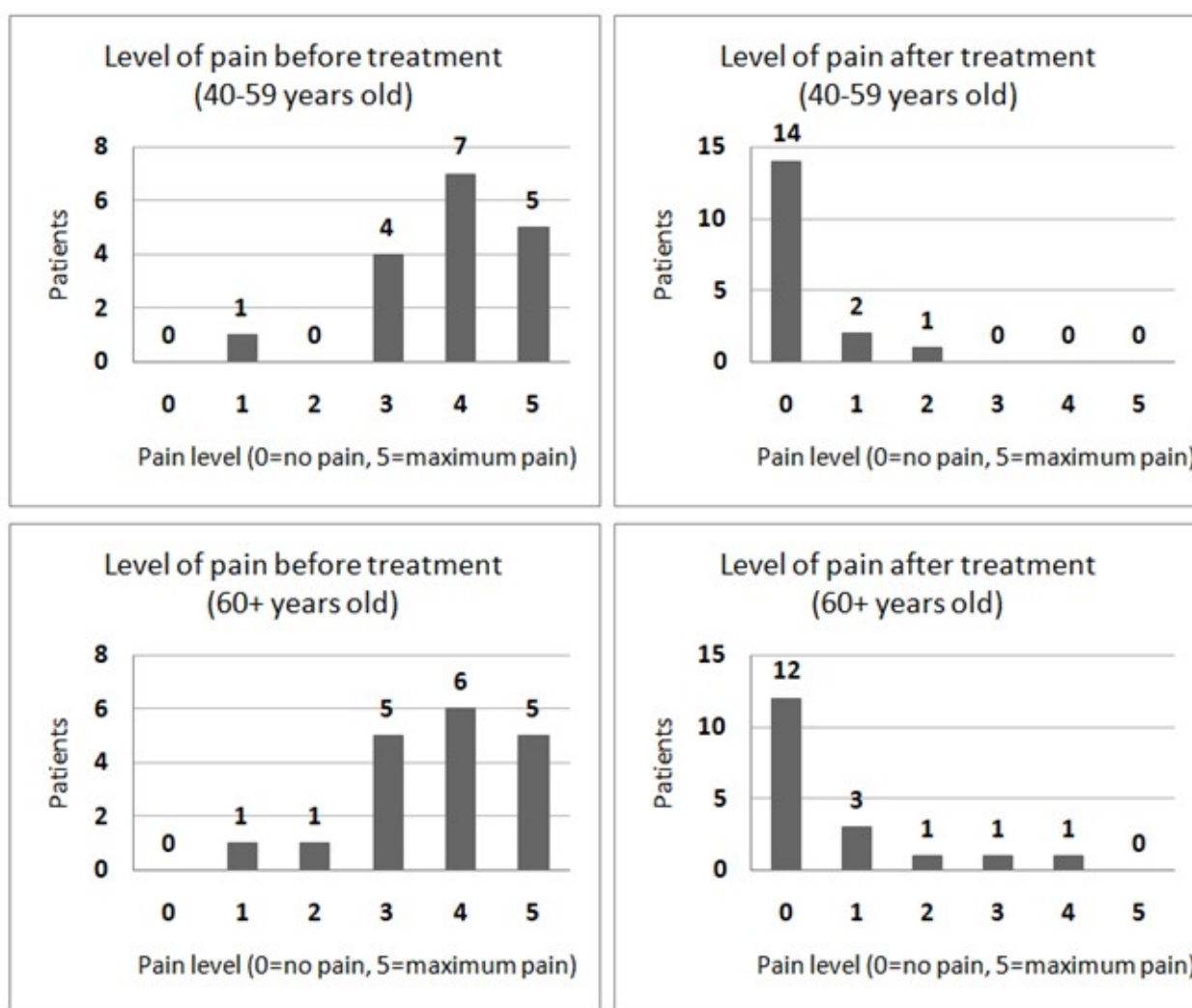
- In the age group 40 – 59 years old, the treated TMJs are distributed as follows: 9 right TMJs and 10 left TMJs, because two (2) patients of this group underwent intra-articular injection on both their TMJs. Accordingly, in the age group 60+ years old, the treated TMJs are distributed as follows: 7 right TMJs and 13 left TMJs, because two (2) patients of this group underwent intra-articular injections on both their TMJs. So, overall, 19 TMJs aged 40 – 59 years old and 20 TMJ aged over 60 years old were treated.
- The number of intra-articular injections needed for each treated TMJ varied, according to the severity of TMJOA of each joint (Table 2).

Table 2. Number of TMJs treated by different number of intra-articular injections (inj) at each age group

Age group	1–2 inj	3–4 inj	5–7 inj	More than 8 inj	Total TMJs :
40 – 59 y.o.	3	6	9	1	= 19 TMJs
Over 60 y.o.	7	4	9	0	= 20 TMJs

Comparing the findings from the medical records with those of the follow-up-visit questionnaires, the following graphs and observations were made:

- With regard to the level of pain before and after the treatment with hyaluronic acid intra-articular TMJ injections, the graphs of Figure 1 present the number of patients and the level of pain they mentioned before and after treatment.



Based on these answers, we are able to calculate the average value of pain level before (APL_1 & APL_3) and after treatment (APL_2 & APL_4) for each age group.

For the patients 40 – 59 years old:

$$APL_1 = \frac{0 * 0 + 1 * 1 + 0 * 2 + 4 * 3 + 7 * 4 + 5 * 5}{17 \text{ patients}} = 3,882$$

$$APL_2 = \frac{14 \cdot 0 + 2 \cdot 1 + 1 \cdot 2 + 0 \cdot 3 + 0 \cdot 4 + 0 \cdot 5}{17 \text{ patients}} = 0,235$$

For the patients over 60 years old:

$$APL_3 = \frac{0 \cdot 0 + 1 \cdot 1 + 1 \cdot 2 + 5 \cdot 3 + 6 \cdot 4 + 5 \cdot 5}{18 \text{ patients}} = 3,722$$

$$APL_4 = \frac{12 \cdot 0 + 3 \cdot 1 + 1 \cdot 2 + 1 \cdot 3 + 1 \cdot 4 + 0 \cdot 5}{18 \text{ patients}} = 0,667$$

When trying to calculate the mean average value of pain level of all patients, regardless of their age, before ($APL_{TOTAL \text{ BEFORE}}$) and after treatment ($APL_{TOTAL \text{ AFTER}}$), the formulas lead to the following results:

$$APL_{TOTAL \text{ BEFORE}} = \frac{APL_1 \cdot 17 + APL_3 \cdot 18}{35 \text{ patients}} = 3,780$$

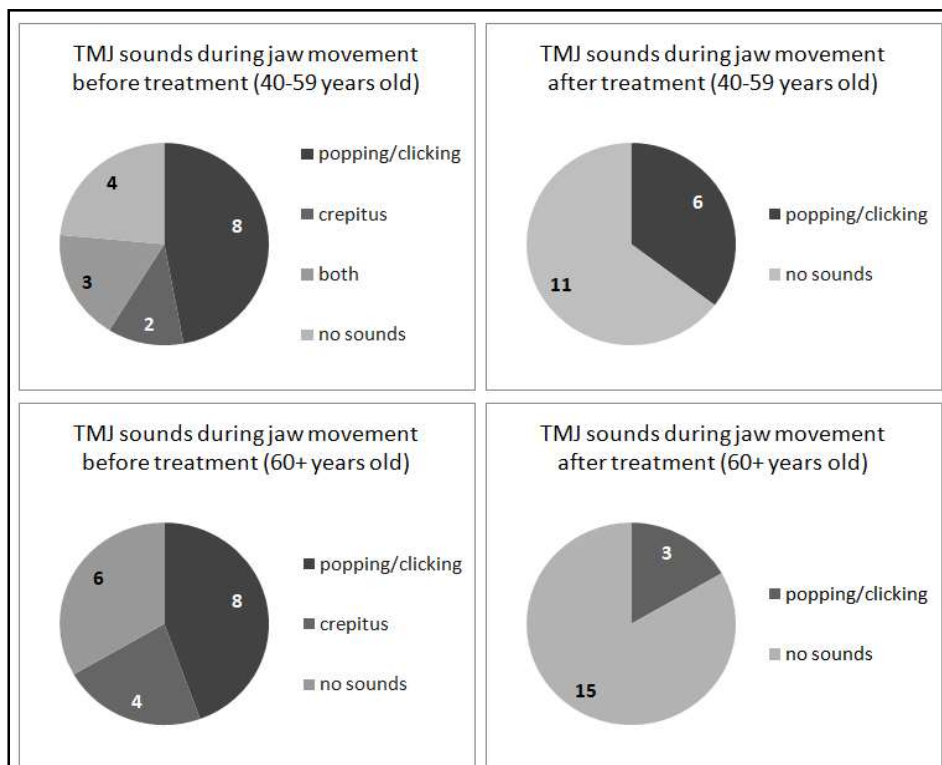
$$APL_{TOTAL \text{ AFTER}} = \frac{APL_2 \cdot 17 + APL_4 \cdot 18}{35 \text{ patients}} = 0,457$$

According to the Graphs 2 and 4, there are 3 patients in age group of 40 – 59 years old and 6 patients in age group of over 60 years old, who still express painful complaints of certainly lower intensity. When those patients were asked about the reason and features of pain, the following answers were gathered:

- 4 patients (2 from each age group) experience automatic pain.
- 3 patients (1 from age group 40 – 59 years old, and 2 from age group 60+ years old) experience pain caused by wide mouth opening.
- 2 patients (both from age group 60+ years old) experience pain caused by chewing hard solid food.
- 3 out of the 9 patients of age group 60+ years old characterize the pain as constant, either automatically triggered (1 out of 3) or caused by chewing hard solid food (2 out of 3).

Judging from the calculations above, it seems that both age groups (40 – 59 and over 60 years old) present significant improvement (Graphs 1 – 4).

Regarding the sounds coming from the diseased TMJs during jaw movement, the graphs of Figure 2 present the number of patients that complain about “popping” / “clicking”, crepitus, both of them, or no sounds before and after treatment.



The answers suggest that the number of patients that do not complain about TMJ noise during the movement of their mandible is increased at both age groups, according to the formula:

$$\Delta x = \frac{\text{new patients with no TMJ sounds after treatment}}{\text{initial number of patients with no TMJ sounds}}$$

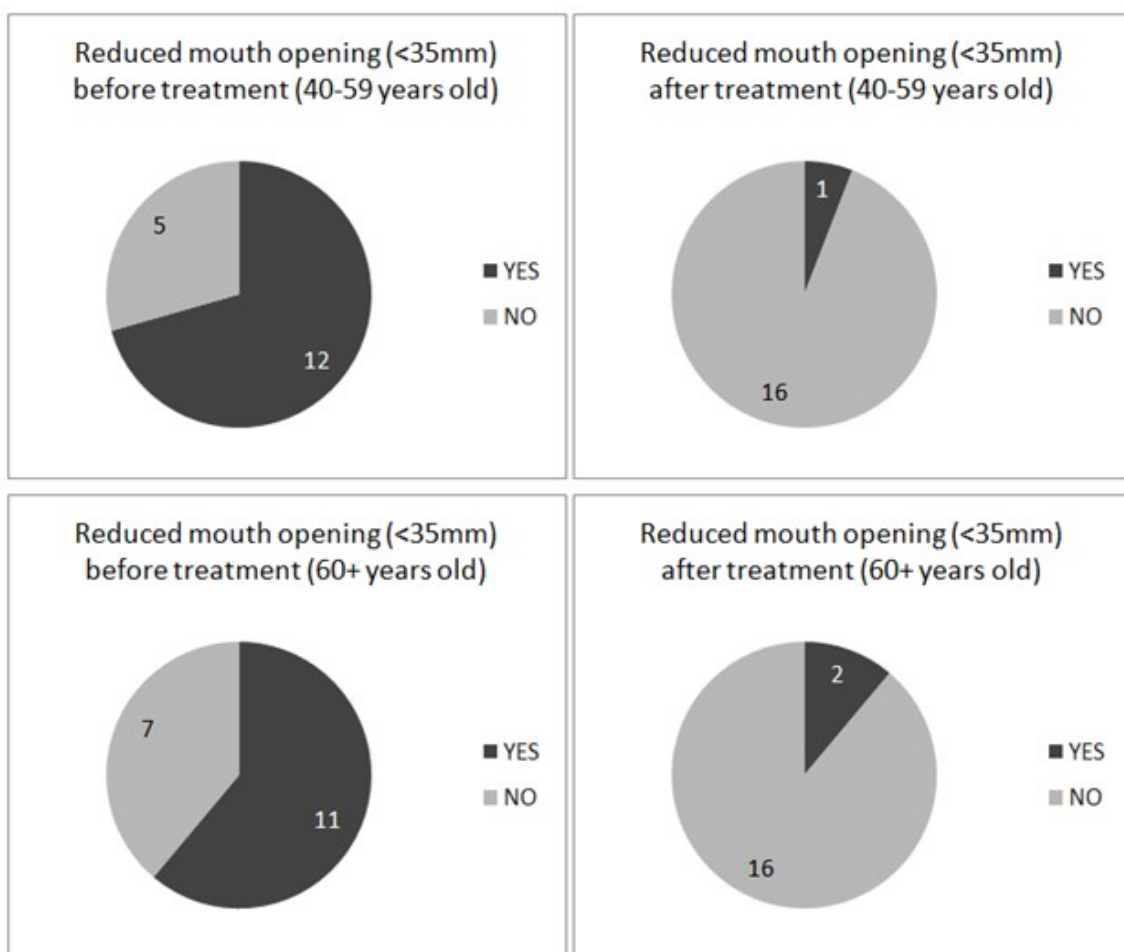
So, in age group 40 – 59 years old, patients that hear no TMJ sounds are more by:

$$\Delta x_1 = \frac{7}{4} = +175\%$$

And in age group over 60 years old, patients that hear no TMJ sounds are more by:

$$\Delta x_2 = \frac{9}{6} = +150\%$$

For the assessment of mouth opening for all patients of the sample, the graphs of Figure 3 have been created and present the number of patients with reduced mouth opening of less than 35mm before and after treatment.



The clinical findings regarding mouth opening are clear about the positive result of intra-articular injections to patients with TMJ osteoarthritis.

DISCUSSION

Osteoarthritis is the most common joint disease, as suggested by the literature (12). It is divided into two types, namely the primary which is idiopathic, and the secondary caused by trauma, iatrogenic factors or infection (3, 13). Osteoarthritis may affect one or more joints of the human body at the same time (3, 14). It is described as a slowly progressive and degenerative joint disease that provokes impairments to all articular structures (articular cartilage, subchondral bone, ligaments, synovial membrane and the adjacent muscular masses (1, 12, 15). The main feature of osteoarthritis is the degradation of the articular cartilage, along with bone erosion, formation of osteophytes and subchondral sclerosis (3, 12, 16, 17). Temporomandibular joint osteoarthritis (TMJOA) is mainly caused by mechanical factors that lead to excessive joint loading, thus traumatizing the joint structures with unbalanced forces (12). Such mechanical factors are injuries, parafunctional habits i.e. nails biting, increased friction within the

TMJ and malocclusion (12). Its prevalence ranges from 8% to 60%, as there are asymptomatic patients with radiographic signs of TMJOA who are not diagnosed, and it seems to affect women more often than men with a female: male ratio of between 7:1 and 9:1 (3, 18). TMJOA's diagnosis is based on the combination of a thorough clinical examination and radiological imaging of TMJs (12). The clinical evaluation includes palpation of preauricular area and the masticatory muscles, observation of the mandible's movement pathways, as well as detection of any TMJ noises during jaw movements (19). The vast majority of patients suffering from TMJOA have to deal with painful symptomatology, which seems to be the most common clinical finding (12, 20). The pain may derive from muscle contraction, according to Hilton's principle, synovitis or bone destruction below the articular cartilage (7, 12, 21). It is localized at the preauricular area and the masticatory muscles (2). Along with pain, usual findings are reduced mouth opening and noises coming from the diseased TMJ (3, 22, 23). The TMJ sounds are often described as "popping", "clicking", "grating" or crepitus (2). Regarding the mouth opening, under normal circumstances a mouth can be up to 40 – 45mm wide open (2,11). This is a mean range of value for normal mouth opening, but clinically a mouth opening of more than 50mm is considered as hyperkinetic, not only for adults but also for children (2). Sometimes, patients with TMOJA also complain about earache, headache, jawache and facial pain (2). It is important to suspect TMJOA after the clinical examination and refer the patient for radiological assessment, in order to avoid complications, such as TMJ ankylosis, joint instability and condylar osteolysis (3, 12, 24). Nevertheless, TMJOA may often be detected by chance, as a small proportion of patients with TMJOA are asymptomatic (12, 25). However, clinical examination alone is characterised by low sensitivity and specificity in diagnosing TMJOA (1, 25, 26). So, the diagnosing procedure is completed with radiographic evaluation of patients' TMJs (3, 27). The initial radiograph taken is usually orthopantomograph, which provides with only a general depiction of the maxillofacial structures, including TMJs, but has no diagnostic value in case of TMJOA (16, 27). For higher diagnostic accuracy, CT or CBCT and MRI are used (1, 12, 26). CT and CBCT seem to have high efficiency in assessment of bony structures, but MRI is considered as the "gold standard" when examining TMJ, as it offers a clear image of the soft tissues, like the articular disk and the muscles of TMJ which are of great interest in various TMDs, as well as the osseous TMJ parts with the ZTE-MRI methodology (16, 19, 25, 28). Taking into account the advantages of both techniques, CT/CBCT and MRI are both valuable for treatment planning in cases of TMJOA (26). Radiographs of patients with TMJOA reveal cortical bone erosion, flattening of condyle and/or glenoid fossa of the temporal bone, sclerosis, osteophytes, and more rarely subchondral cysts (3, 29). When treating TMJOA, the primary purpose is to eliminate or at least reduce patients' three most usual complaints, namely pain, TMJ noises and restricted jaw movements, in order to improve their life quality (9, 12, 30). The management of TMJOA is not always easy and the cooperation of several specialties, such as oral maxillofacial surgeon, orthodontist, prosthodontist, physiotherapist and rheumatologist, may be required (12). The treatment approach often includes not only clinical procedures but also the systematic use of drugs (12). There are specific instructions given to patients after diagnosis of TMJOA that relieve them from the painful symptomatology. Such instructions include dietary modifications, rest, stress avoidance, awareness therapy and the use of a dental splint for muscle relaxation (1). However, these assist only in reducing the intensity of symptoms and by no means do they treat the main disease (1). There have been proposed various methodologies for TMJOA, classified in three groups, based on the severity and complexity of each case: a) conservative treatment, b) less invasive surgical procedures, and c) surgical intervention (12, 30). Intra-articular injections belong to the less invasive surgical procedures and they have been evaluated in the literature with the use of several pharmaceutical substances. Most commonly, hyaluronic acid, corticosteroids and platelet-rich plasma (PRP) are injected in TMJs with osteoarthritis (12). Hyaluronic acid is a hydrophilic acid which is present in the connective tissue extracellular matrix and contributes to joint stabilization and nutrition (12, 31). However, in osteoarthritis, hyaluronic acid is fragmented (31). Intra-articular injections of hyaluronic acid present positive results in reducing or even eliminating the painful symptomatology, as well as in widening the mouth opening (31). According to modern literature, they may be applied either as a complementary or as a primary therapy in cases of TMJOA (12).

CONCLUSION

The results of our study suggest that pain intensity is significantly reduced regardless of the age, but the younger the patient the easier to eliminate pain. Nevertheless, it is important to remember that sometimes patients with temporomandibular osteoarthritis may not express painful complaints and remain asymptomatic. Regardless of the clinical image of TMJOA, the examining physician should suspect it and ask for radiological assessment of patients' TMJs. In this way, more patients with TMJOA will be diagnosed and promptly treated. Among several treatment choices, intra-articular injections with hyaluronic acid seem to be of great value, as they improve patients' life quality.

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