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Do I-PRF adjuvant injections in TMJ arthrocentesis have a cumulative physiological effect? A retrospective cohort study

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Abstract

Objective The aim of this study was to compare the therapeutic outcomes of single versus multiple injectable platelet-rich fibrin (i-PRF) injections after arthrocentesis in patients with temporomandibular joint osteoarthritis (TMJ-OA). The objective was to evaluate and compare TMJ pain and mobility at the 1st, 6th, and 12th months postoperatively.

Methods This retrospective cohort study included 85 female patients (age: 31–73 years, mean ± sd: 54.9 ± 8.8) who underwent arthrocentesis with i-PRF injections from June 2018 to November 2021, diagnosed with osteoarthritis based on the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). Patients had no prior use of occlusal splint. During follow-up visits, pain was evaluated with a visual analog scale (pVAS) during function and maximum interincisal opening (MIO) was measured to assess jaw mobility. The study included patient follow-up records at four time points: preoperative (T0), 1 month postoperative (T1), 6 months postoperative (T2), and 12 months postoperative (T3). The primary outcome variable was pVAS at T3, secondary outcome variables were pVAS at T1 and T2, and MIO at T1, T2, and T3.

Results No significant differences were found in joint pain or mobility between groups at follow-ups (> 0.05).

Conclusions Both groups showed similar outcomes in terms of pain and mobility over a 12-month period. Increasing the frequency of i-PRF injections does not appear to have an impact on therapeutic outcomes in patients with TMJOA. Given the retrospective design of this study, it is important to evaluate the results with caution.

Keywords Arthrocentesis, Temporomandibular joint, Osteoarthritis, Platelet-rich fibrin

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Introduction

Temporomandibular joint osteoarthritis (TMJ-OA) is a prevalent form of arthritis, particularly affecting older women [1]. This multifactorial condition is characterized by the loss of articular cartilage and remodeling of the subchondral bone, progressing through phases of exacerbation and remission before reaching a plateau [2]. Radiographic findings commonly include sclerosis, osteophyte formation, cartilage degradation, and cyst-like changes at the joint margins [1]. Clinically, TMJ-OA presents with joint sounds, pain, restricted jaw movement, and tenderness, primarily driven by excessive mechanical stress and a diminished capacity of the joint cartilage to adapt [2, 3]. In advanced cases, total joint replacement may be required to restore function and alleviate pain [3]. However, there is a growing focus on managing symptoms through minimally invasive interventions, such as arthrocentesis, which involves the insertion of needles into the joint space to irrigate and remove inflammatory byproducts. This procedure can effectively reduce pain and improve mobility, offering relief for patients who are not yet candidates for more extensive surgical options.

Current literature suggests the effectiveness of arthrocentesis and supplemental injections in managing symptoms of temporomandibular joint disorders (TMD) [4]. Intra-articular injections of hyaluronic acid (HA), corticosteroids (CS), and platelet concentrates—such as platelet-rich plasma (PRP) and injectable platelet-rich fibrin (i-PRF)—can be combined with arthrocentesis or used independently as treatment options [5]. These adjunctive injections are administered to enhance the overall efficacy of arthrocentesis.

A rising trend in intra-articular injections involves the use of PRP and i-PRF, both of which are autologous platelet concentrates (APC) derived from patients' whole blood and are rich in cells and growth factors. Although the precise mechanisms of action remain unclear, growth factors are believed to play a significant role in cellular secretion and activation, stimulating and accelerating tissue regeneration [6]. i-PRF, initially introduced by Choukroun et al. [7], does not require chemical manipulation of the patient's blood; rather, it is centrifuged at 700 rpm (60 g) for 3 min. This process reduces the relative centrifugal force and shortens the centrifugation time, thereby preventing the migration of certain cells that are critical for healing and regeneration [8].

The existing literature supports the efficacy of various intra-articular injections; however, ongoing research is focused on understanding the influence of increasing the frequency of these injections on therapeutic outcomes. Although studies have compared single versus repeated applications of hyaluronic acid [9, 10], arthrocentesis alone [11], and PRP injections [12, 13], no studies to date have specifically evaluated the comparative effects of single versus multiple injections of i-PRF. The aim of this retrospective cohort study was to compare the therapeutic outcomes of single versus multiple adjunctive i-PRF injections after TMJ arthrocentesis in patients with TMJ-OA. We hypothesized that multiple i-PRF injections would demonstrate superior efficacy in alleviating pain and dysfunction compared to a single injection in patients with TMJ-OA. The specific objective was to evaluate and compare pain intensity and mandibular mobility following one and three sessions of adjunctive i-PRF injections at the 1st, 6th, and 12th months postoperatively.

Materials and methods

This retrospective cohort study included 85 female patients aged between 31 and 73 years (mean ± sd, 54.9 ± 8.8) who had not received prior occlusal splint therapy and underwent arthrocentesis therapy performed by a single surgeon between June 2018 to November 2021, at the Health Sciences University, Hamidiye Faculty of Dentistry, Department of Oral and Maxillofacial Surgery. This study was authorized by the University of Health Sciences Hamidiye Ethical Committee of Scientific Research in 2023 (2023/4-10)and adhered to the Declaration of Helsinki's guidelines for medical protocol. All patients were informed regarding the treatment and inclusion of their data to the study. Following the disclosure process, their signature was obtained on the informed consent form. The study population involved patients who sought treatment for TMJ-OA and underwent arthrocentesis combined with i-PRF injections in the faculty outpatient clinic. The study sample consisted of patients who met the following inclusion criteria: (1) Female patients between 18 and 75 years with complete records; (2) diagnosed with osteoarthritis based on the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) [14], confirmed with cone-beam computed tomography (CBCT); (3) who reported unilateral arthralgia with a line type visual analog scale (VAS) score for pain of at least 50 mm on a scale of 0–100 mm. The following were listed as exclusion criteria: (1) prior invasive treatment of TMJ (including arthrocentesis, arthroscopy, open surgery, or any surgical procedure involving TMJ); (2) uncontrolled systemic diseases and rheumatic, autoimmune, hematologic, and oncologic diseases; (3) pregnancy or lactation; (4) incomplete patient records; (5) prior use of occlusal splints; (6) presence of temporal and/or masseter muscle myalgia (diagnoses based on DC/TMD); (7) patients who had bilateral arthrocentesis.

In our routine clinical practice, adjunctive injections are commonly recommended following arthrocentesis, with a preference for i-PRF injections (multiple if possible) initially due to their regenerative properties [8]. When patients exhibit reluctance, often stemming from

needle phobia or other reasons, HA injections are offered with the aim of enhancing efficacy. Nonetheless, some patients decline adjunctive injections altogether, leading to a patient-driven decision regarding the type and administration of injections. Our subjects include only i-PRF-injected patients and they were divided into two groups according to the received number of injections; arthrocentesis with a single session of i-PRF injection (i-PRF1) and arthrocentesis plus 3 sessions of i-PRF injections (i-PRF3). The decision on whether patients would receive a single session or three sessions of i-PRF injections was made by the patients themselves. Initially, multiple i-PRF injections in combination with arthrocentesis were suggested by the surgeon to leverage the cumulative effect of the treatment. However, the final decision was left to the patient. In this context, treatment preferences were neither random nor solely directed by the clinician. Instead, patients were informed about the available treatment options, and the choice was entirely based on their personal preferences. While the ultimate determination of injections rests with patients, physicians play a pivotal role in advising and guiding this decision-making process. Subjects and examiners were not blinded to treatment groups due to the retrospective nature of the study.

Following skin disinfection, auriculotemporal nerve anesthesia was administered using 1 mL of articaine hydrochloride (Ultracaine DS, Sanofi Aventis, Istanbul, Turkey). Access to the upper joint space was then established with two needles as described by Nitzan et al. [14]. A total of 100 mL of sodium chloride was used to lavage the upper TMJ space. After completing the arthrocentesis procedure, one needle was removed. In the i-PRF1 group, 1.5 mL of i-PRF was then injected. i-PRF was prepared by drawing 9 mL of venous blood into a sterile, additive-free plastic vacutainer tube, which was centrifuged at 700 rpm for 3 min following the protocol outlined by Wend et al. [8]. After centrifugation, two distinct layers formed: red blood cells settled at the bottom, and a yellowish platelet-rich fraction was observed in the top quarter of the sample. The liquid PRF portion was aspirated into a syringe, and 1.5 mL was used for the injection. The i-PRF3 group received the first i-PRF injection in the same manner as the i-PRF1 group. Over the next two weeks, two additional i-PRF injections were administered weekly, without saline lavage, solely as injections. All patients were prescribed postoperative antibiotics (500 mg amoxicillin and 125 mg clavulanic acid) along with analgesics (25 mg dexketoprofen trometamol) after every procedure.

During follow-up visits, our clinic routinely evaluates treatment efficacy by having patients complete a visual analog scale for pain (pVAS) during functional activities, particularly mouth opening and chewing. The pVAS measures pain intensity on a scale from 0 mm (no pain) to 100 mm (worst imaginable pain). Additionally, maximum interincisal opening (MIO) is measured, which is the distance in millimeters between the incisal edges of the upper and lower central incisors during maximum mouth opening, even if discomfort is present. These evaluations are conducted on a monthly basis.

The study included patient follow-up records at four time points: preoperative (T0), 1 month postoperative (T1), 6 months postoperative (T2), and 12 months postoperative (T3). The primary outcome variable was pVAS at T3, secondary outcome variables were pVAS at T1 and T2, and MIO at T1, T2, and T3.

Patient ages, systemic health status according to the American Society of Anesthesiologists Physical Status system (ASA), previous mandibular molar extraction (Ext), contralateral TMJ pain (CTP), duration of symptoms (DoS) and extravasation as a complication (Comp) during the lavage were collected from patient records.

Sample size calculation was performed by G*Power Software (v.3.1.9.4) (Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany), based on a study by Işık et al. [15]. When power was 0.80, effect size was 1.317, and alpha was set at 0,05 minimum sample size of 17 patients per group was needed. Distribution of the data was checked with the Shapiro-Wilk test. In comparisons of the groups, Student's t-test or Mann-Whitney U test was used depending on normality. Time dependent intra-group data were compared with the Friedman test (Post-hoc, Bonferroni-adjusted Wilcoxon test, $p<.008$). Comparisons of the covariables were done by Chi-square test. Data were summarized as mean and standard deviation. All statistical tests were performed using MedCalc Statistical Software (v.12.7.7) (MedCalc Software bvba, Ostend, Belgium, 2013). A significance level of 0.05 was set.

Results

Out of the 99 patient files, 14 were excluded from the study: 4 due to insufficient data, 2 due to accompanying myalgia, 2 due to bilateral arthrocentesis, 3 due to previous use of occlusal splints, and 3 because they were male patients. The final sample was composed of 85 patients aged between 31 and 73 years (mean sd, 54.9 ± 8.8) and there were no significant differences in age between the groups (mean ± sd, i-PRF1, 54.5 ± 8.9; i-PRF3, 55.3 ± 8.8) ($p>.05$). i-PRF1 group consisted of 45 subjects while i-PRF3 group consisted of 40. The initial (T1) follow-up was the 1st month after the first injection (mean sd, 1 ± 0), and the intermediate (T2) follow-up time ranged between 5th to 7th months (mean sd, 6.1 ± 0.6) and long-term (T3) follow-up time ranged between 11th to 14th months (mean sd, 12.1 ± 0.8). There were no statistically significant differences between groups in follow-up times and in any covariates (Table 1) ($p>.05$).

Table 1 Intergroup comparison of covariates

		i-PRF1		i-PRF3		
		N	%	N	%	p
ASA	1	19	42.2%	16	40.0%	1.000
	2	26	57.8%	24	60.0%	
Ext	NP	13	28.9%	12	30.0%	1.000
	P	32	71.1%	28	70.0%	
CTP*	NP	33	73.3%	25	62.5%	0.353
	P	12	26.7%	15	37.5%	
DoS	Less than a year	10	22.2%	8	20.0%	1.000
	Equal or more than a year	35	77.8%	32	80.0%	
Comp**	NP	37	82.2%	26	65.0%	0.086
	P	8	17.8%	14	35.0%	

Chi-Square test. $p < .05$

ASA, American Society of Anesthesiologists (ASA) physical status classification system; Ext, prior mandibular molar extraction; CTP, contralateral temporomandibular joint pain; DoS, duration of symptoms; Comp, complication; P, Present; NP, Not Present

*CTP VAS score was always below 50 mm

** Extravasation as complication

Table 2 Intergroup and intragroup comparisons of pVAS and MIO

		i-PRF1	i-PRF3	
		Mean ± standard dev. Median (Min.-Max.)	**Mean ± Standard dev. Median (Min.-Max.)**	***p***
pVAS (mm)	T0	71.7 ± 9.9 70- (55–90)	72.4 ± 11.2 70- (50–95)	0.876
	T1	33.3 ± 10.7 30- (15–60)	36.1 ± 13.9 30- (10–80)	0.463
	T2	25.3 ± 10.8 20- (10–55)	24.4 ± 11.7 22.5- (10–55)	0.600
	T3	21.7 ± 16.8 20- (0–70)	18.6 ± 18.3 10- (0–70)	0.065
	p*	**< 0,001**	**< 0,001**	
MIO (mm)	T0	35.6 ± 4.5 37- (23–44)	35.9 ± 4.4 37- (25–45)	0.859
	T1	37.9 ± 2.9 38- (31–44)	37.8 ± 3.5 38- (31–49)	0.673
	T2	38.4 ± 2.7 38- (32–44)	38.9 ± 3.4 39- (32–49)	0.534
	T3	38.5 ± 2.4 38- (34–44)	39.1 ± 3.5 39- (33–52)	0.432
	p*	**< 0,001**	**< 0,001**	

Mann-Whitney U test, Friedman test*

T0, Preoperative; T1, 1st month postoperative; T2, 6th month postoperative, T3, 12th month postoperative

$p < .05$

Table 3 Post-hoc pairwise comparisons of pVAS between follow-ups

	i-PRF1	i-PRF3
T0-T1	< 0,001	< 0,001
T0-T2	< 0,001	< 0,001
T0-T3	**< 0,001**	**< 0,001**
T1-T2	**< 0,001**	**< 0,001**
T1-T3	**< 0,001**	**< 0,001**
T2-T3	0.014	0.014

Wilcoxon test (Bonferroni correction $p < .008$)

T0, Preoperative; T1, 1st month postoperative; T2, 6th month postoperative, T3, 12th month postoperative

Intergroup analyses of pVAS and MIO are presented in Table 2. Preoperatively, there was no statistically significant difference between the groups regarding pVAS, which was 71.7 mm (± 9.9) and 72.4 mm (± 11.2) for i-PRF1 and i-PRF3 respectively ($p > .05$). After treatment, no significant differences were detected between the groups at any of the follow-ups ($p > .05$). At T3 pVAS values decreased to 21.7 mm (± 16.8) for i-PRF1, and 18.6 mm (± 18.3) for i-PRF3 ($p > .05$). Although, on average, pain occurred less in the i-PRF3 group, this difference in pain levels was not statistically significant. Preoperatively, there were no statistically significant differences between groups regarding MIO, which was 35.6 mm (± 4.5) and 35.9 mm (± 4.4) i-PRF1 and i-PRF3 respectively ($p > .05$). Postoperatively, no significant differences were found between groups at any of the follow-ups ($p > .05$). At T3 MIO measurements increased to 38.5 mm (± 2.4) in i-PRF1, and 39.1 mm (± 3.5) in i-PRF-3 ($p > .05$).

Significant differences in intragroup comparison were found between follow-ups in both pVAS and MIO across all groups ($p < .001$) (Table 2). Post hoc analysis indicated significant differences in these variables between T0-T1, T0-T2, T0-T3, T1-T2, and T1-T3 ($p < .008$), excluding T2-T3 ($p > .008$), for both groups and parameters (Tables 3 and 4).

Discussion

The purpose of this study was to compare the effects of arthrocentesis combined with a single session of i-PRF injection versus arthrocentesis combined with three sessions of i-PRF injections in patients with TMJ-OA. Our hypothesis was that multiple injections would yield

Table 4 Post-hoc pairwise comparisons of MIO between follow-ups

	i-PRF1	i-PRF3
T0-T1	< 0,001	< 0,001
T0-T2	< 0,001	< 0,001
T0-T3	**< 0,001**	**< 0,001**
T1-T2	**0.001**	**0.001**
T1-T3	**0.001**	**0.002**
T2-T3	0.234	0.256

Wilcoxon test (Bonferroni corrected $p < .008$)

T0, Preoperative; T1, 1st month postoperative; T2, 6th month postoperative, T3, 12th month postoperative

better results in pain and function variables at the end of 1-year follow-up compared to single injections. As a result of the study, no statistically significant difference was found between the two groups in terms of pain or mouth opening at the end of a 1-year follow-up, therefore our hypothesis was rejected. This suggests that a single session of i-PRF injection after arthrocentesis may be sufficient in terms of pain and function in patients with TMJ-OA compared to multiple sessions. This result should be interpreted with caution due to the limitations of the retrospective nature of the study.

TMJ-OA is an inflammatory and degenerative disorder, leading to the gradual wear and loss of articular cartilage, inflammation of the synovial membrane, and changes in the subchondral bone [2]. This disease causes damage to the tissues and cartilage around the joint, resulting in symptoms such as pain, unusual joint sounds, and functional impairment [3]. The adjunctive injection of i-PRF holds potential hope for this degenerative disease, especially because it contains cells and growth factors believed to be involved in the regeneration process, which are not present in HA and CS [16].

The number of studies applying adjunctive i-PRF injections in TMJ-OA patients is quite limited. Although our study groups did not include various adjunctive injections, it is relevant to reference studies where i-PRF was used in patients with TMJ-OA. In an initial preliminary study, Albilia et al. [17] assessed the effectiveness of i-PRF in patients with TMJ pain and dysfunction over a 12-month follow-up period. They found that 33 out of 47 affected TMJs in 37 patients experienced significant long-term pain relief. Furthermore, the authors noted that the most favorable clinical outcomes from i-PRF injections were observed in TMJ cases classified as Wilkes stages IV and V. In a randomized controlled trial conducted by Karadayı and Gürsoytrak [18], 36 patients who received either arthrocentesis alone or arthrocentesis with additional i-PRF were followed. Both treatments were successful in terms of mouth opening and pain relief. Within the TMJ-OA category (Wilkes stages 4 and 5), the study found a difference in pain between the groups only in the Wilkes stage 5 subgroup, while no difference was observed in the Wilkes stage 4 subgroup. This could potentially be due to the small sample size of 6 patients in each subgroup and the short follow-up period of 3 months. In a retrospective cohort study, Yuce et al. [19] compared arthrocentesis alone, arthrocentesis with HA, and arthrocentesis followed by three i-PRF injections in 47 patients, with each group having a similar distribution of Wilkes stages (ranging from 2 to 5). After a 12-month follow-up period, the i-PRF group showed the most significant improvements in pain reduction and mandibular mobility. Lastly, in a randomized controlled trial conducted by Işık et al. [15], the outcomes of arthrocentesis alone were compared with those of arthrocentesis followed by four consecutive i-PRF injections in 36 patients with TMJ-OA. After a 12-month follow-up period, the group receiving i-PRF injections demonstrated superior improvements in both pain reduction and maximal interincisal opening (MIO). The researchers used i-PRF either as a single injection [18] or as multiple injections [15, 17, 19]. Those who administered multiple injections explained their choice as a means to achieve a *cumulative physiological effect* [17, 19].

While the literature generally indicates that multiple injections are often more effective [9, 11–13, 20], regardless of the preparation, some studies have reported mixed outcomes. Moreover, the lack of high-quality evidence in the existing systematic reviews and meta-analyses comparing multiple- session to single-session treatments with the same or no preparation adds to the uncertainty in the current evidence [20]. In a retrospective study comparing patients with TMJ closed lock treated with single-session arthrocentesis to those treated with double-session arthrocentesis, it was found that the group receiving multiple sessions of arthrocentesis had improved mouth opening and lower pain levels after 6 months [11]. In this study, no additional injections were used, and it suggests that even arthrocentesis alone, when performed multiple times, may be more effective. Similar results have also been observed with treatments involving additional injections. Multiple PRP injections for knee osteoarthritis have been shown in various orthopedic studies to provide better pain control compared to a single injection group [12, 13]. Histological evidence suggests the anti-inflammatory effect from multiple PRP injections was sustained in the long-term, as opposed to a single injection [21], which could be a potential mechanism behind improved pain control. This indicates that when performed, multiple injections may increase treatment efficacy and result in cumulative improvement.

However, there are studies that this "cumulative improvement" could not be seen. A systematic review and meta-analysis conducted by Vilchez-Cavazos found that single and multiple PRP injections in knee arthrocentesis have similar effects on pain [22]. Although some

studies suggest that multiple HA arthrocentesis is more effective than a single HA arthrocentesis in relieving pain [9, 20], there are also studies that have found no significant difference between the two [10, 23]. While there are studies in the literature that compare single and multiple injections of HA and PRP, no publication has yet compared the effects of single versus multiple injections of i-PRF.

Patients were predominantly administered 3 injections of i-PRF as multiple injections in the present study, this preference was based on the findings of Albilia et al. [17]. The authors found that the average number of injections applied for the VAS values to decrease to acceptable levels or zero was 3 for TMJ-OA (Stage IV Wilkes: 2.75 ± 1.13, and Stage V Wilkes: 3.3 ± 1.56). Based on the available data, patients who preferred multiple injections were given recommendations in line with these findings. There were also patients who received less or more than 3 injections, but due to their small sample size, these were not included in the study in order to avoid heterogeneity.

In the present study, it was observed that patients with TMJ-OA who received three sessions of i-PRF did not show better outcomes in terms of pain and function compared to those who received a single session. This result contrasts with the idea that multiple applications of autologous platelet products might offer greater cumulative physiological benefits. Comparable results have been documented in various injection studies as reported in the existing literature. There could be several possible reasons for this outcome. Considering the small sample size, the stage, and the varying severities of the disease, the comparison of treatments could be limited. Additionally, repeating the procedure might lead to more invasive interventions in the joint capsule and surrounding tissues, potentially negating any gains in pain relief and function. These are merely hypotheses and were not tested in this study. Coşkun et al. [24], in their animal study on rabbit TMJ, reported that both multiple-session PRP and single-session PRP groups showed no histological difference in healing indicators. The clinical significance of this histological finding may also translate to our findings in intergroup comparison. However, the heterogeneity in studies, the small sample sizes, and the limitations of existing research currently prevent drawing a definitive conclusion about the benefits of multiple injections. There is a need for further studies to address this issue.

Managing arthrogenous TMDs aims to alleviate pain and restore normal joint movements, typically progressing through several treatment phases. Initially, conservative approaches are employed, including NSAIDs, patient education, occlusal splints, and physiotherapy. If these methods do not resolve the issue, minimally invasive options such as intra-articular injections, arthrocentesis, and arthroscopy are considered [4]. The present study did not include patients who had previously used occlusal splints due to their low numbers, which is partly attributed to patient reluctance and difficulties in accessing these services in other departments. Despite this, our results demonstrated effectiveness in both pain relief and improvement in jaw mobility. According to a network meta-analysis by Al-Moraissi et al. [4], although the quality of evidence is rated as low to moderate, minimally invasive procedures were found to be more effective than conservative treatments for pain reduction and improvement in mouth opening in arthrogenous TMDs. Growing evidence from multiple studies comparing various arthrocentesis modalities—whether performed alone or combined with adjuvant injections—with conservative treatments (such as splints) in TMD patients demonstrates that arthrocentesis with adjuvant injections is superior to conservative treatments for pain relief and at least comparable for improving mouth opening [25–28]. Even in studies reporting no significant differences between the two treatment options [29, 30], we consider arthrocentesis to be the more favorable approach. This perspective stems from the significant time and effort involved in the fabrication of occlusal splints, as well as the challenges in ensuring patient compliance, which is critical to the success of splint therapy. Since arthrocentesis is both faster and less dependent on patient cooperation, we believe it represents a more practical treatment option. As our study did not include patients using occlusal splints, a direct comparison with conservative approaches is not feasible. However, it is worth noting that in the present study arthrocentesis combined with i-PRF injections, when used as a first-line treatment without splints, still resulted in significant pain relief and improved mouth opening. Although the literature provides evidence suggesting that arthrocentesis may be superior to splint-based treatments [26], the authors of the present study believe that it would be premature to adopt a definitive stance on this issue. This is due to the heterogeneity across studies, as well as the existence of reports indicating that splint therapies are more effective, particularly in improving mouth opening [31].

The study's limitations, including its retrospective design and relatively small sample size, suggest that the findings should be interpreted with caution. The absence of blinding due to retrospective design further emphasizes the need for more high-quality research. Self-selection bias may be a concern since the treatment modality was determined based on the patient's preferences following the information provided by the surgeon. The findings are prone to further bias because the multiple injections were suggested by the surgeon and postoperative arthralgia was derived from patients' subjective reports. Follow-up CBCT was not routinely obtained

at T3. Inclusion of CBCT could have provided valuable information regarding hard tissue changes following treatment, which could be considered as another limitation. MRI, with its superior contrast and spatial resolution, offers the best visualization of TMJ soft-tissues, allowing the evaluation of the articular disk and joint effusion. While CBCT effectively visualizes hard tissue structures and changes, it cannot adequately assess soft tissues [32]. MRI was not routinely obtained from patients in the present study, as crepitus was detected during the examination and the osteoarthritis diagnosis was confirmed with CBCT, as recommended by the DC TMD guidelines [33]. However, MRI may offer useful information regarding medullary edema and joint effusion, allowing their correlation to arthralgia to be further studied, as well as the position and form of the articular disc [32].The absence of an MRI also precludes the confirmation of patients' Wilkes classification. The Wilkes classification system for temporomandibular joint disorders relies on both hard and soft tissue assessments, particularly on the status of the articular disc. Since crepitus was present during examination, this would indicate a perforation in the articular disc and place patients of the present study in Wilkes Stage 5 [34]. However without MRI data, it's challenging to confirm this clinical finding. As for a confirmation with CBCT, variations in jaw positioning during CBCT can further complicate assessments of joint space and disc status. Despite limitations, to the best of our knowledge, this is the first study in literature comparing single and multiple i-PRF adjunctive injections.

This study aimed to evaluate the efficacy of single versus multiple adjunctive i-PRF injections following arthrocentesis in patients with TMJ-OA. Both the single-session and three-session i-PRF groups showed similar outcomes in terms of pain and mandibular mobility over a 12-month follow-up period and our hypothesis that multiple injections would yield better results was rejected. This result challenges the notion that multiple i-PRF applications offer greater therapeutic benefits compared to a single session. Given the retrospective design of this study, it is important to evaluate the results with caution, as this design inherently limits the ability to draw definitive conclusions. Future studies should involve randomized controlled trials with larger sample sizes and proper blinding to provide more definitive evidence regarding the benefits of multiple i-PRF injections.

Supplementary Information

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Supplementary Material 1

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Data availability
The dataset supporting the conclusions of this article is included within the supplementary information files.

Declarations

Ethical approval and consent to participate
This study adhered to the Declaration of Helsinki's guidelines for medical protocol. Ethical Board approval was obtained from the University of Health Sciences Hamidiye Ethical Committee of Scientific Research in February 2023 (2023-4/10). All patients were informed regarding the treatment and inclusion of their data to the study and informed consent was obtained from all patients included in the study.

Consent for Publication
NA.

Competing interests
The authors declare no competing interests.

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