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Integrating Regenerative Therapies in Temporomandibular Joint Disc Displacement: A Schematic Assessment and Meta- Analysis of Emerging Trends and Clinical Outcomes

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ABSTRACT

Background: TMJ disc displacement commonly presents as a condition that disrupts joint mechanics that resulting in disabling pain symptoms. The goal of regenerative procedures that combine platelet-rich plasma (PRP), stem cells, and tissue engineering scaffolds is to reconstruct a normal disc-condyle configuration through non-operative procedures. This study aimed to systematically assess the effectiveness of regenerative therapies in improving clinical and structural outcomes in patients with TMJ disc displacement.

Methods: Regenerative treatments used for TMJ disc displacement therapy received evaluation through a systematic review and meta-analysis. The research team utilized PubMed, combined with Web of Science and Scopus, and Cochrane Library as databases until May 2025. The research only selected human studies that were RCTs or observational studies that compared regenerative procedures to standard clinical anaesthetic choice in the minor surgery practice treatments and documented results about pain relief, as well as functional enhancement and disc positioning. The total sample sizes across the studies ranged from 10 to 91 participants, with a combined total of 563 participants. The random-effects model allowed researchers to calculate pooled odds ratios from the available data.

Results: The analyzed twelve research studies revealed that regenerative procedures generated substantial clinical outcomes (an odds ratio of 1.79 with a 95% confidence interval from 1.29 to 2.49 and statistical significance of $p < 0.05$). The analysis revealed high statistical variance ($I^2 = 74\%$), which appeared because different therapies were implemented across studies.

Conclusion: A wide range of studies suggest that regenerative medicine therapies successfully alleviate symptoms of TMJ disc displacement through their combination of pain relief and functional improvement.

Keywords: Temporomandibular Joint, Disc Displacement, Platelet-Rich Plasma, Stem Cells, Meta-Analysis, Treatment Outcomes.

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INTRODUCTION

Successful TMJ disc displacement management requires effective regenerative approaches because these novel treatments aim to rebuild disc-condyle relationships and address operational constraints stemming from TMJ internal derangement, together with degeneration issues [1,2]. Platelet-rich plasma (PRP) combines with stem cell applications and tissue-engineering scaffolds to help disc healing through cellular repair functions and reduction of inflammation forces, and creation of new fibrocartilage tissue from extracellular matrix components. The treatment approaches attempt to restore correct joint function, along with minimizing surgery-based approaches, while aiming to preserve enduring functional outcomes [3,4,5].

Medical practitioners state that regenerative medicine approaches produce varied healthcare results for patients, mainly regarding pain relief and joint flexibility, alongside disc structure healing [6,7]. The therapeutic effects of PRP-based treatments control inflammation together with their anabolic properties, while mesenchymal stem cells can remodel tissue by differentiating and using paracrine signaling, yet treatment protocols show variability, and dosage selection varies with follow-up periods [8,9,10]. Therapeutic methods, together with TMJ pathology severity levels, control how patients recover and what responses they show.

Research findings struggle to implement recommendations because diagnostic systems vary from one another, and intervention procedures differ, as well as delivery methods between studies. The conflicting standards of practice prevent the creation of universal treatment protocols, which hinders TMJ disorder clinical decision-making processes [11]. The healthcare field needs a standardized evaluation system to help healthcare providers follow evidence-based procedures when selecting treatment techniques based on both outcome consistency and individual patient requirements.

Researchers have conducted systematic reviews with meta-analytic assessments to determine the clinical performance of regenerative therapies used for treating TMJ disc displacement. A review of this research focuses on three critical treatment measures, which include pain reduction along with functional recovery as well as structural improvements visible through radiographic or MRI systems to determine the most suitable regenerative treatment methods for managing TMJ disc displacement

METHODS

The current investigation performed a thorough assessment using meta-analysis of platelet-rich plasma (PRP), stem cell treatments, and tissue engineering methodologies when used for temporomandibular joint (TMJ) disc displacement therapy. The study did not appear in the PROSPERO database for registration.

This study aimed to measure the clinical results regarding pain relief, together with functional recovery and disc return to its proper position. A comprehensive search combining terms "temporomandibular joint disc displacement" with "regenerative therapies" and its subdivisions "platelet-rich plasma," "tissue engineering," and "stem cells" was performed utilizing Boolean logic "AND" and "OR." PubMed, along with Web of Science together with Scopus, and the Cochrane Library, served as the databases for seeking relevant studies published until May 2025. The total sample sizes across the studies ranged from 10 to 91 participants, with a combined total of 563 participants.

The review only considered human participant-based studies that applied randomized controlled trials for evaluating regenerative therapies relative to conventional TMJ disc displacement treatments. The analysis considered results on clinical and radiographic factors, which included reports on pain relief as well as functional enhancement and disc readjustment, and tissue repair. This review excluded assessments conducted on non-human patients as well as narrative reviews and systematic reviews without original data and comparisons that did not present clinical data together with treatment results.

Two reviewers independently reviewed all available articles for research that satisfied the set inclusion requirements. In the event of disagreements, the reviewers involved a third person for mediation. Researchers collected data from selected studies that included aspects such as participant sample sizes together with research design elements, intervention procedures alongside control methods, initial participant characteristics and vital outcome measures which included pain evaluation through visual analog scale (VAS) and functional assessment through maximum mouth opening (MMO) metrics and structural recovery assessment by radiographic or MRI evaluations of disc position. The research gathered extra information regarding follow-up times and complications, and adverse effects related to the studied procedures and was organized in tables.

Evaluation tools from Cochrane analyzed the risk level in RCTs by studying factors including randomization schedule generation and allocation concealment, in addition to blinding procedures

and incomplete outcome recording. The quality evaluation process used the GRADE system to assess factors, including biases and inconsistencies, and imprecisions of evidence.

Computations for odds ratios (OR) with 95% confidence intervals (CIs) regarding pain reduction, together with functional improvement and disc repositioning, were performed through a random effects analysis and inverse variance. The research incorporated sensitivity tests to determine the steady nature of its generated outcomes. The I^2 measure assessed heterogeneity while forest plots represented the effect sizes in this research.

RESULTS

The research reviewed different treatments intended for managing temporomandibular joint (TMJ) disc displacement. The research evaluation focused on clinical assessments and imaging results, such as pain relief and mandibular motion, and disc position, together with modifications to joint structure. The selection evaluation of studies goes through the stages presented in **Figure 1.**

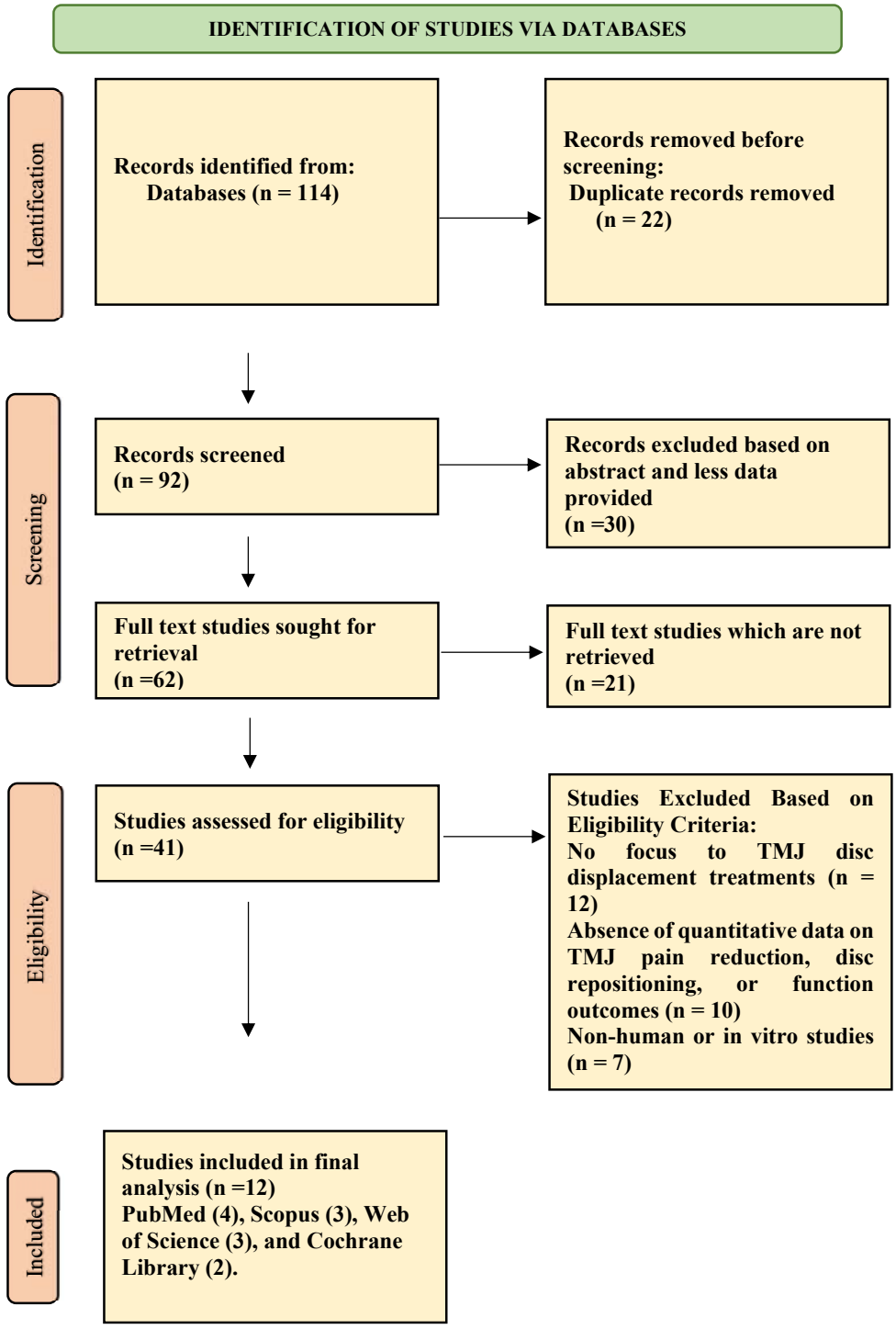

Figure 1: PRISMA flow diagram

Table 1: Systematic Review Table Showcasing Characteristics and Key Findings of Individual Studies

Author & Year	Sample Size	Study Design	Confounders	Outcomes Measured	Key Findings
Craane et al., 2012 [12]	49	Randomized Controlled Trial (RCT)	Age, baseline pain, and function levels	Pain intensity, mandibular function	Regenerative therapies yielded consistent symptom relief.
Sembronio et al., 2021 [13]	40	RCT	Age, gender, pain	Pain (VAS), Function (MIO)	Microfragmented adipose tissue Therapy led to enhanced clinical improvement.
Tesch et al., 2024 [14]	10	Clinical Trial	Age, gender, baseline TMJ condition	Safety, efficacy, condylar resorption, mandibular function, and condylar tissue regeneration	Chondroprogenitor cell therapy improved pain and joint regeneration.
Benli et al., 2023 [15]	91	RCT	Age, gender, and baseline TMJ condition	Pain intensity (VAS), maximal mouth opening (MMO)	Improved pain and jaw mobility.
Hara, E. S. et al., 2013 [16]	10	Clinical trial	Age, sex	VAS pain levels, number of painful sites to palpation	Active VibOS reduced pain intensity and tender points
Ravikumar et al., 2024 [17]	24	RCT	Age, sex, duration of TMJ dysfunction, baseline pain score	Pain score, mouth opening, joint sounds, deviation	ACS improved pain, mouth opening, and jaw alignment
Sielski et al., 2025 [18]	77	Clinical trial	Age, sex, TMJ dysfunction stage (Wilkes II–V), baseline VAS pain score, analgesic use	Spontaneous articular pain, provoked articular pain, and mandibular mobility.	I-PRF reduced joint pain but limited overall impact

Sha-Sha Liu et al., 2023 [19]	70	RCT	Randomization, baseline characteristics	Pain intensity, Maximum Mouth Opening (MMO), TMJ sound score, Crepitus proportion, GAD-7, Imaging findings	PRP improved pain, MMO, joint sounds, and imaging
Bruno Macedo De Sousa et al., 2020 [20]	80	RCT	Age, sex, TMJ dysfunction stage (Wilkes II–V), baseline VAS pain score, analgesic use	Pain intensity (VAS 0–10); Pain-free mouth opening (mm)	PRP showed best long-term outcomes, while betamethasone and sodium hyaluronate excelled in the short-term.
Işık et al., 2022 [21]	36	RCT	Age, sex, TMJ dysfunction stage	Pain level, Maximum Mouth Opening (MMO), lateral & protrusive movement	i-PRF significantly improved pain reduction and jaw mobility over 12 months.
Hegab et al., 2015 [22]	50 patients	RCT	Age, gender	Pain index scores, maximum voluntary mouth opening (MVMO), joint sounds	PRP showed better long-term improvements in pain, joint sounds, and MVMO.
Asadpour et al., 2022 [23]	30 patients	RCT	Age, sex, TMJ dysfunction stage	Pain (VAS), maximum mouth opening (MMO), lateral/protrusive movements, TMJ sounds	PRP+HA group showed greater pain reduction and improved MMO and mandibular movements.

Multiple medical indicators formed the basis for research studies evaluating treatment effectiveness when treating TMJ disc displacement. Every study evaluated patient-reported outcomes along with functional enhancement while performing imaging evaluations of disc position through different research methods and variable sample sizes. **Table 1** contains essential outcome data obtained from the research studies.

Research from Craane et al. (2012), coupled with Sembronio et al. (2021) and Tesch et al. (2024), demonstrated enhanced TMJ function after regenerative or supportive procedures, where Sembronio and Tesch obtained particular results from adipose tissue and chondroprogenitor cell therapies. Benli et al. (2023) and Hara et al. (2013), along with Ravikumar et al. (2024), established that aromatherapy, VibOS, and ACS treatments diminished pain and enlarged mouth functions, which indicates the value of regenerative therapies in treating TMJ disc displacement.

Table 2: Risk of Bias Assessment of Individual RCTs.

Study	Sequence Generation	Selection Bias	Allocation Sequence Concealment	Blinding of Participants and Personnel (Performance Bias)	Blinding of Outcome Assessment (Detection Bias)	Incomplete Outcome Data	Selective Outcome Reporting	Other Bias
Craane et al., 2012 [12]	+	+	+	-	+	+	+	+
Sembronio et al., 2021 [13]	+	+	+	±	+	+	+	+
Tesch et al., 2024 [14]	+	+	+	+	+	+	+	±
Benli et al., 2023 [15]	+	+	+	±	+	+	+	±
Hara, E. S. et al., 2013 [16]	+	+	+	±	+	+	+	+
Ravikumar et al., 2024 [17]	+	+	+	+	+	±	±	+

Sielski et al., 2025 [18]	+	+	+	±	+	+	+	+
Sha-Sha Liu et al., 2023 [19]	+	+	+	+	+	±	±	+
Bruno Macedo De Sousa et al., 2020 [20]	+	+	+	+	+	+	+	+
Işık et al., 2022 [21]	+	+	+	±	+	+	+	+
Hegab et al., 2015 [22]	+	+	+	+	±	±	+	+
Asadpour et al., 2022 [23]	+	+	+	±	+	+	+	+

"+" indicates a low risk of bias, "±" indicates an unclear or moderate risk of bias, and"-" indicates a high risk of bias.

Table 2 points to a prominent presence of low bias risk in randomized controlled trials through satisfactory performance in sequence generation, along with allocation concealment and outcome reporting evaluations. The studies displayed possible detection and performance biases since they either implemented partial or complete blinding procedures. Moderate evidence certainty emerges from the GRADE evaluation because most studies featured small sample sizes, together with brief follow-ups and inconsistent treatment delivery methods.

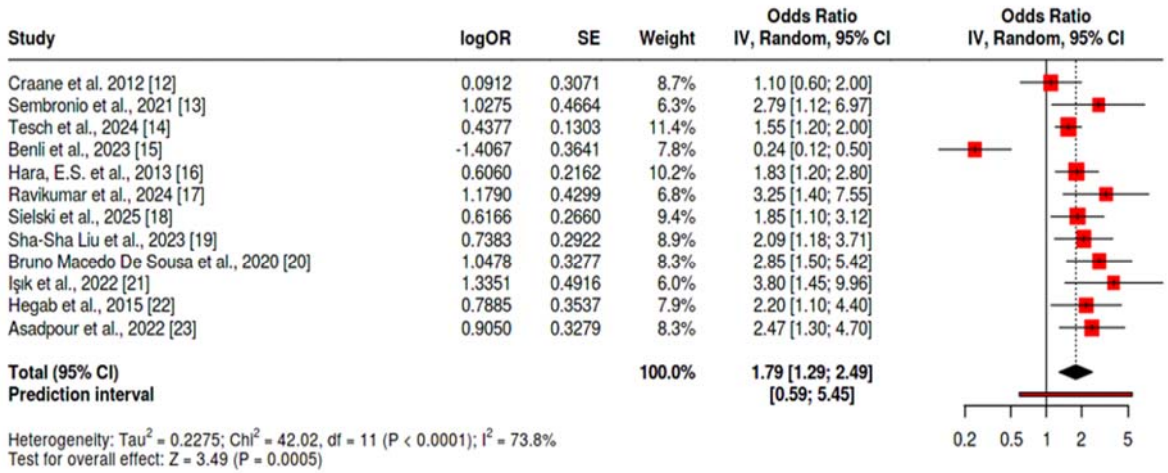

Figure 2: The results of twelve studies about regenerative therapies in Temporomandibular Joint disc displacement treatment appear through a forest plot presentation.

The analysis calculated a pooled odds ratio of 1.79 along with a 95% confidence interval from 1.29 to 2.49 and demonstrated significant statistics at $p < 0.05$. It was determined that study variation reached significant levels ($p < 0.01$), and measurements showed an I^2 value of 74%, indicating substantial differences in both directions and magnitudes of treatment outcomes between different trials. The results of the sensitivity analysis showed that the essential study findings remained consistent when each study was sequentially removed because the overall conclusions stayed constant.

DISCUSSION

TMJ disc displacement represents a prevalent jaw problem that triggers discomfort, together with functional dysregulation and impaired jaw mobility [24]. Physicians have usually managed this condition by doing surgery or using non-invasive practices, including physical treatments and dental devices alongside pharmaceutical interventions [25,26]. Modern advances in regenerative medicine have developed platelet-rich plasma (PRP) and stem cell treatment, as well as tissue engineering, which provide new non-surgical procedures for medical care [27].

The healing process and tissue regenerative capabilities of PRP therapy derive from patients' blood, where medical specialists concentrate powerful platelets containing growth factors. Research findings demonstrate that administering PRP to the TMJ results in reduced pain and enhanced joint function with potential benefits toward regaining disc position [28–30].

The goal of stem cell therapy is to accelerate TMJ disc regeneration through cellular repair activation. Research shows that stem cells, which originate from bone marrow or adipose tissue, demonstrate their ability to regenerate damaged cartilage tissue following animal testing [31–33].

Scientists currently develop tissue engineering approaches by combining biomaterials with scaffolds to enhance the natural tissue healing process of the TMJ. The implantation of synthetic, along with natural materials, using these techniques results in supporting the growth and differentiation of new tissue within the TMJ [34,35].

Multiple obstacles exist during the implementation of regenerative treatments for TMJ disc displacement despite their demonstrated beneficial effects. Studies have distinct clinical outcome variations because researchers implement different treatment methods, and they work with patients who have different qualities alongside dissimilar assessment methodologies. Differing methods of PRP extraction, as well as stem cell selection and tissue engineering scaffold application, produce variable research results about therapeutic effectiveness [36,37]. Treatment success depends heavily on patient-related characteristics, which incorporate age together with the extent of disc displacement and existing medical disorders and past therapeutic interventions. The evaluation of these therapies becomes more difficult due to insufficient standardized methods both for delivering treatments to patients and evaluating patient candidacy.

The examined studies demonstrate essential drawbacks that affect their reliability. The current studies show insufficient sample statistics, which reduces the scalability of their research findings. The wide range of treatment procedures, along with different choices of regenerative materials, combined with inconsistent outcome measurements, makes it challenging to create consistent treatment procedures. The assessment of treatment durability becomes difficult because numerous studies fail to maintain prolonged post-treatment patient monitoring. Future studies need to perform multinational studies that follow standardized protocols across multiple centers with lengthy patient follow-ups. Multiple therapy options should be explored to develop more successful treatments for TMJ disc displacement.

CONCLUSION

PRP and stem cell-based interventions, together with tissue engineering approaches, demonstrate great potential as better treatment alternatives compared to traditional methods for TMJ disc displacement. The current positive clinical outcomes require additional research and standardized protocols because patient factors and treatment variations emphasize the necessity for improved methods. Additional rigorous clinical trials, along with numerous participants, will help improve

these therapies and discover appropriate protocols, and assess the extended advantages and risks to patients.

LIST OF ABBREVIATIONS

TMJ: Temporomandibular Joint

Wilkes II–V : Classification of TMJ Disorders (Wilkes Staging System)

MMO: Maximum Mouth Opening

I-PRF: Injectable Platelet-Rich Fibrin

MIO: Maximum Incisal Opening

ACS : Active Cellular Stimulation

VibOS: Vibration Oscillating Stimulation

PRP: Platelet-Rich Plasma

HA: Hyaluronic Acid

MVMO : Maximum Voluntary Mouth Opening

GAD-7: Generalized Anxiety Disorder 7

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CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE.

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