Inside the joint

Redefining the role of minimally invasive surgery
for temporomandibular joint disorders

Yang Hang Tang

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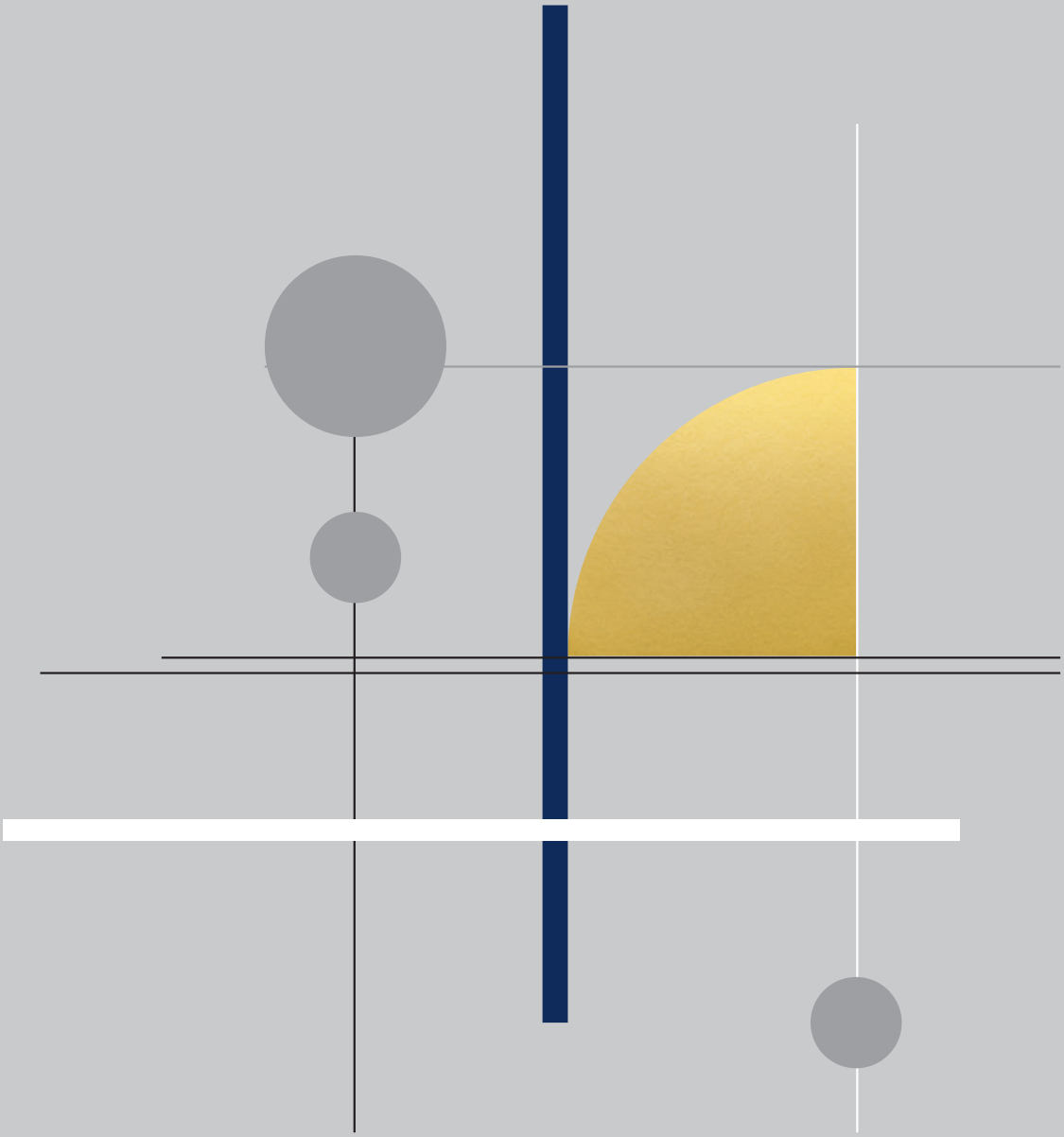
Table of contents



CHAPTER 1

GENERAL INTRODUCTION

The temporomandibular joint (TMJ) is a unique synovial joint that allows both a hinge-like and sliding movement. Anatomically, the joint comprises the mandibular condyle and the mandibular fossa of the temporal bone, enclosed and stabilized by a fibrous capsule and multiple ligaments. The articular disc, a fibrocartilage cushion, divides the joint into an upper and lower compartment and facilitates smooth articulation and effective load distribution during function[1] **(Figure 1)**. Together with the masticatory muscles, these structures cooperate precisely to enable complex mandibular movements required for daily functions while also maintaining occlusal stability[1].

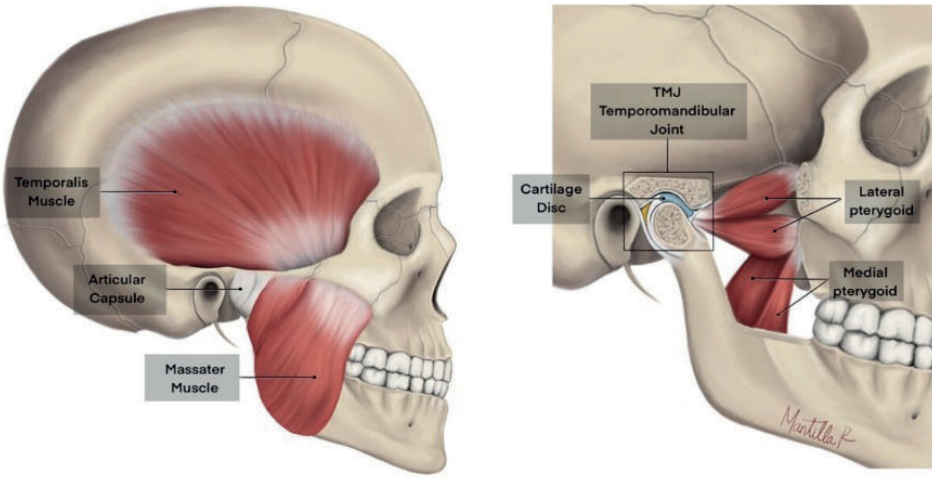


Figure 1. Anatomical structures of the masticatory system, composed of the masticatory muscles and the temporomandibular joint. The articular capsule surrounds and stabilizes the joint. The articular disc allows effective load distribution over the articular surfaces. Source: Buller M, Ibelli TJ, Mantilla-Rivas E, et al. A Plastic Surgeon's Guide to the Temporomandibular Joint: Part I, Anatomy. FACE. 2023;4(2):228-231. Reprint permission pre-approved.

Temporomandibular dysfunction and its classifications

Pathologies arising within the masticatory system are collectively referred to as temporomandibular dysfunction (TMD). According to the American Academy of Orofacial Pain, TMD is defined as "a group of disorders involving the masticatory muscles, the temporomandibular joint and the associated structures"[2]. TMD is one of the most common causes of chronic orofacial pain, affecting 5-16% of the population worldwide and occurring at least twice as often in women, typically between ages of 20 and 40[3,4]. The clinical presentation includes pain, restricted motion, joint locking, and joint noises[4–6], which can significantly impair quality of

life[7,8] and contribute to a considerable socioeconomic burden, with costs estimated to be about twice those of unaffected individuals[9].

Despite its high prevalence and public health significance, the conceptual and clinical understanding of TMD remains ambiguous. In routine clinical practice, the term "TMD" is still often used as an umbrella term for a heterogeneous group of conditions involving distinct anatomical structures and often characterized by distinct pathophysiological mechanisms. This lack of specificity has created ambiguity in research and patient care, as a "one-size-fits-all" approach to diagnosis, management and research is frequently applied. Consequently, treatment outcomes are often suboptimal and external validity of research findings is often limited[10,11].

To address these challenges and improve diagnostic precision, the Diagnostic Criteria for Temporomandibular Dysfunction (DC/TMD)[5] were introduced. This dual-axis framework integrates both a somatic (axis I) and psychosocial (axis II) domain and distinguishes between primarily joint-related and primarily muscle-related disorders. In clinical practice, however, this distinction is often less clear, as symptoms of both myogenous and arthrogenous origin frequently present concurrently[6,11,12]. Nevertheless, accurately identifying the primary origin of symptoms is critical for effective treatment planning and enhancing the specificity of research methodologies[10,11,13].

Temporomandibular joint disorders

Within the DC/TMD, joint-related TMDs are classified as distinct entities. Pain (i.e., arthralgia) is one of the primary symptoms of intra-articular pathology affecting approximately 7% of the population[14]. Although a variety of entities may lead to arthralgia, the most commonly associated diagnoses are disc displacements and degenerative joint disease (DJD)[14,15].

Disc displacement

Disc displacement refers to an abnormal positional relationship between the articular disc and the mandibular condyle, which in almost all cases is characterized by an anterior shift[16]. Two main subtypes are recognized: anterior disc displacements with reduction (ADDwR) and anterior disc displacements without reduction (ADDwoR). In ADDwR, the displaced disc repositions to its "correct" position during mouth opening, whereas in ADDwoR it remains anteriorly displaced. However, the definition of a "correct" disc position remains a subject of debate. While many

consider a 12 o'clock position of the posterior edge of the disc ideal, approximately 30% of asymptomatic individuals exhibit an anteriorly positioned disc, suggesting that the latter may represent a normal anatomical variation or physiological process rather than pathology[16–19]. Since radiologically confirmed anteriorly positioned discs do not consistently correlate with dysfunction or pain[19–21], a clinical and conceptual distinction should be made between an asymptomatic anterior disc *position* and the clinically more relevant symptomatic anterior disc *displacement*[6,18].

Degenerative joint disease

DJD encompasses both osteoarthrosis and osteoarthritis. Whereas in the past a distinction between both terms was made in the dental TMJ literature based on the presence or absence of pain, both nomenclatures are now classified under one term due to inconsistencies in its use. Instead, the process is now described as DJD with or without arthralgia[5]. The condition is characterized by progressive degeneration of the articular cartilage and abnormal remodeling of the underlying bone[15,22]. It has a non-inflammatory origin, unlike pathologies like rheumatoid arthritis[15], but mechanical loading changes often induce a secondary inflammatory response in the joint that contributes to pain and dysfunction[6,15]. Persistent inflammation can lead to bony changes that are detectable through imaging. Given that many individuals with degenerative changes remain asymptomatic and do not seek treatment, it is worth considering whether a distinction should be made between the conceptual and clinical diagnosis of DJD.

Relation between disc displacements and degenerative joint disease

Although disc displacements and DJD are regarded as separate entities, they often coexist and share a strong association[6,23]. Whether disc displacements are the result or the cause of DJD remains debated, and clear associations have not been established to date. Imaging studies suggest that disc displacement increases the likelihood of degenerative changes[24,25], supporting the view that altered biomechanics in the joint induce inflammation and subsequent joint degradation[26]. Contrarily, others suggest that disc displacements are a manifestation of degeneration, where an alteration of the sliding properties of the joint surfaces leads to disc hesitation and displacement[6,27]. Since degenerative changes can be present with a "normal" disc position[6,25] and disc positions other than the 12 o'clock position are often not seen with degenerative changes[23,25], it is likely that neither condition is an exclusive cause of the other.

Taken together, these findings point toward a bi-directional relationship in which disc displacement and DJD likely represent interrelated manifestations of a shared degenerative process. This perspective supports the view that the TMJ is a dynamic, integrated organ in which the articular disc, the synovium and the subchondral bone function as interdependent structures[6]. Mechanical, inflammatory or degenerative alterations in any component can disrupt joint loading and the local biochemical environment, affecting the integrity of the entire system. From this perspective, symptomatic disc displacements and DJD reflect a disturbed homeostatic state of the joint, underscoring the importance of viewing the TMJ as an integrated functional unit rather than focusing on isolated structural findings[6].

Etiology and pathophysiological mechanisms of TMJ disorders

The etiology and pathogenesis of degeneration of the TMJ remains incompletely understood. Historically, considerable emphasis was placed on the role of dental occlusion as a causal factor, a perspective that shaped clinical management for years[28,29]. Although this occlusion-centered approach still influences clinical practice, recent evidence has largely refuted a primary role of dental occlusion as a cause for TMD, suggesting that clinicians should abandon this "old-fashioned gnathological paradigm"[29]. Instead, current research supports a biopsychosocial framework, which views TMDs as multifactorial conditions arising from interactions between biological, mechanical and psychosocial processes[5]. In this model, joint-related disorders such as disc displacements and DJD are thought to be primarily characterized by biomechanical overloading and maladaptive joint responses, leading to inflammation and progressive cartilage and bone degradation[15,30]. These mechanisms operate within a broader biopsychosocial context that recognizes the influence of psychosocial factors on symptom experience and expression[5]. The following sections focus primarily on the mechanical and biological concepts of TMJ disorders, while shortly acknowledging their integration within a wider psychosocial framework.

Mechanical and biological framework

Pathologies of the TMJ are believed to develop from a disturbance in the joint homeostasis, in which mechanical forces exceed the joint's adaptive capabilities for tissue synthesis and repair[6,15]. In healthy joints, mechanical stress induces constant remodeling of the joint's articular surfaces to allow proper loading and maintain joint integrity[15,31]. This dynamic balance may be disturbed in two ways: absolute overloading, where excessive mechanical forces are applied to normally

adaptive tissue (e.g., trauma, parafunction), and relative overloading, where normal mechanical forces act on tissues with reduced adaptive capabilities (e.g., systemic disease, hormonal imbalance or genetic predisposition)[31–33]. From this perspective, TMJ disorders are best understood as existing along a continuum of adaptive and degenerative responses, rather than as isolated pathological states **(Figure 2)**.

Excessive mechanical loading of the joint triggers the release of molecular mediators, including reactive oxygen species, pro-inflammatory cytokines (predominantly interleukin-1 and -6, tumor necrosis factor-α), catabolic enzymes (such as matrix metalloproteinases) and breakdown products into the synovial fluid[15,30,31]. These biochemical changes induce a secondary synovial inflammatory response (i.e., synovitis) and accelerate cartilage and subchondral bone degradation, further disturbing the homeostatic balance of the joint[15,34] **(Figure 2)**.

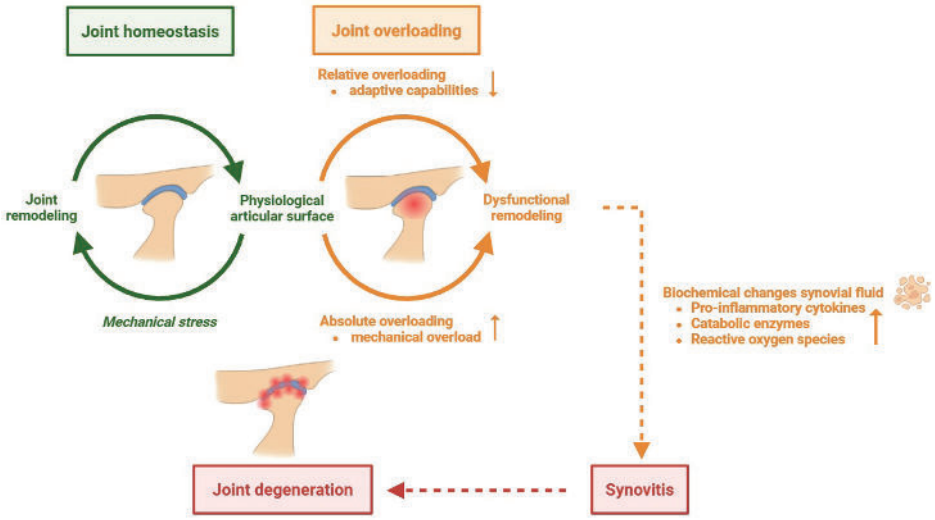


Figure 2. Pathophysiological mechanism of temporomandibular joint degeneration. Under physiological circumstances, mechanical stress induces joint remodeling that maintains homeostasis. Joint overloading of the joint occurs when the adaptive capabilities of the joint are compromised (relative overloading) or when excessive mechanical forces are applied (absolute overloading), resulting in maladaptive remodeling. This triggers biochemical changes in the synovial fluid, including release of pro-inflammatory cytokines, catabolic enzymes and reactive oxygen species, resulting in synovitis and progressive cartilage and bone degeneration.

This inflammatory cascade is now considered the primary cause of clinical symptoms in TMJ disorders. Contrary to earlier assumptions, joint pain arises primarily from inflammatory processes rather than mechanical interferences such as disc displacements. Elevated levels of pro-inflammatory cytokines and pain mediators following joint overloading are the main cause of synovitis and pain[19,35–37]. Likewise, a restricted mouth opening, traditionally attributed to mechanical impingement from a non-reducing displaced disc[5,19,38], is instead associated with synovitis-induced fibrous adhesions or an analgesic muscle inhibition reflex, a protective mechanism that deactivates the muscles around the joints with pain and inflammation[19]. Collectively, these findings suggest that synovitis and its associated intra-articular molecular cascades play a central role in the pathogenesis of TMJ disorders.

Psychosocial framework

Psychosocial factors play a significant role in modulating pain perception and disease experience in TMJ disorders. Growing evidence indicates a mutually strengthening relationship between mental health and TMJ pathology, contributing to a complex disease process[39]. Patients with TMJ disorders frequently show elevated levels of psychological distress, pain catastrophizing, depression, anxiety, somatization and maladaptive coping behaviors[5,39–41]. These factors can influence pain perception by altering pathophysiological mechanisms of pain modulation, especially when nociceptive signals are prolonged.

Clinical course

The clinical course of TMJ disorders is variable but generally favorable[4]. Longitudinal studies show that, in most patients, symptoms resolve spontaneously without specific interventions[42,43]. This self-limiting course is attributed to the adaptive capacities of the joint, whereby structural and functional remodeling allows changes in mechanical loading and gradually restores homeostasis[6].

However, a subset of patients follows a less favorable trajectory[44]. In these cases, delayed or inadequate treatment may result in prolonged periods of pain and functional impairments. A persistent nociceptive stimulation can induce peripheral sensitization, characterized by increased excitability of pain receptors[45,46]. When this nociceptive input continues, it subsequently may lead to central sensitization, in which neuroplastic changes within the central nervous system lower pain thresholds and increase pain responses, such as allodynia and hyperalgesia, even after the initial pain stimulus has resolved[47,48]. These mechanisms increase the likelihood of

pain chronicity and explain why symptoms may persist despite management of the primary joint pathology[45,46].

A proper understanding of the factors that influence this variable course is therefore crucial for optimizing patient care. Identifying patients at risk of symptom chronicity and structural degeneration remains challenging, underscoring the need for high-quality, longitudinal research to determine prognostic factors for TMJ disease progression.

Current treatment paradigm for TMJ disorders

Effective management of TMJ disorders begins with a systematic diagnostic process, including a detailed anamnesis and clinical examination consistent with the DC/TMD framework[5]. Imaging is used to confirm specific subdiagnoses. Magnetic resonance imaging (MRI) is preferred for evaluating the position of the articular disc and other soft tissue to diagnose disc displacements. Cone-beam computed tomography (CBCT) or conventional computed tomography (CT) is used to detect osseous changes consistent with DJD[5,49].

"Form follows function"

As discussed in the previous paragraphs, current evidence indicates that pain and dysfunction are mostly associated with synovitis, capsular pathology and biochemical alterations within the joint, rather than disc malposition itself. Consequently, TMJ disorders are regarded primarily as functional disturbances rather than purely structural pathologies. Therefore, initial treatments should prioritize symptom relief and restoration of function, moving away from earlier disc-focused paradigms that aimed to correct joint anatomy[19,35,50]. This treatment concept aligns with the principle that ***"form follows function"***: once normal joint function is restored, the surrounding morphology may adapt to a new state of homeostasis without the need for anatomical correction.

Stepwise treatment approach

Within the current function-focused treatment paradigm, first-line treatments consist of reversible, conservative treatments like patient education, physical therapy, anti-bruxism splints and pharmacological treatments (e.g., nonsteroidal anti-inflammatory drugs, muscle relaxants and antidepressants)[35,51,52]. These interventions aim to reduce joint loading and inflammation while retaining function, and they are sufficient for the majority of patients.

Minimally invasive surgical methods, such as arthrocentesis and arthroscopy, are often only indicated when conservative treatments provide insufficient symptom relief[35,52]. Arthrocentesis involves the lavage of the upper TMJ space[53] to promote tissue recovery by removing inflammatory cytokines and matrix-degrading enzymes which are thought to be responsible for symptoms[54,55]. It is usually performed through two needles using saline or Ringer's lactate solution as irrigant. The ideal lavage volume needs yet to be determined, but evidence suggests at least 300ml is necessary to achieve optimal removal of inflammatory cytokines[55]. Reported success rates average around 83.5%[56]. Arthrocentesis emerged as a simplified, derivative of arthroscopy, developed after arthroscopic studies demonstrated that symptomatic improvement could be achieved without disc repositioning[57], suggesting that lavage has a central therapeutic role.

TMJ arthroscopy involves inserting a small endoscope into the upper TMJ compartment, allowing visualization of the intra-articular structures and performance of targeted therapeutic maneuvers such as lysis of adhesions, deposition of medication into inflamed tissue and electrocauterization of redundant and hyperaemic tissue. During the procedure, continuous lavage is performed to distend the joint space and provide clear vision **(Figure 3)**. Since its introduction, technical advancements have led to different arthroscopic levels based on complexity and invasiveness. These range from simple diagnostic arthroscopy (level I) or arthroscopic lysis and lavage (ALL) under local anesthesia, to more advanced arthroscopic surgery (AS), without (level II) or with (level III) disc repositioning and fixation procedures under general anesthesia[58,59]. Reported success rates range between 50% and 96%[60].

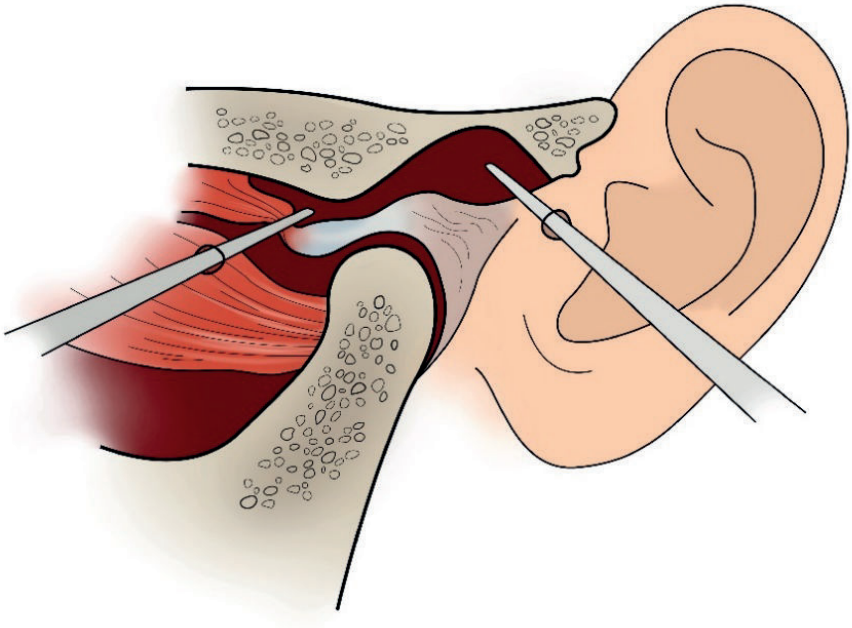


Figure 3. Introduction of two portals during TMJ arthroscopy into the upper joint space. The upper and lower joint spaces are enlarged for illustrative purposes. Source: Tang YH, van Bakelen NB, Spijkervet FKL. [Minimally invasive treatments and open joint surgery for disorders of the temporomandibular joint]. Ned Tijdschr Tandheelkd. 2024 May;131(5):223-230. Dutch.

Finally, open joint surgery is only reserved for a few advanced or refractory cases involving severe structural damage, ankylosis or severely debilitating end-stage DJD. These interventions include discectomy, arthroplasty, or when no other option remains, total joint replacement. Contemporary position statements, including those from the American Association of Oral and Maxillofacial Surgeons (AAOMS) emphasize that these irreversible surgical methods should be only undertaken after exhausting all conservative and minimally invasive surgical options[35,51,52].

Limitations and evidence gaps in current treatment paradigm

Despite the widespread acceptance of a stepwise treatment approach, its clinical implementation remains inconsistent and characterized by several knowledge gaps. The first knowledge gap concerns the timing of treatment escalation when conservative interventions fail. Currently, no consensus exists on how to define treatment failure or when to proceed to minimally invasive surgery. Consequently, clinicians often rely on individual judgement rather than standardized, evidence-based criteria, resulting in variability in practice. Furthermore, because TMJ disorders are often self-limiting, treatment escalation in patients who could benefit from earlier intervention is often delayed. This delay can lead to prolonged pain and dysfunction and increases the risk of chronicity, which in turn may reduce responsiveness to subsequent interventions[61]. Extended conservative treatments also place a greater burden on healthcare resources[62] and requires sustained patient compliance. Identifying the optimal timing for minimally invasive surgery is therefore crucial to optimizing patient care. Although a growing body of evidence suggests that earlier intervention may enhance recovery and functional outcomes[63,64], the ideal timing for minimally invasive treatments and their comparative results with conservative treatments are still lacking[65].

The second knowledge gap involves the selection of minimally invasive surgical technique. While arthroscopy and arthrocentesis demonstrate high efficacy in symptom reduction, their relative effectiveness compared with each other and indications remain understudied. Arthrocentesis offers simplicity and lesser invasiveness, whereas arthroscopy allows for diagnostic visualization and targeted therapeutic maneuvers. Few studies have directly compared the two modalities, leaving clinicians without clear evidence to guide the choice between them.

The third knowledge gap concerns the management of patients who do not respond sufficiently to initial minimally invasive surgery. While a few studies have reported beneficial outcomes of re-arthroscopy[66,67], research evaluating the full spectrum of subsequent treatments remains scarce. Specifically, no study has comprehensively investigated the retreatment outcomes after unsuccessful initial arthrocentesis. Gaining insights into retreatment success rates, predictors of treatment success and the optimal sequencing of retreatments may contribute to a more structured, evidence-based pathway for managing refractory cases.

Thesis outline and aims

While the current stepwise approach provides a framework for TMJ disorder management, its clinical application is hindered by a few challenges: 1) the absence of consensus for treatment escalation after conservative treatments, 2) the lack of comparative evidence between minimally invasive surgical methods and 3) the uncertainty regarding retreatment strategies after failed initial arthrocentesis. The purpose of this thesis is to redefine the role of minimally invasive surgery for TMJ disorders by addressing these three gaps. Chapters **2-4** address the first knowledge gap, chapters **5-7** the second and chapter **8** the third. Specifically, the study aims are as follows:

1. To systematically review the current literature to evaluate the clinical efficacy of arthrocentesis for symptomatic TMJ disorders, by comparing it to conservative treatment at all endpoints and for all clinical outcomes (**Chapter 2)**.

2. To evaluate the long-term efficacy of arthrocentesis as treatment for temporomandibular joint arthralgia compared to conservative treatments in a randomized controlled trial **(Chapter 3)**

3. To assess whether the timing of initial arthrocentesis for TMJ arthralgia affects treatment outcomes in a cohort study (**Chapter 4)**

4. To systematically review the current literature to evaluate the clinical efficacy of arthroscopy for symptomatic TMJ disorders, by comparing it to arthrocentesis as well as to conservative treatment at all endpoints and for all clinical outcomes (**Chapter 5, Chapter 6)**.

5. To evaluate the efficacy of arthroscopy as treatment for TMJ pain and dysfunction compared to arthrocentesis in a randomized controlled trial (**Chapter 7)**

6. To examine the prevalence and success rates of retreatments in TMJ arthralgia patients who did not achieve adequate symptom relief with initial arthrocentesis in a cohort study (**Chapter 8**).

References

1. Buller M, Ibelli TJ, Mantilla-Rivas E, et al. A Plastic Surgeon's Guide to the Temporomandibular Joint: Part I, Anatomy. *Face*. 2023;4(2):228-231. doi:10.1177/27325016231171619
2. de Leeuw R, G K. *Orofacial Pain: Guidelines for Assessment, Diagnosis, and Management*. 6th ed. Quintessence; 2018.
3. National Institute of Dental and Craniofacial Research. Temporomandibular Disorders and Jaw Pain. Accessed November 8, 2025. https://www.nidcr.nih.gov/research/data-statistics/temporomandibular-disorders-jaw-pain
4. Kapos F, Exposto F, Oyarzo J, Durham J. Temporomandibular disorders: a review of current concepts in aetiology, diagnosis and management. *Oral Surg*. 2020;13(4):321-334. doi:10.1111/ors.12473
5. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *J oral facial pain headache*. 2014;38(1):6-27.
6. Stegenga B. Osteoarthritis of the Temporomandibular Joint Organ and Its Relationship to Disc Displacement. *J Orofac Pain*. 2001;15(3):193-205.
7. Dahlstrom L, Carlsson G. Temporomandibular disorders and oral health-related quality of life. A systematic review. *Acta Odontol Scand*. 2010;68(2):80-85. doi:10.3109/00016350903431118
8. Almoznino G, Zini A, Zakuto A, et al. Oral health-related quality of life in patients with temporomandibular disorders. *J oral facial pain headache*. 2015;29(4):231-241. doi:10.11607/ofph.1413
9. White B, Williams L, Leben J. Health Care Utilization and Cost among Health Maintenance Organization Members with Temporomandibular Disorders. *J Orofac Pain*. 2001;15(2):158-169.
10. Laskin D. Putting order into temporomandibular disorders. *J Oral Maxillofac Surg*. 1998;56(2):121. doi:10.1016/S0278-2391(98)90846-1
11. Laskin D. Temporomandibular disorders: a term past its time? *J Am Dent Assoc*. 2008;139(2):124-128. doi:10.14219/jada.archive.2008.0115
12. Slade GD, Bair E, Greenspan JD, et al. Signs and symptoms of first-onset TMD and sociodemographic predictors of its development: The OPPERA prospective cohort study. *J Pain*. 2013;14(12 SUPPL.). doi:10.1016/j.jpain.2013.07.014
13. Garstka AA, Kozowska L, Kijak K, et al. Accurate Diagnosis and Treatment of Painful Temporomandibular Disorders: A Literature Review Supplemented by Own Clinical Experience. *Pain Res Manag*. 2023;2023. doi:10.1155/2023/1002235
14. Valesan L, Da-Cas C, Réus J, et al. Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. *Clin Oral Investig*. 2021;25(2):441-453. doi:10.1007/s00784-020-03710-w

15. Tanaka E, Detamore MS, Mercuri LG. Degenerative disorders of the Temporomandibular joint: etiology, diagnosis, and treatment. *J Dent Res*. 2008;87(4):296-307. doi:10.1177/154405910808700406

16. Poluha RL, De La Torre Canales G, Costa YM, Grossmann E, Bonjardim LR, Conti PCR. Temporomandibular joint disc displacement with reduction: A review of mechanisms and clinical presentation. *J Appl Oral Sci*. 2019;27. doi:10.1590/1678-7757-2018-0433

17. Pereira F, Lundh H, PL W. Morphologic changes in the temporomandibular joint in different age groups: An autopsy investigation. *Oral Surgery, Oral Med Oral Pathol*. 1994;78(3).

18. Türp JC, Schlenker A, Schröder J, Essig M, Schmitter M. Disk displacement, eccentric condylar position, osteoarthrosis - misnomers for variations of normality? Results and interpretations from an MRI study in two age cohorts. *BMC Oral Health*. 2016;16(1). doi:10.1186/s12903-016-0319-4

19. Mercuri L, Greene C, Manfredini D. The temporomandibular joint disc: A complex fable about an elusive butterfly. *Cranio*. Published online 2025:1-8. doi:https://doi.org/10.1080/08869634.2025.2477963

20. Leeuw R de, Boering G, Kuijl B van der, Stegenga B. Hard and soft tissue imaging of the temporomandibular joint 30 years after diagnosis of osteoarthrosis and internal derangement. *J Oral Maxillofac Surg*. 1996;54:1270-1280.

21. Dolwick MF. Intra-articular disc displacement part I: Its questionable role in temporomandibular joint pathology. *J Oral Maxillofac Surg*. 1995;53(9):1069-1072. doi:10.1016/0278-2391(95)90126-4

22. Zarb G, Carlsson G. Temporomandibular Disorders: Osteoarthritis. *J Orofac Pain*. 1999;13(4):295-306.

23. Silva MAG, Pantoja LLQ, Dutra-Horstmann KL, et al. Prevalence of degenerative disease in temporomandibular disorder patients with disc displacement: A systematic review and meta-analysis. *J Cranio-Maxillofacial Surg*. 2020;48(10):942-955. doi:10.1016/j.jcms.2020.08.004

24. Dias IM, Coelho PR, Assis NMSP, Leite FPP, Devito KL. Evaluation of the correlation between disc displacements and degenerative bone changes of the temporomandibular joint by means of magnetic resonance images. *Int J Oral Maxillofac Surg*. 2012;41(9):1051-1057. doi:10.1016/j.ijom.2012.03.005

25. Roh HS, Kim W, Kim YK, Lee JY. Relationships between disk displacement, joint effusion, and degenerative changes of the TMJ in TMD patients based on MRI findings. *J Cranio-Maxillofacial Surg*. 2012;40(3):283-286. doi:10.1016/j.jcms.2011.04.006

26. Cortés D, Exss E, Marholz C, Millas R, Moncada G. Association between disk position and degenerative bone changes of the temporomandibular joints: An imaging study in subjects with TMD. *Cranio - J Craniomandib Sleep Pract*. 2011;29(2):117-126. doi:10.1179/crn.2011.020

27. de Bont LGM, Stegenga B. Pathology of temporomandibular joint internal derangement and osteoarthrosis. *Int J Oral Maxillofac Surg*. 1993;22(2):71-74. doi:10.1016/S0901-5027(05)80805-7

28. Turp J, Greene C, Strub J. Dental occlusion: a critical reflection on past, present and future concepts. *J Oral Rehabil.* 2008;35:446-453.

29. Manfredini D, Lombardo L, Siciliani G. Temporomandibular disorders and dental occlusion. A systematic review of association studies: end of an era? *J Oral Rehabil.* 2017;44(11):908-923. doi:10.1111/joor.12531

30. Wang XD, Zhang JN, Gan YH, Zhou YH. Current understanding of pathogenesis and treatment of TMJ osteoarthritis. *J Dent Res.* 2015;94(5):666-673. doi:10.1177/0022034515574770

31. Stegenga B. Nomenclature and classification of temporomandibular joint disorders. *J Oral Rehabil.* 2010;37(10):760-765. doi:10.1111/j.1365-2842.2010.02146.x

32. Slade GD, Ohrbach R, Greenspan JD, et al. Painful temporomandibular disorder: decade of discovery from OPPERA studies. *J Dent Res.* 2016;95(10):1084-1092.

33. Delpachitra S, Dimitroulis G. Osteoarthritis of the temporomandibular joint: a review of aetiology and pathogenesis. *Br J Oral Maxillofac Surg.* 2022;60:387-396.

34. Haskin CL, Milam SB, Cameron IL. Pathogenesis of degenerative joint disease in the human temporomandibular joint. *Crit Rev Oral Biol Med.* 1995;6(3):248-277. doi: 10.1177/10454411950060030601

35. Bouloux GF, Chou J, DiFabio V, et al. The Contemporary Management of Temporomandibular Joint Intra-Articular Pain and Dysfunction. *J Oral Maxillofac Surg.* 2024;82(6):623-631. doi:10.1016/j.joms.2024.01.003

36. Herb K, Cho S, Stiles MA. Temporomandibular joint pain and dysfunction. *Curr Pain Headache Rep.* 2006;10(6):408-414. doi:10.1007/s11916-006-0070-7

37. Hamada Y, Kondoh T, Holmlund AB, et al. Inflammatory cytokines correlated with clinical outcome of temporomandibular joint irrigation in patients with chronic closed lock. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology.* 2006;102(5):596-601. doi:10.1016/j.tripleo.2005.11.010

38. Sidebottom A. How do I manage restricted mouth opening secondary to problems with the temporomandibular joint? *Br J Oral Maxillofac Surg.* 2012;51:469-472.

39. Wan J, Lin J, Zha T, et al. Temporomandibular disorders and mental health: shared etiologies and treatment approaches. *J Headache Pain.* 2025;26(1). doi:10.1186/s10194-025-01985-6

40. Dougall AL, Jimenez CA, Haggard RA, Stowell AW, Riggs RR, Gatchel RJ. Biopsychosocial Factors Associated With the Subcategories of Acute Temporomandibular Joint Disorders. *J Orofac Pain.* 2012;26(817):7-16.

41. Yap AUJ, Tan KBC, Kiam Chua E, Tan HH. Depression and somatization in patients with temporomandibular disorders The evaluation of psychological profiles. *J Prosthet Dent.* 2002;88(5):479-484.

42. Kurita K, Westesson P, Yuasa H, Toyama M, Machida J, Ogi N. Natural Course of Untreated Symptomatic Temporomandibular Joint Disc Displacement without Reduction. *J Dent Res.* 1998;77(2):361-365.

43. Sato S, Kawamura H, Nagasaka H, Motegi K. The natural course of anterior disc displacement without reduction in the temporomandibular joint: Follow-up at 6, 12, and 18 months. *J Oral Maxillofac Surg.* 1997;*55*(3):234-238. doi:10.1016/S0278-2391(97)90531-0

44. Schiffman EL, Ahmad M, Hollender L, et al. Longitudinal Stability of Common TMJ Structural Disorders. *J Dent Res*. 2017;96(3):270-276. doi:10.1177/0022034516679396

45. Furquim BD, Flamengui LMSP, Conti PCR. TMD and chronic pain: A current view. *Dental Press J Orthod.* 2015;20(1):127-133. doi:10.1590/2176-9451.20.1.127-133.sar

46. Merrill RL. Central Mechanisms of Orofacial Pain. *Dent Clin North Am.* 2007;51(1):45-59. doi:10.1016/j.cden.2006.09.010

47. Cayrol T, Van Den Broeke EN, Gerard E, et al. Chronic temporomandibular disorders are associated with higher propensity to develop central sensitization: A case-control study. *Pain*. 2023;164(5):E251-E258. doi:10.1097/j.pain.0000000000002803

48. La Touche R, Paris-Alemany A, Hidalgo-Pérez A, López-de-Uralde-Villanueva I, Angulo-Diaz-Parreño S, Muñoz-García D. Evidence for Central Sensitization in Patients with Temporomandibular Disorders: A Systematic Review and Meta-analysis of Observational Studies. *Pain Pract.* 2018;18(3):388-409. doi:10.1111/papr.12604

49. Ahmad M, Hollender L, Anderson Q, et al. Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD): Development of Image Analysis Criteria and Examiner Reliability for Image Analysis. 2009;107(6):844-860. doi:10.1016/j.tripleo. 2009.02.023.

50. Dolwick MF. Intra-articular disc displacement part I. Its questionable role in temporomandibular joint pathology. *J Oral Maxillofac Surg.* 1995;53(9):1069-1072. doi:10.1016/0278-2391(95)90126-4

51. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain*. 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5

52. Bouloux G, Greene C, Mercuri L. Intraarticular TMJ pain and dysfunction – 2024 – invited guest editorial. *Cranio*. 2024;42(5):481-482.

53. Nitzan D, Dolwick M, Martinez G. Temporomandibular joint arthrocentesis: A simplified treatment for severe, limited mouth opening. *J Oral Maxillofac Surg*. 1991;49(11):1163-1167. doi:10.1016/0278-2391(91)90409-F

54. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006

55. Kaneyama K, Segami N, Nishimura M, Sato J, Fujimura K, Yoshimura H. The ideal lavage volume for removing bradykinin, interleukin-6, and protein from the temporomandibular joint by arthrocentesis. *J Oral Maxillofac Surg.* 2004;62(6):657-661. doi:10.1016/j.joms.2003.08.031

56. Monje-Gil F, Nitzan D, González-Garcia R. Temporomandibular joint arthrocentesis. Review of the literature. *Med Oral Patol Oral Cir Bucal.* 2012;17(4). doi:10.4317/medoral.17670

57. Nitzan D, Dolwick M, Heft M. Arthroscopic lavage and lysis of the temporomandibular joint: A change in perspective. *J Oral Maxillofac Surg.* 1990;48(8):798-801. doi:10.1016/0278-2391(90)90335-Y

58. Hakim M, McCain J, Ahn D, Troulis M. Minimally Invasive Endoscopic Oral and Maxillofacial Surgery. *Oral Maxillofac Surg Clin North Am.* 2019;31(4):561-567.

59. González-García R. Categorizing temporomandibular joint arthroscopic procedures for a better clinical practice and teaching. *J Stomatol Oral Maxillofac Surg.* 2024;125(5). doi:10.1016/j.jormas.2024.101808

60. González-García R. The Current Role and the Future of Minimally Invasive Temporomandibular Joint Surgery. *Oral Maxillofac Surg Clin North Am.* 2015;27(1):69-84. doi:10.1016/j.coms.2014.09.006

61. Emshoff R, Rudisch A. Determining predictor variables for treatment outcomes of arthrocentesis and hydraulic distention of the temporomandibular joint. *J Oral Maxillofac Surg.* 2004;62(7):816-823. doi:10.1016/j.joms.2003.12.020

62. Vos L, Stegenga B, Stant A, Quik E, Huddleston Slater J. Cost Effectiveness of Arthrocentesis Compared to Conservative Therapy for Arthralgia of the Temporomandibular Joint: A Randomized Controlled Trial. *J Oral Facial Pain Headache.* 2018;32(2).

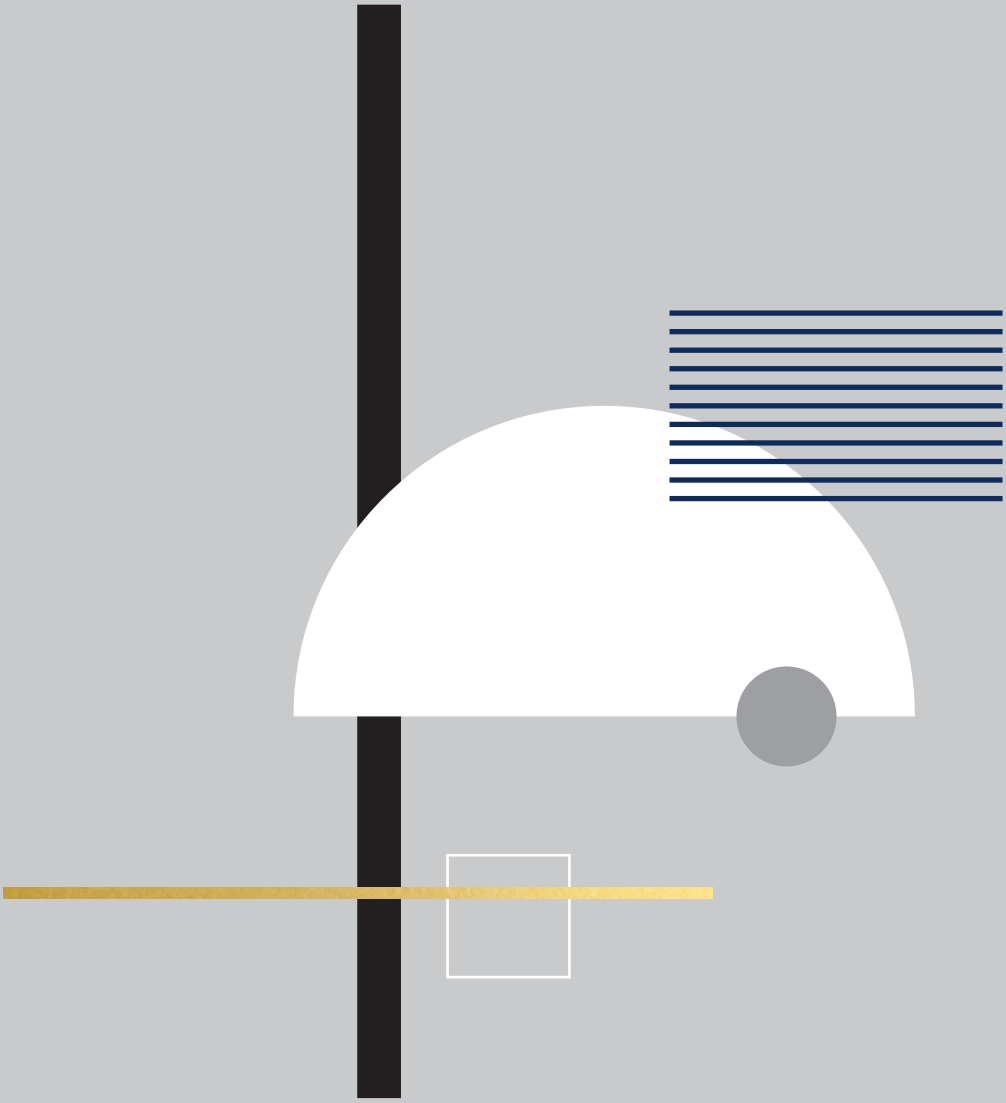
63. Al-Moraissi E, Wolford L, Ellis E, Neff A. The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *J Cranio-Maxillofacial Surg.* 2020;48(1):9-23. doi:10.1016/j.jcms.2019.10.004

64. Tran C, Ghahreman K, Huppa C, Gallagher J. Management of temporomandibular disorders: a rapid review of systematic reviews and guidelines. *Int J Oral Maxillofac Surg.* 2022;51:1211-1225.

65. Li D, Wong N, Li S, McGrath C, Leung Y. Timing of arthrocentesis in the management of temporomandibular disorders: an integrative review and meta-analysis. *Int J Oral Maxillofac Surg.* 2021;50:1078-1088.

66. Martin Granizo R, Correa Muñoz DC, Varela Reyes E. Rearthroscopy of the temporomandibular joint: A retrospective study of 600 arthroscopies. *J Cranio-Maxillofacial Surg.* 2018;46(9):1555-1560. doi:10.1016/j.jcms.2017.12.007

67. Mancha de la Plata M, Muñoz-Guerra M, Escorial Hernandez V, Martos Diaz P, Gil-Diez Usandizaga JL, Rodriguez-Campo FJ. Unsuccessful Temporomandibular Joint Arthroscopy: Is a Second Arthroscopy an Acceptable Alternative? *J Oral Maxillofac Surg.* 2008;66(10):2086-2092. doi:10.1016/j.joms.2008.06.043



CHAPTER 2

ARTHROCENTESIS VERSUS CONSERVATIVE TREATMENTS FOR TEMPOROMANDIBULAR JOINT DISORDERS

A systematic review with meta-analyses and trial sequential analyses

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Abstract

This systematic review aimed to evaluate the efficacy of arthrocentesis compared to conservative treatments for symptomatic temporomandibular joint disorders. A systematic search for randomized, prospective and retrospective controlled trials was undertaken in five electronic databases. Various patient outcomes and economic evaluations were analyzed for short-term (<6 months), intermediate-term (6 months to 5 years) and long-term (≥5 years) follow-up periods. Primary meta-analyses were performed for randomized controlled trials using random-effects models. Arthrocentesis was superior to conservative treatments regarding pain reduction at short-term (MD 14.5 (95% CI 9.7; 19.4), k= 9 RCTs, n= 545 patients, I^2= 48%, high quality of evidence) and intermediate-term follow-up (MD 14.2 (95% CI 7.3; 21.1), k=9 RCTs, n= 547 patients, I^2= 81%, moderate quality of evidence). Furthermore, arthrocentesis was superior to conservative treatment regarding maximum mouth opening improvement at short-term (MD 2.4 mm (95% CI 0.8; 4.1), k= 8 RCTs, n= 472 patients, I^2= 80%, moderate quality of evidence) and intermediate-term follow-up (MD 2.2 mm (95% CI 0.5; 3.9), k= 8 RCTs, n= 468 patients, I^2= 75%, moderate quality of evidence). Trial sequential analysis supported the conclusions of all primary meta-analyses. Results were clinically relevant for pain improvement, but not for maximum mouth opening improvement. Results at long-term follow-up and for other study outcomes were either lacking or too heterogeneous for meta-analysis, highlighting the need for more standardized, high-quality research.

Introduction

Temporomandibular joint (TMJ) disorders affect approximately one third of the general population and manifest primarily as disc displacements (DD) and/ or degenerative joint disease (DJD)[1]. The majority of patients experience minor symptoms, however, more severe symptoms may substantially impact quality of life. This is attributed to the interference with essential functions such as eating, speaking and laughing[2]. Typically, conservative treatments such as counselling, dental splint application, physiotherapy and medication (e.g., non-steroidal anti-inflammatory drugs and muscle relaxants) are first-line treatments due to their low risk of side effects. Within this context, arthrocentesis is usually only considered when non-surgical treatments have failed[3]. During this procedure, lavage of the upper TMJ space is facilitated[4] with the aim to reduce symptoms by removing pro-inflammatory cytokines, degradation products and matrix degrading enzymes[5,6]. Recent studies have advocated to perform arthrocentesis at an earlier stage[7–9], since patients with chronic symptoms (e.g., after prolonged ineffective conservative treatment) are less likely to respond positively to subsequent surgical interventions[10,11]. To address this, a pair-wise systematic review comparing arthrocentesis versus conservative treatments for TMJ disorders has been performed previously[12]. This study focused on joint pain and mouth opening at 6 months follow-up. However, systematic reviews reporting on long-term results as well as other patient outcomes and economical evaluations are lacking. This systematic review with meta-analysis and trial sequential analysis therefore aimed to guide evidence-based clinical decisions comparing arthrocentesis versus conservative treatments for symptomatic TMJ disorders, including short-, intermediate- and long-term outcomes of objective (i.e., maximum mouth opening, joint blocks and noises, protrusive and lateral mandibular movements and costs/ cost-effectiveness) and subjective (i.e., joint pain, mandibular function and quality of life) outcomes.

Materials and methods

The present study was conducted in compliance with the Cochrane handbook for systematic reviews[13] and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[14]. The study protocol was registered in the International Prospective Register of Systematic Review (PROSPERO; CRD42022355646) before the literature search.

Eligibility criteria and data items

The selection of study records through the in- and exclusion criteria was done using the PICOTS format. Studies were included with (P) patients suffering from symptomatic TMJ disorders as classified by the Diagnostic Criteria for Temporomandibular Disorders[15]: TMJ arthralgia, disc displacements with and/or without reduction and degenerative joint disease. The (I) intervention group consisted of TMJ arthrocentesis using any technique, with or without concomitant therapies or injections, whereas the (C) control group consisted of conservative, non-surgical treatments in any modality, such as medication, physical therapy, oral splints or any combination of conservative treatment methods. (O) The primary study outcome for the current study was pain during mandibular movement and/or function using a continuous numeric scale. The secondary outcomes included pain at rest using a continuous numeric scale, maximum mouth opening (MMO) measured as interincisal distance in millimeters, mandibular function (e.g., using the mandibular function impairment questionnaire (MFIQ)[16] or chewing ability), joint blocks and noises, protrusive and lateral movements, quality of life and costs/cost-effectiveness. (T) Measurements of study outcomes were divided into three follow-up ranges: short-term (<6 months), intermediate-term (6 months–5 years) and long-term (≥5 years). The latest outcome measure in each follow-up range was used. (S) Randomized controlled trials (RCTs), prospective non-randomized controlled trials and retrospective cohort studies with a control group were eligible for inclusion. Additionally, all studies must have included at least 10 participants and been published in peer-reviewed journals. There were no language or publication date restrictions. The exclusion criteria were case reports, conference abstracts, reviews, experts' opinions, letters-to-editors or patients younger than 16 years of age, with congenital or acquired dentofacial deformities, rheumatic disorders, connective tissue disorders or bony ankylosis of the TMJ.

Search strategy and information sources

Five electronic databases (Pubmed, Embase, Web of Science, Cochrane Library, Scopus) were systematically searched using controlled vocabulary (MeSH) and free text terms with the help of a biomedical literature specialist (SvdW) **(appendix A)**. In addition, the grey literature was searched. A reference check of relevant trials and reviews on the same topic was performed and experts on the study subject (NBvB and FKLS) were inquired about potentially relevant study articles. The last search was performed on the 2nd of August 2024. No language or publication date restrictions were applied.

Study selection process

Records identified after the literature searches were de-duplicated using the method of Bramer et al.[17]. Hereafter, two reviewers (YHT and NBvB) independently screened all titles and abstracts for full-text assessment eligibility and did the subsequent full-text assessment. A consensus meeting was held to resolve disagreements. A third reviewer (FKLS) was consulted if no agreement could be reached. In each stage, the inter-observer agreement was indicated using the Cohen's kappa statistic and the percentage of agreement was described. Kappa value was interpreted as slight (0–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80) or high (>0.81).

Data collection process

Data collection from the included studies was done using a predefined standardized form. After the data was completely collected by one reviewer (YHT), 15% of the records were independently collected by a second reviewer (NBvB) and compared to the corresponding data of the first reviewer. If agreement between the reviewers was <90%, the second reviewer had to assess the remaining records followed by another consensus meeting. The following data were collected from the included records: authors, publication date, study design, study outcomes at baseline and follow-up, characteristics of study participants (number of patients, gender, age), duration of symptoms, treated diagnosis and treatment specifications (treatment modality, technique, co-interventions and the pre- and post-operative treatment regimen). All the pain scores reported on a continuous scale were recalculated to a visual analog scale (VAS)-score of 0–100 mm (higher score equals severer pain) to allow more accurate between-study comparisons and quantitative analyses.

If additional data from included records was required for quantitative analysis, corresponding authors[18–20] were contacted via email in March 2023 and January 2024 in attempts to retrieve the data. If the requested data were unavailable, no reply was received or when no contact could be established, the records were excluded from quantitative analyses.

Quality assessment

The risk of bias assessment for RCTs was performed using the Cochrane Risk of Bias Tool for Randomized Trials, version 2 (RoB2)[21]. Here, studies were judged either a low risk of bias, some concerns or a high risk of bias, based on five different domains. For the risk of bias assessment of non-randomized studies, the validated Methodological Index for Non-Randomized Studies (MINORS)[22] was used. Studies

were assessed on 12 items, which were each scored either 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). Risk of bias assessment of studies from the current research group were performed by a third, independent and unaffiliated researcher (JAMS; see acknowledgement).

For the assessment of clinical heterogeneity between studies in each meta-analysis, the Clinical Diversity In Meta-Analyses (CDIM) tool was utilized[23]. Using this tool, each study was evaluated on four domains (i.e., setting diversity, population diversity, intervention diversity and outcome diversity) with a total of 11 items. Each item was assigned an equal weight and scored 0 (low diversity), 1 (moderate diversity or unknown) or 2 (high diversity), adding up to a score of 0–22. A total score of 0–11 indicated a low clinical heterogeneity, 12 to 18 indicated a moderate clinical heterogeneity and 19 to 22 indicated a high clinical heterogeneity between the studies.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE)-approach was used to rate the certainty of evidence for outcomes[24,25]. The quality of evidence was rated either high, moderate, low or very low.

Abovementioned quality assessments were carried out independently by two reviewers (YHT an NBvB) and any disagreements were resolved in a consensus meeting. Due to the nature of each tool/approach, Risk of Bias assessments were performed for all included studies, whereas the assessments of the clinical heterogeneity and the certainty of evidence were performed for each primary meta-analysis.

Effect measures and data synthesis

Primary meta-analyses were performed based on the highest available evidence (RCTs only). The a priori drafted study protocol included non-randomized studies in case insufficient evidence could be gathered from RCTs during the data collection process. In that case, evidence of non-randomized studies would be presented as accessory data to ensure comprehensive coverage of the topic. Summary effect measures were calculated if ≥ 2 studies reported on the same study outcome[13]. For the continuous variables suitable for quantitative analysis, the mean difference (MD) and corresponding 95% confidence intervals (CI) were computed[13]. Due to an expected presence of heterogeneity between studies, a random-effects model with the DerSimonian-Laird estimator[26] was used for the meta-analyses[27]. Statistical

heterogeneity between studies per meta-analysis was evaluated through I^2 and was considered substantial if ≥ 50%[13].

If only standard deviations (SDs) of the baseline and follow-up scores were reported, the SDs of the changes were estimated from those measurements using a correlation coefficient of 0.5[13,28]. Furthermore, if studies were included with three or more arms from which at least two suited a single intervention group as defined for the current review, similar groups were combined to allow pair-wise meta-analysis[13]. If studies only reported on medians with range, these were recalculated to means with SD before the synthesis of summary effect estimates[13,29]. Similarly, standard errors were transformed into SDs if these were the only estimates reported in a study[13].

A priori defined subgroup analyses were performed for *(1)* the duration of symptoms, i.e., acute (<3 months) or chronic (≥3 months), *(2)* the use of co-medication during arthrocentesis, e.g., hyaluronic acid and *(3)* the diagnosis, e.g., only for disc displacement without reduction (DDwoR). Sensitivity analyses were performed where *(1)* high risk of bias studies were excluded and where *(2)* each study was omitted one by one from the primary meta-analysis to evaluate the individual effects of the studies. All meta-analyses and forest-plots were synthesized in R, version 4.2.2 (R Core team), using the *meta*-package, version 6.1-0[30].

In addition, trial sequential analyses (TSA) were performed due to the susceptibility of conventional meta-analyses to type-I errors (i.e., false positive findings)[31]. A random-effects model TSA using the DerSimonian-Laird estimator was performed with Trial Sequential Analysis Viewer, version 0.9.5.10 Beta (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet[32]). A required information size (RIS; i.e., the required sample size for the meta-analysis) was determined for each primary meta-analysis to provide an indication of the robustness of the conclusions drawn. A p-value <0.05 was considered statistically significant in all analyses.

Results

Study selection

After removal of duplicates, 1876 unique records were screened by title and abstract (**Figure 1**) and 34 reports were selected for full-text reads. The inter-observer agreement was substantial (Cohen›s kappa coefficient (κ) = 0.78; percentage of agreement = 99.3%).

Following full text-assessment (high inter-observer agreement: κ = 0.87; percentage of agreement = 93.9%) and expert consultation, 21 records were deemed suitable for inclusion. From those records 16 were used for qualitative analyses and meta-analyses[19,33–47] and five for qualitative analyses[9,18,20,48,49]. Excluded records after full-text reads are presented in **appendix B**, together with the reasons for exclusion. For the data collection process, the agreement was 100% between the two reviewers. The third reviewer was not consulted throughout the study screening and selection procedure.

Study characteristics

From the included records, three involved the reporting of different outcomes or follow-up from a single RCT[9,43,49], leading to the inclusion of 19 unique studies. Of these, ten studies were RCTs[9,37,48,49,38–40,43–47] and nine non-randomized studies[18–20,33–36,41,42]. Publication years ranged from 1995 to 2024. A total of 2725 study participants were included in the review (ranging from 24 to 1752 participants per study), from who 622 were participating in RCTs. Reported follow-up moments and study participants characteristics of each study are shown in **Table 1**. Arthrocentesis techniques between studies exhibited a degree of similarity, but the use of co-interventions, such as hyaluronic acid, oral splints or medication, varied considerably between studies. Additionally, a substantial variability in conservative methods was present between the studies (**Table 1**).

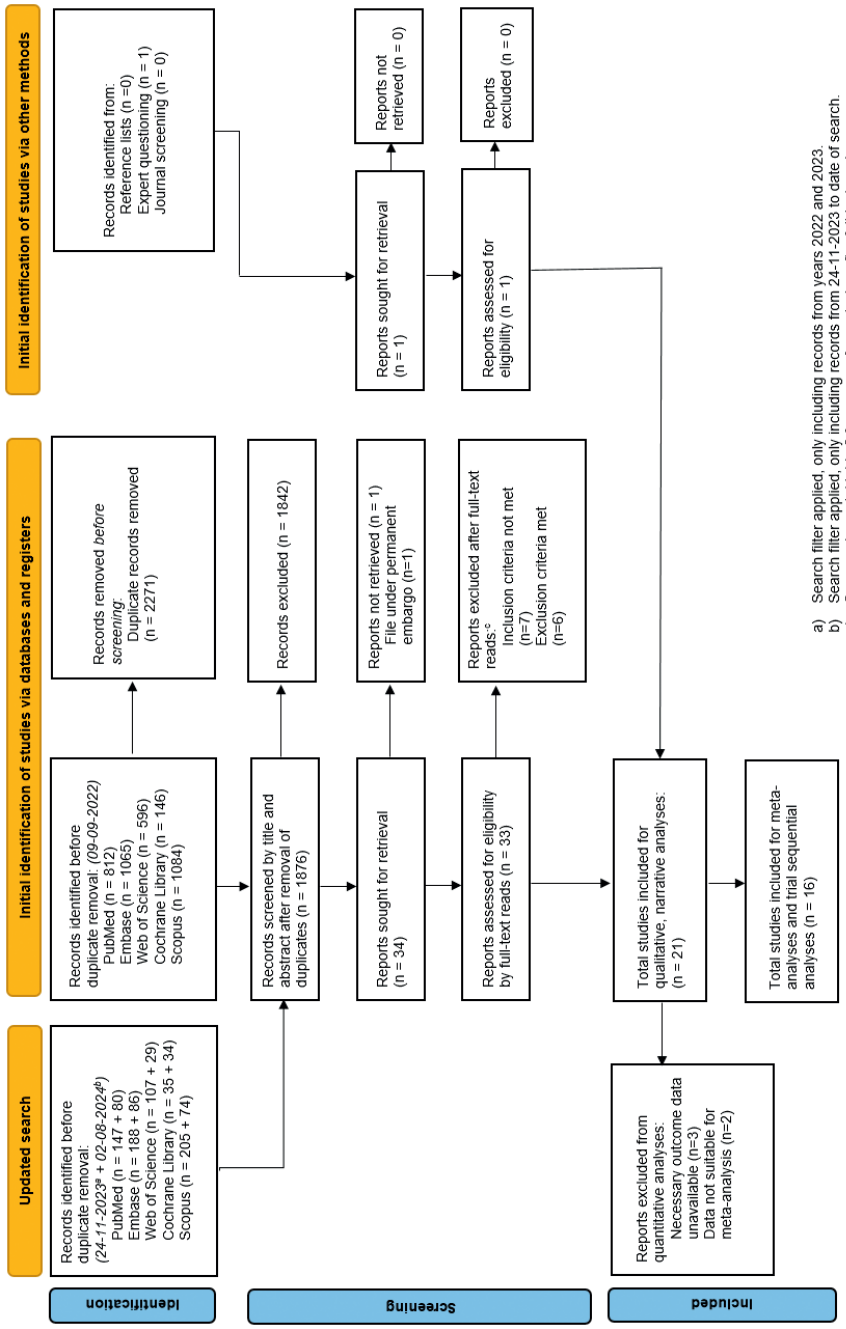

Figure 1. Flow diagram of the study record identification and selection process.

Table 1. Study characteristics of included studies.

Study	FU months			Diagnosis	Arthrocentesis	Irrigation fluid	CI	Conservative treatment
	S	I	L					
Randomized controlled trials								
Guarda-Nardini et al. (2005)[48]	3	6		OA	Five sessions; double needle	Ringer	HA	SS
Diracoglu et al. (2009)[40]	3	6		DDwoR	Single session; double needle	Ringer	x	SS & heat therapy & HE
Hosgor et al. (2017)[44]	3	6		DDwR & DDwoR	Single session; double needle	Ringer	x	(SS or NSAIDs or LLLT) & HE
Tatli et al. (2017)[45]	3	6		DDwoR	Single session; double needle; with/ without SS	NaCl	HA	SS & NSAIDs
Malekzadeh et al. (2019)[46]	3	12		DDwoR	Single session; double needle	NaCl	x	CBT & HE. NSAIDs (pain) or SS (bruxism)
Abbasgholizadeh et al. (2020)[47]	3	6		DDwR & DDwoR	Single session; ultrasound guided & SS	NaCl	HA	SS or LLLT
de Almeida et al. (2023)[37]	1	12		DDwoR with OA	Single session; single needle	NaCl	HA	PT
Vos et al. (2014)[43]	3	6		Arthralgia	Single session; double needle	NaCl	x	NSAIDs. SS (pain) or PT (restricted MMO)
Vos et al. (2018)[49]								
Tang et al. (2023)[9]			74					
Correa-Silva et al. (2024)[38]	3	6		Arthralgia	Single session; double needle	Ringer	CS	SS
Li et al. (2024)[39]	3	12		DDwR & DDwoR	Single session; double needle & SS	NaCl	x	SS
Non-randomized studies								
Murakami et al. (1995)[33]		6		DDwoR	Single session; double needle	Ringer	CS	NSAIDs & muscle relaxants & ARS
Onder et al. (2009)[41]	2	6		OA	Single session; double needle & SS	Ringer	x	SS & NSAIDs
Machon et al. (2011)[18]	3			OA	Single session; double needle; with/ without SS	Ringer	HA	SS or NSAIDs
Lee et al.(2013)[42]	3	6		DDwoR	Single session; double needle & SS	Ringer	HA	SS & NSAIDs

Table 1. Study characteristics of included studies. *Continued.*

Study	FU months			Diagnosis	Arthrocentesis	Irrigation fluid	CI	Conservative treatment
	S	I	L					
Non-randomized studies								
Malachovsky et al. (2019)[19]	3	12		Arthralgia	Single session; double needle	Ringer or NaCl	x	NSAIDs
Yilmaz et al. (2019)[35]		6		DDwR & DDwoR	Single session; double needle	Ringer	HA	Rest
Goyal et al. (2020)[34]	3			Arthralgia	Single session; with/ without SNRI	Ringer	x	SNRI
Altaweel et al. (2021)[20]	3	6		DDwoR	Single session; double needle & SS or ARS	Ringer	HA	SS or ARS
Helal et al. (2021)[36]		6		DDwoR	Single session, double needle	Ringer	x	ARS

Abbr.: FU follow-up; S short-term, I intermediate-term; L long-term; OA osteoarthritis; DDwoR disc displacement without reduction; DDwR disc displacement with reduction; SS stabilization splint; SNRI selective serotonin and noradrenalin reuptake inhibitor; ARS anterior repositioning splint; Ringer Ringer's lactate; NaCl sodium chloride solution; CI co-intervention; HA hyaluronic acid; CS corticosteroids; HE Home exercise; NSAIDs nonsteroidal anti-inflammatory drugs; LLLT low-level laser therapy; CBT cognitive behavior therapy; PT Physical therapy.

Risk of bias assessment

Risk of bias assessment resulted in a 'high risk of bias' judgement for two reports due to a high risk of bias in the randomization process[48] or deviations from the intended interventions[46]. The remaining nine reports had a 'some concerns' assessment, primarily due to missing information regarding the randomization process, deviations from the intended intervention and/or the measurement of the outcome result (i.e., measurement of the subjective outcome pain with non-blinded study participants) (**Table 2**). The risk of bias assessment of non-randomized studies was performed in nine studies. Studies scored between 10 and 19 on a scale of 0–24, with a lower score reported in studies with a retrospective design (**Table 3**).

Table 2. Risk of bias assessment of randomized controlled trials using the Cochrane Risk of Bias Tool 2.

Author (year)	D1	D2	D3	D4	D5	Overall Bias
Guarda Nardini et al. (2005)[48]	−	+	+	!	+	−
Diracoglu et al. (2009) [40]	!	+	+	!	+	!
Vos et al. (2014[43], 2018)[49]	+	!	+	!	+	!
Hosgor et al. (2017) [44]	!	+	+	!	+	!
Tatli et al. (2017)[45]	!	+	+	!	+	!
Malekzadeh et al. (2019)[46]	+	−	+	!	+	−
Abbasgholizadeh et al. (2020)[47]	!	+	+	!	!	!
De Almeida et al. (2023)[37]	+	+	+	!	+	!
Tang et al. (2023)[9]	+	!	+	!	+	!
Correa Silva et al. (2024)[38]	!	+	+	!	+	!
Li et al. (2024)[39]	+	!	+	!	+	!

+ Low risk of bias
! Some concerns
− High risk of bias

D1 Randomization process; D2 Deviations from intended interventions; D3 Missing outcome data; D4 Measurement of the outcome result; D5 Selection of the reported results.

Table 3. Risk of Bias assessment of non-randomized studies using the Methodological Index for Non-randomized Studies.

Author (year)	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the study aim	Unbiased assessment of the study endpoint	Follow-up period appropriate to study aim	Lost to follow-up <5%	Prospective calculation of study size	Adequate control group	Contemporary groups	Baseline equivalence	Adequate statistical analysis	Total
Murakami et al. (1995)[33]	2	2	0	2	0	1	0	0	2	2	2	2	15
Onder et al. (2009)[41]	2	0	0	2	0	1	0	0	2	2	1	1	11
Machon et al. (2011)[18]	2	0	2	2	0	1	0	0	2	2	1	2	14
Lee et al. (2013)[42]	2	0	0	2	0	1	0	0	2	0	2	2	11
Malachovsky et al. (2019)[19]	0	2	0	2	0	1	0	0	2	2	0	2	11
Yilmaz et al. (2019)[35]	2	2	2	2	2	1	0	0	2	2	2	2	19
Goyal et al. (2020)[34]	2	0	0	2	0	1	0	0	2	1	0	2	10
Altaweel et al. (2021)[20]	2	0	2	2	0	1	0	0	2	2	2	2	15
Helal et al. (2021)[36]	2	0	2	2	2	1	0	0	2	2	1	2	16

0 not reported; 1 reported but inadequate; 2 reported and adequate.

Primary outcome

Pain during mandibular movement and/or function

Pain during mandibular movement and/or function was presented in 19 reports. Of those, 15 were used for quantitative analyses (**Figure 2**, **Figure 3**). Remaining studies lacked sufficient information[18,20,48] or were the only study in the follow-up range[9]. Of the studies reporting on pre- and post-operative differences for each treatment arm, 13 reports showed improvement of pain scores over time in both the

arthrocentesis and conservative treatment groups[9,20,46–48,33,37,39,40,42–45], three studies showed improvement over time in only the arthrocentesis group[19,35,41], one study showed no statistical significant improvement over time in both groups[38] and two studies did not adequately report pre- and post-operative differences[18,34].

At short-term follow-up (range 1 to 3 months) treatment effect of arthrocentesis was superior to conservative treatments in pain reduction (MD 14.5 (95% CI 9.7; 19.4), *k*= 9 RCTs, *n*= 545 patients, I^2= 48%, high quality of evidence). Including non-randomized studies resulted in larger differences accompanied by higher statistical heterogeneity (MD 18.8 (95% CI 13.8; 23.8), *k*= 13 studies, *n*= 2382 patients, I^2= 89%) (**Figure 2**). At intermediate-term follow-up (range 6 to 12 months), arthrocentesis was superior to conservative treatments in pain reduction (MD 14.2 (95% CI 7.3; 21.1), *k*= 9 RCTs, *n*= 547 patients, I^2= 81%, moderate quality of evidence). Including non-randomized studies resulted in larger differences accompanied by higher statistical heterogeneity (MD 22.3 (95% CI 11.5; 33.1), *k*= 14 studies, *n*= 2490 patients, I^2= 99%) (**Figure 3**). One RCT reported on pain reduction at long-term follow-up (median of 6.2 years)[9]. In that study, arthrocentesis was found more efficacious in pain reduction (−10.23 (95% CI -17.86;-2.60), p= 0.009) compared to conservative treatment over the entire follow-up period.

Sensitivity analyses revealed a lower statistical heterogeneity (I^2= 0% at both short-term and intermediate-term follow-up) in the RCT-only meta-analyses after excluding the study of Diracoglu et al.[40]. No methodological or clinical explanation could be given for this outlier, therefore not warranting the exclusion of this study. No substantial differences were observed after exclusion of the study[46] with a high risk of bias assessment.

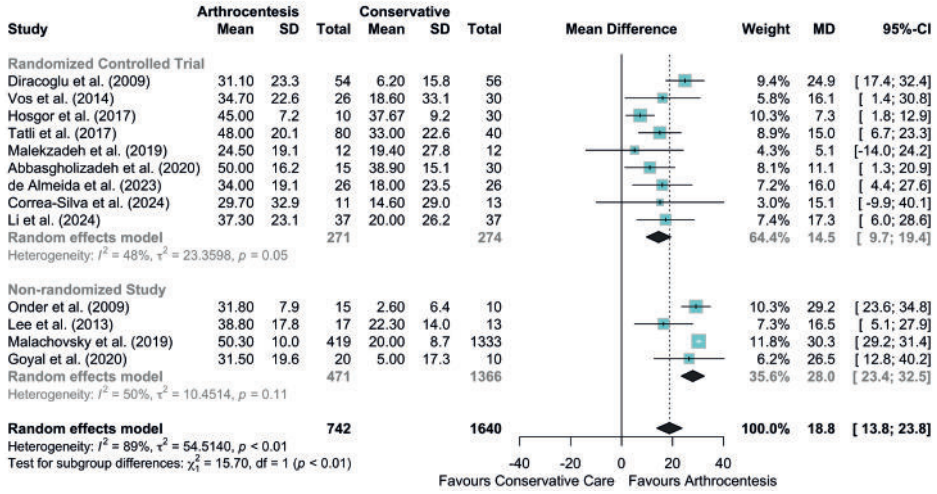

Figure 2. Forest plot of pain reduction (visual analog scale, 0–100) at short-term follow-up (<6 months). Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% confidence interval.

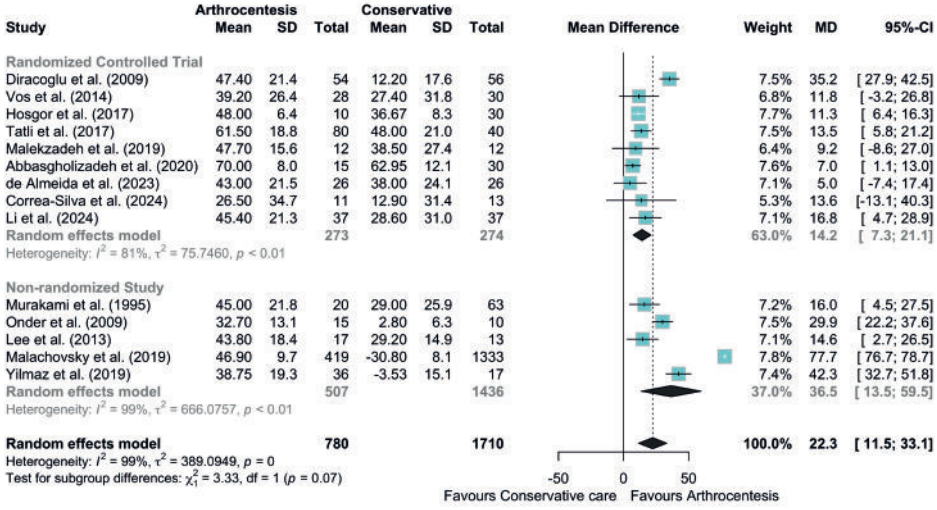

Figure 3. Forest plot of pain reduction (visual analog scale, 0–100) at intermediate-term follow-up (6 months–5 years). Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% confidence interval.

Secondary outcomes

Maximum mouth opening

MMO measured as interincisal distance was reported in 19 reports. Of those, 15 were used for quantitative analyses (**Figure 4**, **Figure 5**). Of the studies reporting on pre- and post-operative differences for each treatment arm, 11 reports showed MMO improvement over time in both the arthrocentesis and conservative treatment groups[20,33,47,36,37,39,40,42,43,45,46], five studies showed improvement over time in only the arthrocentesis group[19,35,41,44,48], one study showed no statistical significant improvement over time in both groups[38] and two studies did not adequately report pre- and post-operative differences[18,34].

At short-term follow-up (range 1 to 3 months) a significantly greater effect in MMO improvement of arthrocentesis was observed compared to conservative treatments after pooling RCTs (MD 2.4 mm (95% CI 0.8; 4.1), *k*= 8 RCTs, *n*= 472 patients, I^2= 80%, moderate quality of evidence), which maintains when including non-randomized studies (**Figure 4**). At intermediate-term follow-up (range 6 to 12 months), arthrocentesis was superior to conservative treatments after pooling RCTs (MD 2.2 mm (95% CI 0.5; 3.9), *k*= 8 RCTs, *n*= 468 patients, I^2= 75%, moderate quality of evidence), which maintains when including non-randomized studies (**Figure 5**). No studies reported on long-term results for MMO improvement.

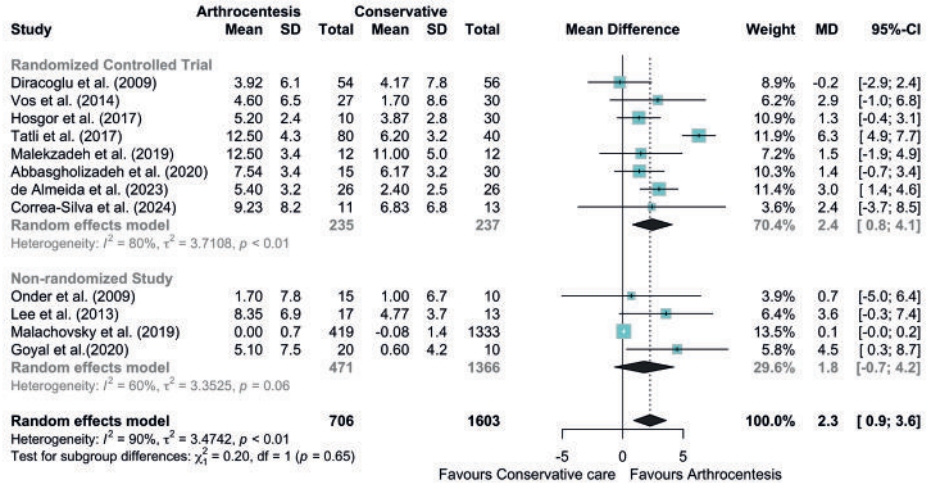

Figure 4. Forest plot of maximum mouth opening improvement (millimeters) at short-term follow-up (<6 months). Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% confidence interval.

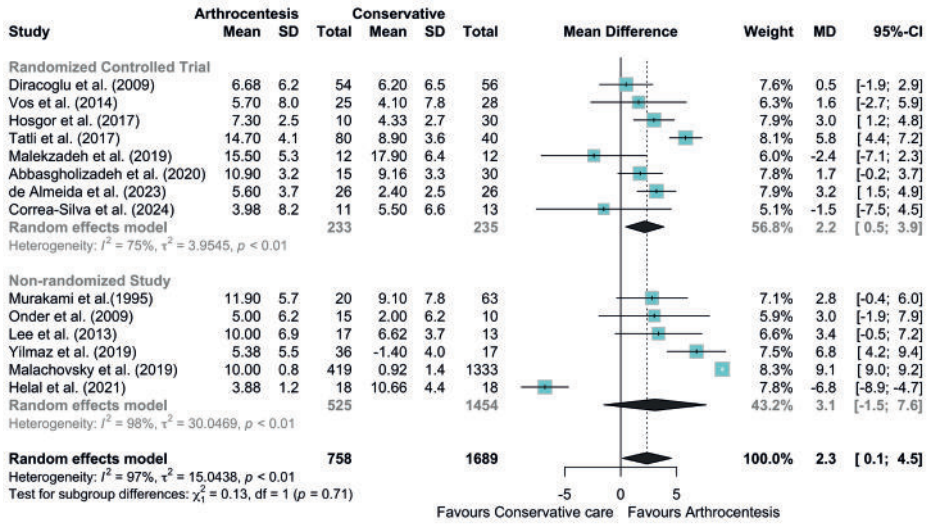

Figure 5. Forest plot of maximum mouth opening improvement (millimeters) at intermediate-term follow-up (6 months–5 years). Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% confidence interval.

Sensitivity analyses revealed a substantially lower statistical heterogeneity (I^2= 0% at short-term and I^2= 36% at intermediate-term follow-up) in the RCT-only meta-analyses after excluding the study of Tatli et al.[45]. No methodological or clinical explanation could be given for this outlier, therefore not warranting the exclusion of this study. No substantial differences were observed after exclusion of the study[46] with a high risk of bias assessment.

Joint pain at rest

Joint pain at rest was described in four records[9,35,43,48]. Reduction of pain at rest over time was seen in both the arthrocentesis and conservative treatment group in three reports[9,43,48], whereas in another study, only the arthrocentesis group improved over time[35]. No difference was observed between groups at intermediate-term follow-up in two studies[35,48]. When considering the entire length of the follow-up period (median 6.2 years), arthrocentesis was superior over conservative treatment (−8.39 (95% CI -13.70;-3.08), p= 0.002)[9] **(appendix C).**

Mandibular function

Mandibular function was described in six reports using various measurement tools. In four reports, both arthrocentesis and conservative intervention improved the mandibular function over time[9,33,43,48], whereas in two studies only the arthrocentesis group improved mandibular function[35,38]. On short-term follow-up, no differences

between groups were observed[38,43,48]. At intermediate-term follow-up, two studies reported superiority of arthrocentesis over conservative treatment[35,43] and three reported no differences between groups[33,38,48]. At long-term follow-up, no differences were reported between both groups[9] **(appendix C)**.

Joint blocks and noises

The severity of joint noises and blocks was reported in six studies[34,35,38,41,42,44]. From those, three studies reported no within group improvement[34,41,44], one reported improvement in both groups[42], one reported only improvement in joint blocks in the arthrocentesis group[38] and one reported only improvement in the arthrocentesis group in a subgroup involving patients with disc displacement with reduction[35]. Between group comparisons showed no differences in all studies at the short-term and intermediate-term follow-up **(appendix C)**.

Lateral and protrusive movements

Lateral and protrusive mandibular movement improvement were reported in four studies[36,40,45,47]. Within-group improvements in both treatment groups were observed in all studies. Regarding lateral movements, one study reported no between-group differences at short- and intermediate-term follow-up[40], two study reported statistical significant superiority of arthrocentesis over splints at short- and intermediate-term follow-up[45,47], whereas another study reported the superiority of splints over arthrocentesis at intermediate-term follow-up[36]. Regarding protrusive movements, no differences were reported in two studies between the two treatments at short- and intermediate-term follow-up[36,40] **(appendix C)**.

Quality of life

Quality of life was reported in five studies[35,37,38,43,45]. Measurement tools included the oral health impact profile (OHIP) questionnaire[37,43], the disability questions from the Research Diagnostic Criteria for Temporomandibular Joint Disorders (RCD/TMD) Axis II biobehavioral questionnaire[45], a psychosocial status score[38] and a VAS[35]. Quality of life improvement was observed in both groups in three studies[37,43,45], and only in the arthrocentesis group in two studies[35,38]. For between-group comparison, arthrocentesis resulted in superior quality of life improvement compared to conservative treatment in three studies at short- and intermediate-term follow-up[35,37,45], whereas no difference between groups was seen in the remaining studies at short- and intermediate-term follow-up[38,43] **(appendix C)**.

Costs and cost-effectiveness

Costs, cost-effectiveness and cost-utility were analyzed in one study[49]. The mean societal cost (i.e., direct and indirect medical and nonmedical cost) was lower for arthrocentesis (795 United States dollars) compared to conservative interventions (2266 United States dollars). Furthermore, arthrocentesis resulted in higher cost-effectiveness (for outcome pain during movement) and cost-utility (using quality adjusted life years) compared to conservative treatments **(appendix C)**.

Subgroup analyses

The effect estimates of type of intervention on pain reduction between the subgroups acute symptoms subgroup versus chronic symptoms at short-term follow-up were not significantly different (p= 0.30). Also at intermediate-term follow-up, acute symptoms and chronic symptoms were not statistically significantly different from each other regarding pain reduction (p= 0.08) **(appendix D).** Furthermore, effect estimates on maximum mouth opening improvement between acute and chronic symptoms did not significantly differ at short-term (p= 0.86) or intermediate-term follow-up (p= 0.54) **(appendix E)**. Regarding the use of hyaluronic acid, no statistically significant difference in effect estimates on pain reduction was found between the application of hyaluronic acid as adjuvant to arthrocentesis and when no hyaluronic acid was applied at short-term (p= 0.86) or intermediate-term follow-up (p= 0.13) **(appendix F).** Furthermore, maximum mouth opening improvement in the group with adjuvant hyaluronic acid application did not significantly differ from the group with no hyaluronic acid application at short-term (p= 0.12) or intermediate-term follow-up (p= 0.12) **(appendix G).**

Analyses with studies involving participants suffering from DDwoR resulted in the superiority of arthrocentesis over conservative treatment in pain reduction at short-term (MD 17.6 (95% CI 10.6; 24.6)) and intermediate-term follow-up (MD 16.6 (95% CI 2.7; 30.5) and an equal efficacy in MMO improvement between the treatment groups at short-term (MD 2.8 mm (95% CI 0.0; 5.7)) and intermediate-term follow-up (MD 2.2 mm (95% CI -1.0; 5.4) **(appendix H).** There was insufficient data available to perform subgroup analysis regarding other diagnoses.

Certainty of evidence

Clinical diversity among studies was assessed as low in all primary meta-analyses. For both pain during mandibular movement and/or function and MMO the CDIM score was 10 (short-term follow-up) or 11 (intermediate-term follow-up) out of 22 **(appendix I).** Despite a 'low clinical diversity' judgement, heterogeneity was

observed between studies in the 'intervention' domain, primarily regarding the techniques and timing of arthrocentesis and conservative treatments (**appendix I**).

TSA was performed for the primary meta-analyses. In all TSA the RIS, i.e., the required sample size in meta-analysis was reached **(appendix J)**. Hence, TSA suggests that the available evidence from the meta-analyses are not subject to potential false neutral outcomes and, thus, supports the conclusions of these meta-analyses **(appendix J)**.

Assessment of the certainty of evidence using the GRADE-approach resulted in a high quality of evidence for the primary meta-analysis for pain improvement at short-term follow-up. A moderate quality of evidence judgement was given for the remaining three primary meta-analyses involving the outcomes pain improvement at intermediate-term follow-up and MMO improvement at both follow-ups. All outcomes had an initial assessment of high quality of evidence due to the inclusion of solely RCTs. Downgrading of one level occurred due to inconsistency in the results, as no plausible explanation could be identified during full-text reading and CDIM-assessment, despite the presence of a substantial statistical heterogeneity ($I^2 \geq 50\%$) in all primary analyses (**Table 4**).

Table 4. Summary of findings of primary meta-analyses (randomized controlled trials only).

Outcome	Follow-up (months)	MD (95% CI) between interventions	Nº of participants (studies)	Certainty of the evidence (GRADE)
Pain reduction (VAS, 0-100; higher is worse)	Short-term (1-3)	14.5 (9.7;19.4)	545 (9)	⊕⊕⊕⊕ High
	Intermediate-term (6-12)	14.2 (7.3;21.1)	547 (9)	⊕⊕⊕◯ Moderate[1]
MMO improvement (mm)	Short-term (1-3)	2.4 (0.8;4.1)	472 (8)	⊕⊕⊕◯ Moderate[1]
	Intermediate-term (6-12)	2.2 (0.5;3.9)	468 (8)	⊕⊕⊕◯ Moderate[1]

Abbr.: MD mean difference; 95% CI 95% confidence interval; GRADE Grading of Recommendations Assessment, Development and Evaluation; VAS visual analog scale; MMO maximum mouth opening.[1]Downgraded one level due to inconsistency: unexplained heterogeneity that were not accounted for in the analyses ($I^2 \geq 50\%$).

Discussion

This systematic review evaluated the efficacy of arthrocentesis compared to conservative, non-surgical treatments in any modality for symptomatic TMJ disorders. Meta-analyses of RCTs showed that arthrocentesis is statistically superior to conservative treatments regarding pain reduction at short-term follow-up (high quality of evidence; RIS reached with TSA) and intermediate-term follow-up (moderate quality of evidence; RIS reached with TSA), and regarding MMO improvement at short- and intermediate-term follow-up (moderate quality of evidence; RIS reached with TSA).

Several previous studies have researched the clinical importance of changes in pain scores and emphasize the importance of taking baseline scores into consideration when evaluating pain scores. Reductions in chronic pain scores of 10–20% may reflect the minimally clinically important difference (MCID), whereas 30% reduction indicate a moderate clinically important difference[50]. A more recent study determined the MCID for pain VAS in TMD patients is determined to be 12 mm[51]. Therefore, pain during mandibular function reduction at short- (MD 14.5 mm) and intermediate-term follow-up (MD 14.2 mm) in this study were not only statistically significant, but also clinically relevant: baseline pain scores in the groups ranged between 35.4 and 74.0 on the VAS, translating to a 20%–41% difference at short-term and a 19%–40% difference at intermediate-term follow-up between the arthrocentesis and conservative treatments. As for MMO-improvement, the MCID is determined to be between 6 and 9 mm[52]. However, this range does not consider the baseline MMO. Yet, since the statistical significant differences in MMO improvement between treatment groups were 2.4 mm (short-term follow-up) and 2.2 mm (intermediate-term follow-up), and baseline values ranged between 27.2 and 39.0 mm (translating to a difference between groups of 6%–9% and 6%–8%), it is not likely that these differences are clinically relevant.

The observation that arthrocentesis is superior to conservative treatments in reducing pain aligns with the hypothesis that joint lavage aids in eliminating pro-inflammatory cytokines and degradation products responsible for synovitis[5,6,53]. Since synovitis has been linked to the severity of pain patients experience[54], the current results suggest that the superior pain reduction observed with arthrocentesis could be attributed to its efficiency in eliminating inflammatory mediators from the upper joint space. In TMJ disorders, a restricted mouth opening may result from biomechanical issues within the joint, such as intra-articular adhesion formation

or a non-reducing displaced disc, or pain originating from the joint or masticatory muscles[55,56]. In the current results, the equal effect found between both treatment groups could indicate that arthrocentesis is equally efficacious compared to conservative treatments in addressing the articular disc or intra-articular adhesions. Alternatively, since arthrocentesis targets the joint, it may be possible that it addresses the biomechanical issues superiorly, but is less efficacious at alleviating masticatory muscle pain compared to conservative treatments.

Results for the outcomes joint pain at rest, mandibular function, joint blocks and noises, lateral and protrusive movements, quality of life and costs/cost-effectiveness were too scarce or heterogeneous, therefore disallowing meta-analysis. Nevertheless, for the outcomes pain at rest, mandibular function, lateral and protrusive movements and quality of life, the general tendency was that after both arthrocentesis and conservative treatments an improvement over time was seen. When observing between-group comparisons, results were mixed. Generally, arthrocentesis was either superior or equal to conservative treatments for all clinical outcome measurements. An outcome of particular interest is quality of life. Seemingly, a more invasive treatment does not negatively impact the subjective well-being of patients. Lastly, the only study available on the economical perspective of treatments suggests that arthrocentesis may be superior over conservative treatments regarding cost-effectiveness[49].

The current results are in partial agreement with those of a recently published study by Thorpe et al.[12]. In their study, the authors reported a borderline statistically significant superiority of arthrocentesis over conservative treatment for pain reduction and MMO improvement after six months follow-up, but stated that these results might not be clinically relevant. The discrepancy observed between that study and the current review could be attributed to the inclusion of two new RCTs[38,39] and the exclusion of a RCT that used a synovial fluid aspiration as control group[57] in the current review. The authors of the current paper argue that a synovial fluid aspiration does not align with the definition of conservative treatment and have, therefore, not included this specific study in the current review.

The subgroup analysis performed based on the duration of symptoms yielded no statistical differences between studies treating acute or chronic symptoms for pain reduction or MMO-improvement. This finding contradicts the notion that chronic symptoms are less responsive to arthrocentesis[10]. However, since a sizeable effect difference was seen between the subgroups for pain improvement, it may

be possible that the limited number of studies included might have provided an insufficient sample size to detect a significant difference. Additionally, subgroup analysis involving adjuvant hyaluronic acid injection after arthrocentesis did not result in greater symptom improvement than when only performing arthrocentesis. This finding aligns with the current evidence, indicating that while hyaluronic acid may be effective as monotherapy, its use as an addition to arthrocentesis does not further alleviate symptoms[58–60]. Results from the subgroup analyses for studies involving only DDwoR did not clinically differ from the primary analysis, likely because the majority of studies involved participants were suffering from DDwoR, thus significantly influencing the overall results. Subgroup analyses based on other diagnoses, however, were not possible due to the between-study heterogeneity and limited available data. It is important to emphasize that the results from the subgroup analyses are merely hypothesis generating, since they are derived from indirect, between-study comparisons and a limited amount of studies, and should therefore be interpreted with caution[13].

Besides the magnitude of treatment effects, several other factors need to be considered before decision-making regarding the optimal treatment choice may take place, such as the safety, the feasibility and the (societal) costs. In terms of safety, arthrocentesis is widely considered to be a safe procedure, with a minimum risk of severe complications. Nevertheless, the risk of complications, although mostly transient and mild in nature, are not absent[61]. Concerning feasibility, the success of arthrocentesis may not be as dependent on patient compliance and time-consuming as conservative treatments, which frequently require extended periods of treatment. Regarding (societal) costs, the current evidence of costs and cost-effectiveness is limited to a single study and necessitates further research. The assessment of long-term economic implications in relation to potential health outcomes is necessary to make informed clinical decisions about optimal treatment choices.

To objectify clinical heterogeneity, the validated CDIM-tool was used indicating low overall clinical heterogeneity. Despite this, a heterogeneity was observed between studies included in the quantitative analyses in patient diagnoses and techniques regarding arthrocentesis and conservative treatments. Therefore, a limitation of the current study is that it cannot be ruled out for certain that the pooling of all TMJ disorders (i.e., DD, DJD, arthralgia) as well as the various conservative treatment types may have influenced the generalizability of the current results. However, TMJ disorders are often closely related and concurrently occurring, sharing similar treatment indications. As such, the conclusions drawn may reflect the clinical

reality, where these diagnoses are not always distinctly separated. Furthermore, the decision to pool the different conservative treatment types was made to ensure the feasibility of the statistical analysis, given the variability in treatment approaches and durations used across institutions. Since many healthcare providers implement their own patient-tailored versions of conservative treatments, pooling these diverse treatment regimens provides a more realistic representation of how conservative treatments are applied in practice for TMJ disorders.

Currently, several directions for further research may be relevant. The optimal timing for arthrocentesis to date remains a subject of debate. Since no consensus exists regarding how long conservative treatment needs to be employed before deemed ineffective, there is a risk that patients are subjected to them for an unnecessarily long period, decreasing the success chances of subsequent treatments and wasting time and resources. One systematic review investigating the optimal timing for arthrocentesis has been performed[62]. In that study, no definitive conclusion could be drawn due to the lack of high quality studies and the indirect evidence presented. Future research identifying at-risk patients with disease symptoms refractory to conservative treatment and/or comparing different timings of arthrocentesis in a single clinical trial may aid in the determination of which patients may perhaps benefit from earlier arthrocentesis. To date, study outcomes other than pain and MMO, such as the mandibular function or the quality of life have been scarcely investigated or assessed using highly varied measurement tools. Intensifying research efforts and using validated measurement tools, such as the MFIQ[16] or the OHIP[63], could result in a more comprehensive understanding of the true therapeutical effects of different treatments for TMJ disorders. Moreover, the considerable clinical variation observed regarding the execution of treatments across different institutions underscores the importance of adhering to rigorously developed protocols and guidelines. A standardized approach for treatment techniques, use of co-interventions, timing, outcome registration, statistical analysis and data reporting allows for more robust study results. Finally, the absence of long-term study results highlights the need for research designs that include extended follow-up periods.

In conclusion, arthrocentesis is statistically significantly superior to conservative treatments regarding improvement of pain during mandibular movement and/or function and MMO at short- and intermediate-term follow-up for symptomatic TMJ disorders. Results of pain improvement were clinically relevant, whereas this was not the case for MMO improvement. Long-term results and outcomes regarding pain at rest, mandibular function, joint blocks and noises, protrusive and lateral movements,

quality of life and costs/cost-effectiveness were lacking or too heterogeneous for meta-analyses, but revealed a general trend of an equal to superior effect of arthrocentesis.

Author contributions (Credit)

Tang YH: Conceptualization, Methodology, Formal Analysis, Investigation, Writing – Original Draft. Van Bakelen NB: Conceptualization, Methodology, Investigation, Writing – Review and editing. Gareb B: Formal Analysis, Writing – Review and editing. Spijkervet FKL: Conceptualization, Methodology, Writing – Review and editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

1. Valesan L, Da-Cas C, Réus J, et al. Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. *Clin Oral Investig*. 2021;25(2):441-453. doi:10.1007/s00784-020-03710-w
2. Almoznino G, Zini A, Zakuto A, et al. Oral health-related quality of life in patients with temporomandibular disorders. *J oral facial pain headache*. 2015;29(4):231-241. doi:10.11607/ofph.1413
3. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain*. 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5
4. Nitzan D, Dolwick M, Martinez G. Temporomandibular joint arthrocentesis: A simplified treatment for severe, limited mouth opening. *J Oral Maxillofac Surg*. 1991;49(11):1163-1167. doi:10.1016/0278-2391(91)90409-F
5. Kaneyama K, Segami N, Nishimura M, Sato J, Fujimura K, Yoshimura H. The ideal lavage volume for removing bradykinin, interleukin-6, and protein from the temporomandibular joint by arthrocentesis. *J Oral Maxillofac Surg*. 2004;62(6):657-661. doi:10.1016/j.joms.2003.08.031
6. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006
7. Al-Moraissi E, Wolford L, Ellis E, Neff A. The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *J Cranio-Maxillofacial Surg*. 2020;48(1):9-23. doi:10.1016/j.jcms.2019.10.004
8. Tran C, Ghahreman K, Huppa C, Gallagher J. Management of temporomandibular disorders: a rapid review of systematic reviews and guidelines. *Int J Oral Maxillofac Surg*. 2022;51:1211-1225.
9. Tang Y, Vos L, Tuin A, et al. Arthrocentesis versus non- surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. *Int J Oral Maxillofac Surg*. 2023;52:595-603.
10. Emshoff R, Rudisch A. Determining predictor variables for treatment outcomes of arthrocentesis and hydraulic distention of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62(7):816-823. doi:10.1016/j.joms.2003.12.020
11. Israel H, Behrman D, Friedman J, Silberstein J. Rationale for Early Versus Late Intervention With Arthroscopy for Treatment of Inflammatory/Degenerative Temporomandibular Joint Disorders. *J Oral Maxillofac Surg*. 2010;68:2661-2667.
12. Thorpe A, Haddad Y, Hsu J. A systematic review and meta- analysis of randomized controlled trials comparing arthrocentesis with conservative management for painful temporomandibular joint disorder. *Int J Oral Maxillofac Surg*. 2023;52:869-896.
13. Higgins J, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions, version 6.3 (updated February 2022). *Cochrane*. 2022.

14. Page M, McKenzie J, Bossuyt P, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;29;372:n71. doi:10.1136/bmj.n71

15. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *J oral facial pain headache*. 2014;38(1):6-27.

16. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*. 1993;7(2):183-195.

17. Bramer W, Giustini D, Jonge G de, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. *J Med Libr Assoc*. 2016;104(3):240-243. doi:http://dx.doi.org/10.3163/1536-5050.104.3.014

18. Machon V, Hirjak D, Lukas J. Therapy of the osteoarthritis of the temporomandibular joint. *J Cranio-Maxillofacial Surg*. 2011;39(2):127-130. doi:10.1016/j.jcms.2010.04.010

19. Malachovsky I, Statelova D, Stasko J, Mikuskova K, Smatanova M, Janíčková M. Therapeutic effects of arthrocentesis in treatment of temporomandibular joint disorders. *Bratislava Med J*. 2019;120(3):235-239. doi:10.4149/BLL_2019_052

20. Altaweel A, Ismail H, Fayad M. Effect of simultaneous application of arthrocentesis and occlusal splint versus splint in management of non-reducing TMJ disc displacement. *J Dent Sci*. 2021;16:732-737.

21. Sterne J, Savovic J, Page M, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *Res Methods Report*. 2019;366(14898).

22. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (Minors): Development and validation of a new instrument. *ANZ J Surg*. 2003;73(9):712-716. doi:10.1046/j.1445-2197.2003.02748.x

23. Barbateskovic M, Koster T, Eck R, et al. A new tool to assess clinical diversity in meta-analyses (CDIM) of internventions. *J Clin Epidemiol*. 2021;135:29-41. doi:doi:10.1016/j.jclinepi.2021.01.023

24. Atkins D, Best D, Briss P, Eccles M, Falck-Ytter Y, Flottorp S. Grading quality of evidence and strength of recommendations. The GRADE Working Group. *Br Med J (Clin Res Ed)*. 2004;(June):328(7454):1490.

25. Duhailib Z, Granholm A, Alhazzani W, Oczkowski S, Belley-Cote E, Moller M. GRADE pearls and pitfalls—Part 1: Systematic reviews and meta-analyses. *Acta Anaesthesiol Scand*. 2024:1-9.

26. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188. doi:10.1016/0197-2456(86)90046-2

27. Borenstein M, Hedges L, Higgins J, HR Rothstein. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1:97-111.

28. Smaïl-Faugeron V, Fron-Chabouis H, Courson F, Durieux P. Comparison of intervention effects in split-mouth and parallel-Arm randomized controlled trials: A meta-epidemiological study. *BMC Med Res Methodol.* 2014;14(1). doi:10.1186/1471-2288-14-64

29. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol.* 2005;5(13). doi:10.1186/1471-2288-5-13

30. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Heal.* 2019;22:153-160. doi:10.1136/ebmental-2019-300117

31. Wetterslev J, Jakobsen J, Gluud C. Trial sequential analysis in systematic reviews with meta-analysis. *BMC Med Res Methodol.* 2017;17(39):1-18.

32. Thorlund K, Engstrom J, Wetterslev J, Brok J, Imberger G, Gluud C. *User Manual for Trial Sequential Analysis (TSA).* Copenhagen, Denmark; 2011.

33. Murakami K, Hosaka H, Moriya Y, Segami N, Iizuka T. Short-term treatment outcome study for the management of temporomandibular joint closed lock. A comparison of arthrocentesis to nonsurgical therapy and arthroscopic lysis and lavage. *Oral Surgery, Oral Med Oral Pathol Oral Radiol.* 1995;80(3):253-257. doi:10.1016/S1079-2104(05)80379-8

34. Goyal P, Singh R, Gangwar S, Mohammad S, Pal U, Singh G. Effect of duloxetine in temporomandibular joint disorders: A comparison with arthrocentesis. *Natl J Maxillofac Surg.* 2020;11(2):219-223.

35. Yilmaz O, Korkmaz Y, Tuzumer T. Comparison of treatment efficacy between hyaluronic acid and arthrocentesis plus hyaluronic acid in internal derangements of temporomandibular joint. *J Cranio-Maxillofacial Surg.* 2019;47:1720-1727.

36. Helal M, Agou S, Bayoumi A, Imam A, Hassan A. Management of internal derangement of temporomandibular joint disc displacement with reduction using two different lines of treatment. *Brazilian Dent Sci.* 2021;24(2):1-8. doi:10.14295/bds.2021.v24i2.2080

37. de Almeida A, Botelho J, Machado V, Mendes J, Manso C, Gonzalez-Lopez S. Comparison of the Efficacy of Two Protocol Treatments in Patients with Symptomatic Disc Displacement without Reduction: A Randomized Controlled Trial. *J Clin Med.* 2023;12(3228).

38. Corrêa-Silva M, de Carvalho T, Zambon C, Peres M, Machado G. Is there a superiority between arthrocentesis and stabilizing occlusal splint for the treatment of anterior disc displacement with reduction and intermittent block and anterior disc displacement without reduction in TMJ? Randomized clinical trial. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2024;138(2):244-254. doi:10.1016/j.oooo.2024.04.001

39. Li D, Luo L, Li K, Su Y, Durham J, Leung Y. Early Arthrocentesis for Temporomandibular Joint Arthralgia: A Superiority Trial. *Int Dent J.* 2024. doi:10.1016/j.identj.2024.04.015

40. Diracoglu D, Saral I, Keklik B, et al. Arthrocentesis versus nonsurgical methods in the treatment of temporomandibular disc displacement without reduction. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;108(1):3-8. doi:10.1016/j.tripleo.2009.01.005

41. Onder M, Tuz H, Kocygit D, Kisnisci R. Long-term results of arthrocentesis in degenerative temporomandibular disorders. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107:1-5.

42. Lee H, Baek H, Song D, et al. Effect of simultaneous therapy of arthrocentesis and occlusal splints on temporomandibular disorders: anterior disc displacement without reduction. *J Korean Assoc Oral Maxillofac Surg*. 2013;39(1):14. doi:10.5125/jkaoms.2013.39.1.14

43. Vos L, Huddleston Slater J, Stegenga B. Arthrocentesis as initial treatment for temporomandibular joint arthropathy: A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2014;42(5):e134-e139. doi:10.1016/j.jcms.2013.07.010

44. Hosgor H, Bas B, Celenk C. A comparison of the outcomes of four minimally invasive treatment methods for anterior disc displacement of the temporomandibular joint. *Int J Oral Maxillofac Surg*. 2017;46(11):1403-1410. doi:10.1016/j.ijom.2017.05.010

45. Tatli U, Benlidayi M, Ekren O, Salimov F. Comparison of the effectiveness of three different treatment methods for temporomandibular joint disc displacement without reduction. *Int J Oral Maxillofac Surg*. 2017;46:603-609.

46. Malekzadeh B, Cahlin B, Widmark G. Conservative therapy versus arthrocentesis for the treatment of symptomatic disk displacement without reduction: a prospective randomized controlled study. *Oral Surgery, Oral Med Oral Pathol Oral Radiol*. 2019;128:18-24.

47. Abbasgholizadeh Z, Evren B, Ozkan Y. Evaluation of the efficacy of different treatment modalities for painful temporomandibular disorders. *Int J Oral Maxillofac Surg*. 2020;49:628-635.

48. Guarda-Nardini L, Masiero S, Marioni G. Conservative treatment of temporomandibular joint osteoarthrosis: Intra-articular injection of sodium hyaluronate. *J Oral Rehabil*. 2005;32(10):729-734. doi:10.1111/j.1365-2842.2005.01505.x

49. Vos L, Stegenga B, Stant A, Quik E, Huddleston Slater J. Cost Effectiveness of Arthrocentesis Compared to Conservative Therapy for Arthralgia of the Temporomandibular Joint: A Randomized Controlled Trial. *J Oral Facial Pain Headache*. 2018;32(2):198-207. doi:10.11607/ofph.1457

50. Dworkin R, Turk D, Wyrwich K, et al. Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. *J pain*. 2008;9(2):105-121.

51. Calixtre L, Oliveira A, Alburquerque-Sendin F, Armijo-Olivo S. What is the minimal important difference of pain intensity, mandibular function, and headache impact in patients with temporomandibular disorders? Clinical significance analysis of a randomized controlled trial. *Musculoskelet Sci Pract*. 2020;46:2020.

52. Kropmans T, Dijkstra P, Stegenga B, Stewart R, Bont L de. Smallest detectable difference of maximal mouth opening in patients with painfully restricted temporomandibular joint function. *Eur J Oral Sci*. 2000;108:9-13.

53. Nishimura M, Segami N, Kaneyama K, Suzuki T, Miyamaru M. Proinflammatory cytokines and arthroscopic findings of patients with internal derangement and osteoarthritis of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2002;40:68-71.

54. Celotti C, Martin-Granizo R, De La Sen O. Correlation of arthroscopic findings with clinical–radiological signs and symptoms of temporomandibular joint dysfunction: retrospective study of 829 joints. *Int J Oral Maxillofac Surg*. 2022;51:1069-1073.

55. Murakami K, Segami N, MOryia Y, Iizuka T. Correlation Between Pain and Dysfunction and Intra-articular Adhesions in Patients With Internal Derangement of the Temporomandibular Joint. *J Oral Maxillofac Surg*. 1992;50:705-708.

56. Sidebottom A. How do I manage restricted mouth opening secondary to problems with the temporomandibular joint? *Br J Oral Maxillofac Surg*. 2012;51:469-472.

57. Ritto F, Cueto A, dos Santos Canellas J, et al. Arthrocentesis versus nonsurgical methods in the management of temporomandibular joint closed lock and pain: a double-blind randomized controlled trial. *Oral Surgery, Oral Med Oral Pathol Oral Radiol*. 2022;133(4):369-376.

58. Ferreira N, Masterson D, Lopes de Lima R, et al. Efficacy of viscosupplementation with hyaluronic acid in temporomandibular disorders: A systematic review. *J Cranio-Maxillofacial Surg*. 2018;46:1943-1952.

59. Derwich M, Mitus-kenig M, Pawlowska E. Mechanisms of action and efficacy of hyaluronic acid, corticosteroids and platelet-rich plasma in the treatment of temporomandibular joint osteoarthritis—a systematic review. *Int J Mol Sci*. 2021;22(14). doi:10.3390/ijms22147405

60. Siewert-Gutowska M, Pokrowiecki R, Kaminski A, Zawadzki P, Stopa Z. State of the Art in Temporomandibular Joint Arthrocentesis—A Systematic Review. *J Clin Med*. 2023;12.

61. Vaira LA, Raho MT, Soma D, et al. Complications and post-operative sequelae of temporomandibular joint arthrocentesis Complications and post-operative sequelae of temporomandibular joint arthrocentesis. *Cranio*. 2018;36(4):264-267.

62. Li D, Wong N, Li S, McGrath C, Leung Y. Timing of arthrocentesis in the management of temporomandibular disorders: an integrative review and meta-analysis. *Int J Oral Maxillofac Surg*. 2021;50:1078-1088.

63. Slade GD. Derivation and validation of a short-form oral health impact profile. *Community Dent Oral Epidemiol*. 1997;25(4):284-290. doi:10.1111/j.1600-0528.1997.tb00941.x

Appendix A. Overview of search queries per electronic database.

Database	Search terms	Hits (09-09-2022)	Hits (24-11-2023	Hits (02-08-2024)
Pubmed	("Temporomandibular Joint"[Mesh] OR "Craniomandibular Disorders"[Mesh] OR Temporomand*[tiab] OR temporo-mand*[tiab] OR tmj[tiab] OR craniomandibular*[tiab] OR myofascial[tiab]) AND ("Arthrocentesis"[Mesh] OR Arthrocentes*[tiab] OR "Therapeutic Irrigation"[Mesh] OR lavage*[tiab] OR irrigat*[tiab] OR lysis[tiab] OR minimally invasiv*[tiab] OR minimal invasiv*[tiab])	812	147	80
Embase	('temporomandibular joint'/exp OR 'temporomandibular joint disorder'/exp OR Temporomand*:ab,ti,kw OR 'temporo-mand*':ab,ti,kw OR tmj:ab,ti,kw OR craniomandibular*:ab,ti,kw OR myofascial:ab,ti,kw) AND ('arthrocentesis'/exp OR 'lavage'/exp OR Arthrocentes*:ab,ti,kw OR lavage*:ab,ti,kw OR irrigat*:ab,ti,kw OR lysis OR 'minimally invasiv*':ab,ti,kw OR 'minimal invasiv*':ab,ti,kw)	1065	188	86
Web of Science	TS= (Temporomand*OR temporo-mand* OR tmj OR craniomandibular* OR myofascial) AND TS= (Arthrocentes* OR lavage* OR irrigat* OR lysis OR "minimally invasiv*" OR "minimal invasiv*")	596	107	29
Cochrane Library	(Temporomand* OR "temporo-mand*" OR tmj OR craniomandibular* OR myofascial) AND (Arthrocentes* OR lavage* OR irrigat* OR lysis OR "minimally invasiv*" OR "minimal invasiv*")	146	35	34
Scopus	TITLE-ABS-KEY (Temporomand* OR "temporo-mand*" OR tmj OR craniomandibular* OR myofascial) AND TITLE-ABS-KEY (Arthrocentes* OR lavage* OR irrigat* OR lysis OR "minimally invasiv*" OR "minimal invasiv*")	1084	205	74

Appendix B. Overview of excluded reports after full-text screening.

Author (year)	Reason for exclusion	Regarding
Al-Rifae et al. (2021[1])1	Intervention does not fit current review	Inclusion criteria
Bilici et al. (2018)[2]	Intervention performed when control group failed	Inclusion criteria
Diracoglu et al. (2008)[3]	Conference abstract	Exclusion criteria
Hasson et al. (2000)[4]	Review paper	Exclusion criteria
Isik et al. (2023)[5]	Control group does not fit current review	Inclusion criteria
Kholakiya et al. (2015)[6]	Conference abstract	Exclusion criteria
Moreno-Sanchez et al. (2022)[7]	Review paper	Exclusion criteria
Ritto et al. (2022)[8]	Control group does not fit current review (joint aspiration)	Inclusion criteria
Rodrigues et al. (2023)[9]	Control group does not fit current review	Inclusion criteria
Sato et al. (1997)[10]	Control group does not fit current review	Inclusion criteria
Vos et al. (2013)[11]	Conference abstract	Exclusion criteria
Yucel et al. (2014)[12]	Outcome measurement does not fit current review	Inclusion criteria
Cueto (2020)[13]	Study protocol	Exclusion criteria

Appendix C. Individual results from included studies.

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement (mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Murakami et al. (1995)[14]	Intermediate (6)	AC	20	MD ±SD	45.0 ±21.8*	-	11.9 ±5.7*	7.3[a]/ 5.3[b]	-	-	-	-	-	-
		NSAID + SS	63	MD ±SD	29.0 ±25.9*	-	9.1 ±7.8*	3.9[a]/ 2.7[b]	-	-	-	-	-	-
Guarda Nardini et al. (2005)[15]	Short (3)	AC	20	MD	40.0	39.0	4.2	2.6[c]	-	-	-	-	-	-
		SS	20	MD	51.0	26.0	5.8	3.1[c]	-	-	-	-	-	-
		Rest	20	MD	-	-	-	-	-	-	-	-	-	-
	Intermediate (6)	AC	20	MD	42.0	36.0	7.0	2.5[c]	-	-		-	-	-
		SS	20	MD	52.0	28.0	6.4	3.0[c]	-	-	-	-	-	-
		Rest	20	MD	2.0	1.0	-1.7	-1.3[c]	-	-	-	-	-	-
Diracoglu et al. (2009)[16]	Short (3)	AC	54	MD ±SD	31.1 ±23.3	-	3.9 ±6.1	-	-	0.7	1.0[e]/ 0.7[f]	-	-	-
		SS + HE	56	MD ±SD	6.2 ±15.8	-	4.2 ±7.8	-	-	0.2	0.7[e]/ -0.6[f]	-	-	-
	Intermediate (6)	AC	54	MD ±SD	47.4 ±21.4	-	6.7 ±6.2	-	-	1.2	1.8[e]/ 1.5[f]	-	-	-
		SS + HE	56	MD ±SD	12.2 ±17.6	-	6.2 ±6.5	-	-	1.1	2.2[e]/ -0.1[f]	-	-	-

Appendix C. Individual results from included studies. *Continued.*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement (mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Onder et al. (2009)[17]	Short (2)	AC + SS	15	MD ±SD	31.8 ±7.9*	-	1.7 ±7.8*	-	0.1[d]	-	-	-	-	-
		SS	10	MD ±SD	2.6 ±6.4*	-	1.0 ±6.7*	-	0.1[d]	-	-	-	-	-
	Intermediate (6)	AC + SS	15	MD ±SD	32.7 ±13.1*	-	5.0 ±6.2*	-	0.1[d]	-	-	-	-	-
		SS	10	MD ±SD	2.8 ±6.3*	-	2.0 ±6.2*	-	0.1[d]	-	-	-	-	-
Machon et al. (2011)[18]	Short (3)	AC + SS	20	MD ±SD	*bin*	-	*bin*	-	-	-	-	-	-	-
		AC	20	MD ±SD	*bin*	-	*bin*	-	-	-	-	-	-	-
		SS	20	MD ±SD	*bin*	-	*bin*	-	-	-	-	-	-	-
		Rest	20	MD ±SD	*bin*	-	*bin*	-	-	-	-	-	-	-

Abbr.: FU follow-up; AC arthrocentesis; NSAID nonsteroidal anti-inflammatory drugs; SS stabilization splint; N number of subjects; MD difference between baseline and follow-up means; SD standard deviation; Pain M pain during mandibular movement or function; VAS visual analog scale; bin binary study outcome (not presented for sake of simplicity); Pain R pain at rest; MMO maximum mouth opening; QoL quality of life. *SD imputed for quantitative analysis using a correlation coefficient of 0.5. [a] Activities and Daily Living score, scale 0–72 (higher is worse). [b] Jaw function score, scale 0–20 (higher is worse).
[c] Mastication efficiency, scale 0-10 (higher is better). [d] Joint sounds, scale 0-2 (higher is worse). [e] Right lateral movement. [f] Left lateral movement.

Appendix C. Individual results from included studies. *Continued*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Lee et al. (2013)[19]	Short (3)	AC + SS	17	MD ±SD	38.8 ±17.8*	-	8.4 ±6.9*	-	0.97[a]	-	-	-	-	-
		SS	13	MD ±SD	22.3 ±14.0*	-	4.8 ±3.7*	-	1.46[a]	-	-	-	-	-
	Intermediate (6)	AC + SS	17	MD ±SD	43.8 ±18.4*	-	10.0 ±6.9*	-	0.73[a]	-	-	-	-	-
		SS	13	MD ±SD	29.2 ±14.9*	-	6.6 ±3.7*	-	1.54[a]	-	-	-	-	-
Hosgor et al. (2017)[20]	Short (3)	AC	10	MD ±SD	45.0 ±7.2*	-	5.2 ±2.4*	-	ANA	-	-	-	-	-
		SS	10	MD ±SD	36.0 ±10.2*	-	4.1 ±2.3*	-	ANA	-	-	-	-	-
		NSAID	10	MD ±SD	32.0 ±5.9*	-	2.0 ±2.8*	-	ANA	-	-	-	-	-
		LLLT + SS	10	MD ±SD	45.0 ±6.2*	-	5.5 ±2.3*	-	ANA	-	-	-	-	-
	Intermediate (6)	AC	10	MD ±SD	48.0 ±6.4*	-	7.3 ±2.5*	-	ANA	-	-	-	-	-
		SS	10	MD ±SD	38.0 ± 9.7*	-	4.0 ±2.3*	-	ANA	-	-	-	-	-
		NSAID	10	MD ±SD	32.0 ±6.4*	-	3.0 ±2.7*	-	ANA	-	-	-	-	-
		LLLT + SS	10	MD ±SD	40.0 ±7.1*	-	6.0 ±2.3*	-	ANA	-	-	-	-	-

Appendix C. Individual results from included studies. *Continued*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Tatli et al. (2017)[21]	Short (3)	AC	40	MD ±SD	51.0 ±20.0*	-	11.8 ±3.3*	-	-	-	1.8[b]/ 4.5[c]	-	37.0[d]	-
		AC + SS	40	MD ±SD	45.0 ±20.0*	-	13.2 ±5.0*	-	-	-	1.9[b]/ 4.5[c]	-	36.6[d]	-
		SS	40	MD ±SD	33.0 ±22.6*	-	6.2 ±3.2*	-	-	-	1.1[b]/ 2.0[c]	-	25.4[d]	-
	Intermediate (6)	AC	40	MD ±SD	63.0 ±19.3*	-	13.7 ±4.1*	-	-	-	2.7[b]/ 5.2[c]	-	50.6[d]	-
		AC + SS	40	MD ±SD	60.0 ±18.3*	-	15.7 ±3.9*	-	-	-	2.4[b]/ 4.7[c]	-	46.6[d]	-
		SS	40	MD ±SD	48.0 ±21.0*	-	8.9 ±3.7*	-	-	-	1.3[b]/ 2.5[c]	-	40.0[d]	-

Abbr.: FU follow-up; AC arthrocentesis; SS stabilization splint; NSAID nonsteroidal anti-inflammatory drugs; LLLT low-level laser therapy; HE home exercise; N number of subjects; MD difference between baseline and follow-up means; SD standard deviation; Pain M pain during mandibular movement or function; VAS visual analog scale; Pain R pain at rest; MMO maximum mouth opening; ANA analyzed in the included study but data not available for extraction; QoL quality of life. *SD imputed for quantitative analysis using a correlation coefficient of 0.5. [a] Joint noise, tool and scale not reported. [b] Ipsilateral mandibular movement. [c] Contralateral mandibular movement. [d] Using disability questions from the Research Diagnostic Criteria for Temporomandibular Disorders (RCD/TMD) Axis II biobehavioral questionnaire, scale 0-60 (higher is worse).

Appendix C. Individual results from included studies. *Continued*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Malachovsky et al. (2019)[22]	Short (3)	AC	419	MD ±SD	50.3 ±10.0*	-	0.0 ±0.7*	-	-	-	-	-	-	-
		NSAID	1333	MD ±SD	20.0 ±8.7*	-	-0.1 ±1.4*	-	-	-	-	-	-	-
	Intermediate (12)	AC	419	MD ±SD	46.9 ±9.7*	-	10.0 ±0.8*	-	-	-	-	-	-	-
		NSAID	1333	MD ±SD	-30.8 ±8.1*	-	0.9 ±1.4*	-	-	-	-	-	-	-
Malekzadeh et al. (2019)[23]	Short (3)	AC + HE	12	MD ±SD	24.5 ±19.1*	-	12.5 ±3.4*	-	-	-	-	-	-	-
		SS + HE	12	MD ±SD	19.4 ±27.8*	-	11 ±5.0*	-	-	-	-	-	-	-
	Intermediate (12)	AC + HE	12	MD ±SD	47.7 ±15.6*	-	15.5 ±5.3*	-	-	-	-	-	-	-
		SS + HE	12	MD ±SD	38.5 ±27.4*	-	17.9 ±6.4*	-	-	-	-	-	-	-
Yilmaz et al. (2019)[24]	Intermediate (6)	AC 1#	18	DM	50.0	20.0	4.5	4.0[a]	1.0[b]	-	-	-	3.0[a]	-
		Rest 1#	9	DM	0.0	0.0	-4.0	1.0[a]	0.0[b]	-	-	-	-0.5[a]	-
		AC 2#	18	DM	60.0	20.0	10.0	4.0[a]	1.0[b]	-	-	-	4.5[a]	-
		Rest 2#	8	DM	-5.0	-5.0	-0.5	0.0[a]	0.0[b]	-	-	-	0.3[a]	-

Appendix C. Individual results from included studies. *Continued*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Abbasgholi-zadeh et al. (2020)[25]	Short (3)	AC + SS	15	MD ±SD	50.0 ±16.2*	-	7.5 ±3.8*	-	-	-	2.7[c]	-	-	-
		SS	15	MD ±SD	36.7 ±16.7*	-	6.0 ±2.9*	-	-	-	2.1[c]	-	-	-
		LLLT + SS	15	MD ±SD	41.1 ±13.5*	-	6.3 ±3.5*	-	-	-	2.3[c]	-	-	-
	Intermediate (12)	AC + SS	15	MD ±SD	70.0 ±8.0*	-	10.9 ±3.2*	-	-	-	3.7[c]	-	-	-
		SS	15	MD ±SD	59.3 ±13.5*	-	8.4 ±3.0*	-	-	-	2.5[c]	-	-	-
		LLLT + SS	15	MD ±SD	66.6 ±9.5*	-	9.9 ±3.5*	-	-	-	3.7[c]	-	-	-

Abbr.: FU follow-up; AC arthrocentesis; NSAID nonsteroidal anti-inflammatory drugs; SS stabilization splint; HE home exercise; LLLT low-level laser therapy; N number of subjects; MD difference between baseline and follow-up means; SD standard deviation; DM difference of medians; Pain M pain during mandibular movement or function; VAS visual analog scale; Pain R pain at rest; MMO maximum mouth opening; QoL quality of life.

#Group 1 involves subjects suffering from disc displacement with reduction, group 2 subjects suffering from disc displacement without reduction. *SD imputed for quantitative analysis using a correlation coefficient of 0.5. [a] Based on visual analog scale, scale 0-10 (higher is better). [b] Based on scale 0-2 (higher is better). [c] Contralateral mandibular movement.

Appendix C. Individual results from included studies. *Continued*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Goyal et al. (2020)[26]	Short (3)	AC	10	MD ±SD	20.0 ±13.6*	-	3.2 ±6.2*	-	ANA	-	-	-	-	-
		AC + SNRI	10	MD ±SD	43.0 ±11.5*	-	7.0 ±8.5*	-	ANA	-	-	-	-	-
		SNRI	10	MD ±SD	5.0 ±17.3*	-	0.6 ±4.2*	-	ANA	-	-	-	-	-
Altaweel et al. (2021)[27]	Short (3) & Intermediate (12)	AC + SS	10	MD ±SD	ANA	-	ANA	-	-	-	-	-	-	-
		AC + ARS	10	MD ±SD	ANA	-	ANA	-	-	-	-	-	-	-
		SS	10	MD ±SD	ANA	-	ANA	-	-	-	-	-	-	-
		ARS	10	MD ±SD	ANA	-	ANA	-	-	-	-	-	-	-
Helal et al. (2021)[28]	Short (3)	AC	18	MD ±SD	-	-	3.9 ±1.2	-	-	1.5 ±0.6	2.7 ±1.6[a]/ 2.2 ±1.2[b]	-	-	-
		ARS	18	MD ±SD	-	-	10.7 ±4.4	-	-	1.7 ±0.6	4.3 ±0.8[a]/ 3.2 ±1.5[b]	-	-	-

Appendix C. Individual results from included studies. *Continued*

Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
De Almeida et al. (2023)[29]	Short (1)	AC	26	MD ±SD	34.0 ±19.1*	-	5.4 ±3.2	-	-	-	-	-	12.9[c]	-
		HE	26	MD ±SD	18.0 ±23.5*	-	2.4 ±2.5	-	-	-	-		13.3[c]	-
	Intermediate (12)	AC	26	MD ±SD	43.0 ±21.5*	-	5.6 ±3.7	-	-	-	-	-	10.0[c]	-
		HE	26	MD ±SD	38.0 ±24.1*	-	2.4 ±2.5	-	-	-	-	-	8.8[c]	-

Abbr.: FU follow-up; AC arthrocentesis; SNRI Serotonin-norepinephrine reuptake inhibitor; SS stabilization splint; ARS anterior repositioning splint; HE home exercise; N number of subjects; MD difference between baseline and follow-up means; SD standard deviation; Pain M pain during mandibular movement or function; VAS visual analog scale; ANA analyzed in the included study but data not available for extraction; Pain R pain at rest; MMO maximum mouth opening; QoL quality of life. *SD imputed for quantitative analysis using a correlation coefficient of 0.5. [a] Right lateral movement. [b] Left lateral movement. [c] Using Oral Health Impact Profile 14 questionnaire, scale 0-56 (higher is worse).

Appendix C. Individual results from included studies. *Continued*

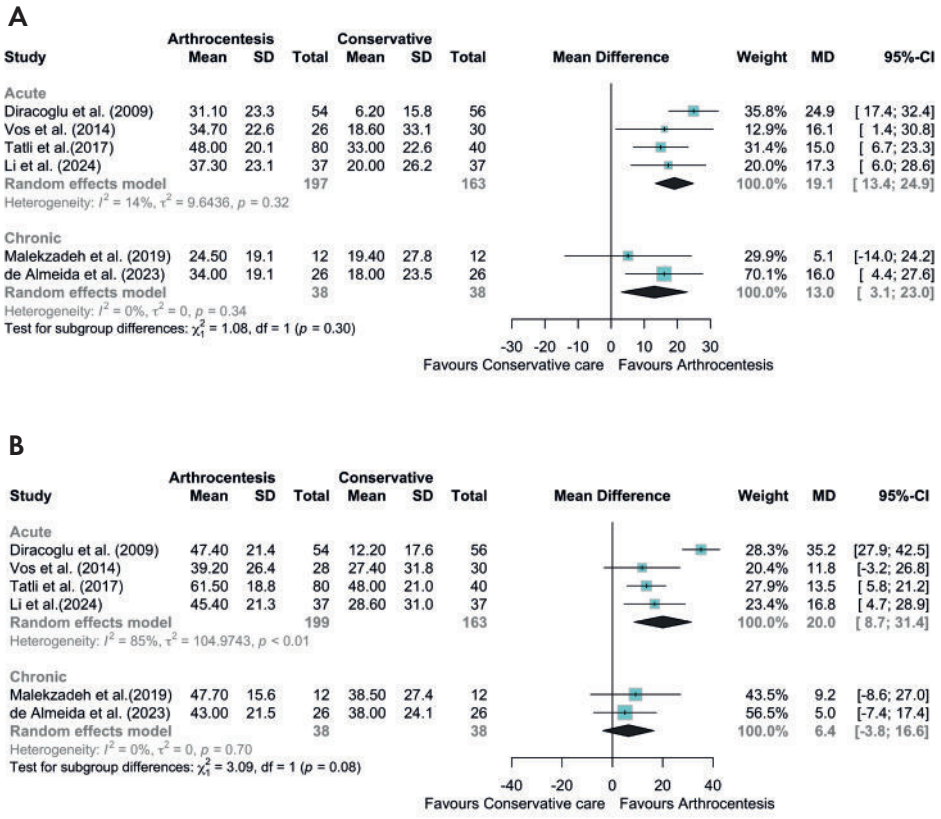
Author (year)	FU (months)	Study arm		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Vos et al. (2014)[30] & (2018)[31]	Short (3)	AC	MD ±SD	34.7 ±22.6*	14.4 ±19.2*	4.6 ±6.5*	17.1 ±22.2*,[a]	-	-	-	-	12.9 ±20.3*,[b]	-
			N	26	26	27	20	-	-	-	-	21	-
		PT + SS	MD ±SD	18.6 ±33.1*	0.5 ±28.8*	1.7 ±8.6*	12.5 ±26.1*,[a]	-	-	-	-	6.7 ±28.0*,[b]	-
			N	30	30	30	17	-	-	-	-	17	-
	Intermediate (6.5)	AC	MD ±SD	39.2 ±26.4*	13.7 ±20.4*	5.7 ±8.0*	41.6 ±13.4*,[a]	-	-	-	-	17.7 ±20.1*,[b]	589[c]
			N	28	28	25	10	-	-	-	-	10	30
		PT + SS	MD ±SD	27.4 ±31.8*	7.4 ±27.3*	4.1 ±7.8*	19.1 ±23.1*,[a]	-	-	-	-	10.6 ±18.1*,[b]	2266[c]
			N	30	30	28	15	-	-	-	-	14	31
Tang et al. (2023)[32]	Long (74)	AC	MD ±SD	42.2 ±22.4*	10.2 ±17.4*	-	40.4 ±17.7*,[a]	-	-	-	-	-	-
			N	21	20	-	18	-	-	-	-	-	-
		PT + SS	MD ±SD	30.6 ±33.1*	8.6 ±26.9*	-	32.2 ±23.4*,[a]	-	-	-	-	-	-
			N	24	24	-	23	-	-	-	-	-	-

Abbr.: FU follow-up; AC arthrocentesis; PT Physical therapy; SS stabilization splint; N number of subjects; MD difference between baseline and follow-up means; SD standard deviation; Pain M pain during mandibular movement or function; VAS visual analog scale; Pain R pain at rest; MMO maximum mouth opening; QoL quality of life. *Mean and standard deviation calculated directly from original database of the study. [a] Using Mandibular Function Impairment Questionnaire, scale 0-100 (higher is worse). [b] Using Oral Health Impact Profile 14 questionnaire, scale 0-56 (higher is worse). [c] Estimated mean total (societal) cost over 26 weeks, in United States Dollars.

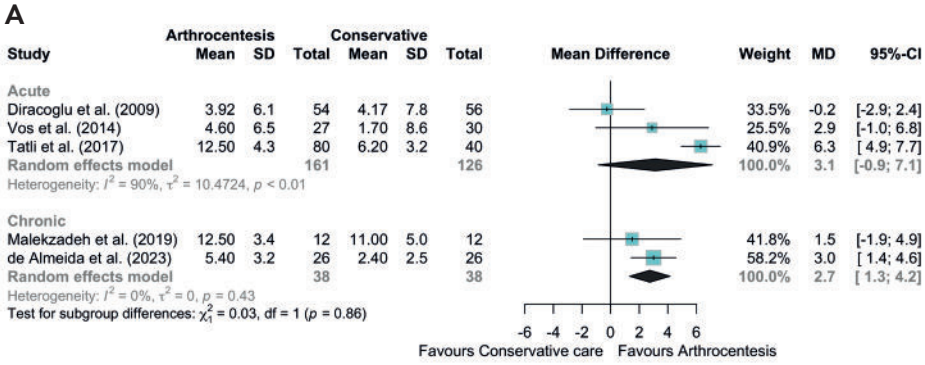
Appendix C. Individual results from included studies. *Continued*

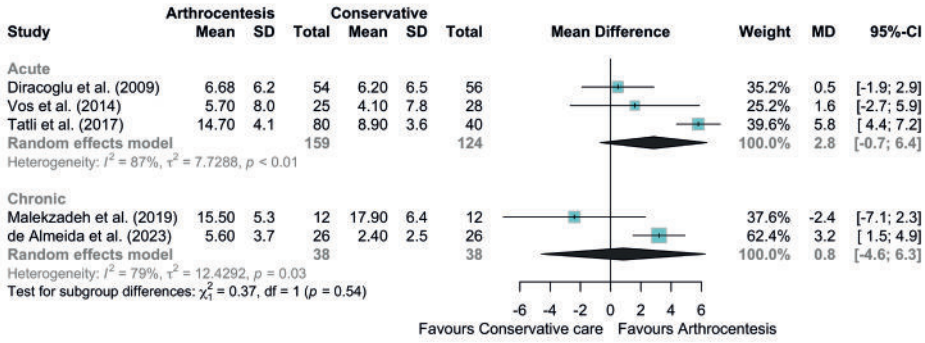
Author (year)	FU (months)	Study arm	N		Pain M (VAS 0-100)	Pain R (VAS 0-100)	MMO improvement (mm)	Mandibular function	Joint blocks and noises	Protrusive movement improvement (mm)	Lateral movement improvement(mm)	Blocks and noises	QoL	Costs/Cost-effectiveness
Correa-Silva et al. (2024)[33]	Short (3)	AC	11	MD ±SD	29.9 ±32.9*	-	9.2 ±8.2*	4.0[a]	*bin*	-	-	-	6.5[b]	-
		SS	13	MD ±SD	14.6 ±29.0*	-	6.8 ±6.8*	2.1[a]	*bin*	-	-	-	4.6[b]	-
	Intermediate (6)	AC	11	MD ±SD	26.5 ±34.7*	-	4.0 ±8.2*	2.2[a]	*bin*	-	-	-	9.0[b]	
		SS	13	MD ±SD	12.9 ±31.4*	-	5.5 ±6.6*	4.3[a]	*bin*	-	-	-	3.8[b]	
Li et al. (2024)[34]	Short (3) &	AC + SS	37	MD ±SD	37.3 ±23.1#	-	ANA	-	-	-	-	-	-	-
		SS	37	MD ±SD	20.0 ±26.2#	-	ANA	-	-	-	-	-	-	-
	Intermediate (12)	AC + SS	37	MD ±SD	45.5 ±21.3#	-	ANA	-	-	-	-	-	-	-
		SS	37	MD ±SD	28.6 ±31.0#	-	ANA	-	-	-	-	-	-	-

Abbr.: FU follow-up; AC arthrocentesis; SS stabilization splint; N number of subjects; MD difference between baseline and follow-up means; SD standard deviation; Pain M pain during mandibular movement or function; VAS visual analog scale; Pain R pain at rest; MMO maximum mouth opening; ANA analyzed in the included study but data not available for extraction; bin binary study outcome (not presented for sake of simplicity); QoL quality of life. *SD imputed for quantitative analysis using a correlation coefficient of 0.5. # SD imputed from standard error and sample size. [a] Food limitation score, tool and scale not reported. [b] Psychosocial status score, tool and scale not reported.

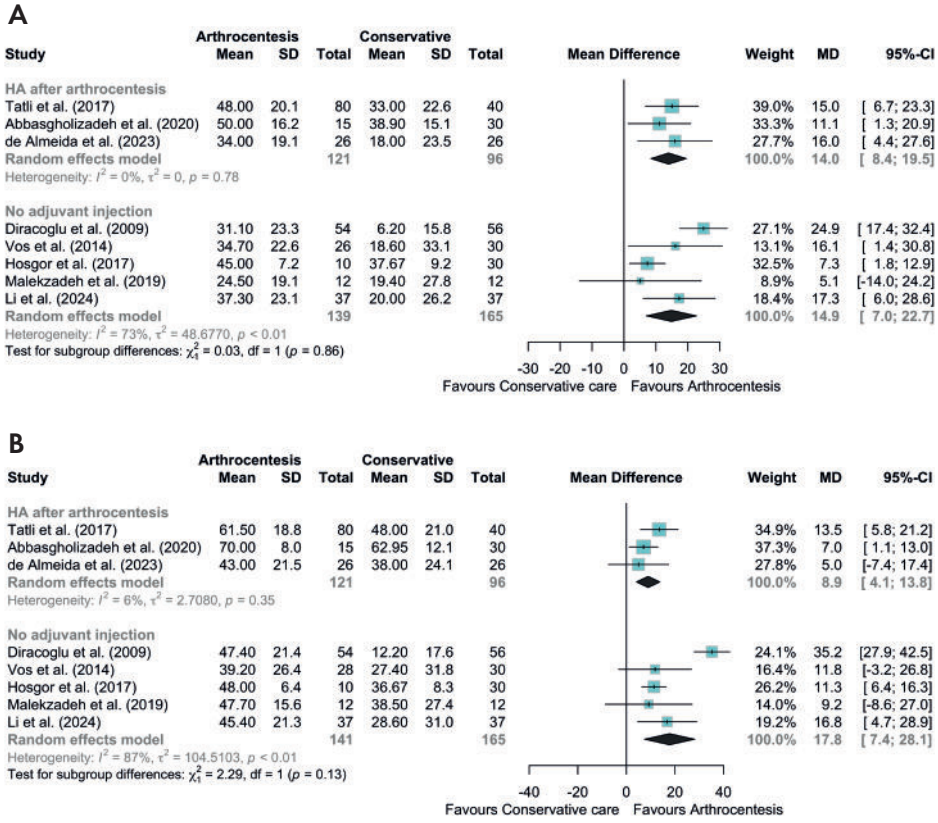


Appendix D. Forest plots of pain reduction (visual analog scale, 0-100) comparing subgroups with patients with acute symptoms (<3 months) and chronic symptoms (≥3 months) at (A) short-term and (B) intermediate-term follow-up. Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% Confidence interval.

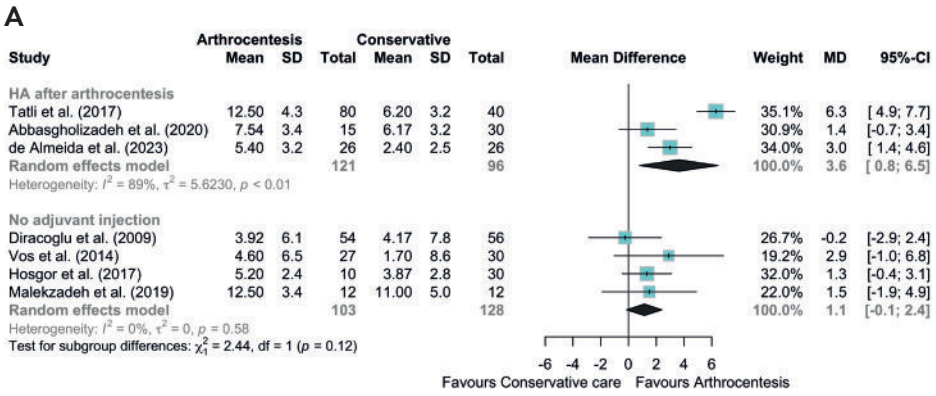


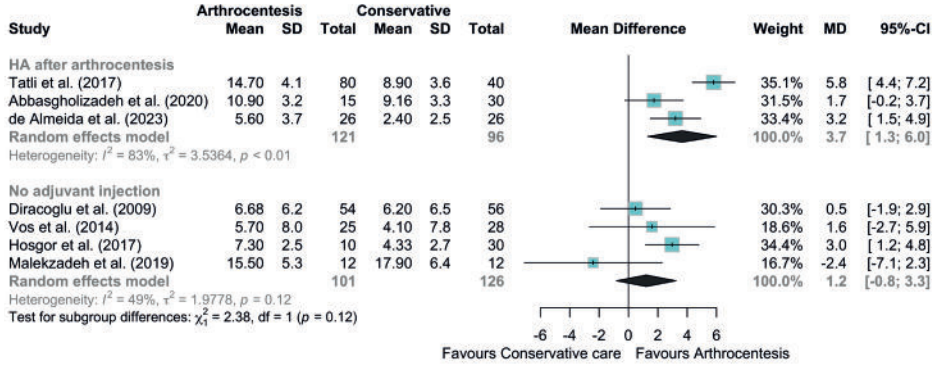


Appendix E. Forest plots of maximum mouth opening improvement (mm) comparing subgroups with patients with acute symptoms (<3 months) and chronic symptoms (≥3 months) at (A) short-term and (B) intermediate-term follow-up. Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% Confidence interval.



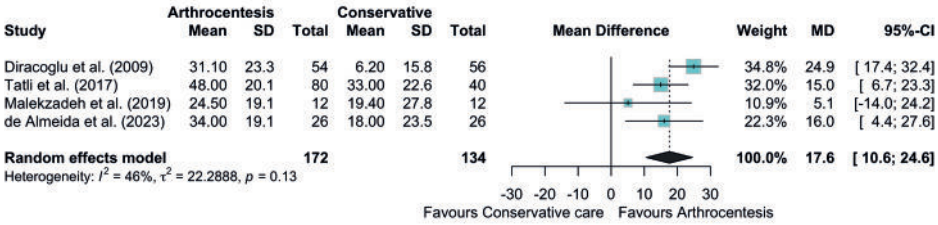
Appendix F. Forest plots of pain reduction (visual analog scale, 0-100) comparing subgroups involving adjuvant hyaluronic acid after arthrocentesis and no hyaluronic acid use at (A) short-term and (B) intermediate-term follow-up. Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% Confidence interval; HA hyaluronic acid.





Appendix G. Forest plots of maximum mouth opening improvement (mm) comparing subgroups involving adjuvant hyaluronic acid after arthrocentesis and no hyaluronic acid use at (A) short-term and (B) intermediate-term follow-up. Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% Confidence interval; HA hyaluronic acid.

A



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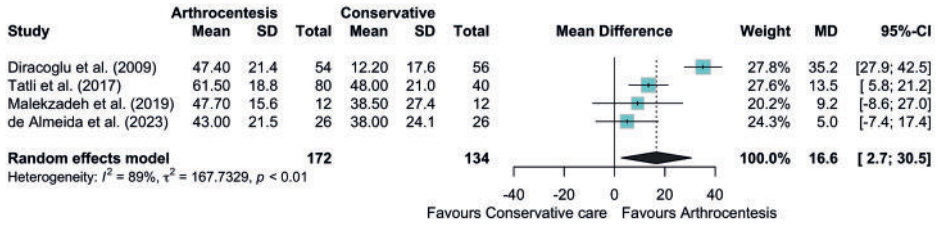

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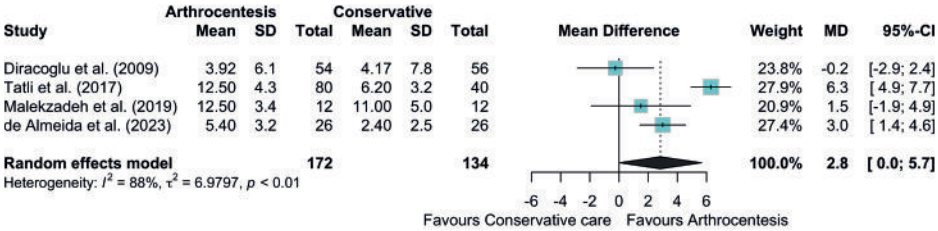
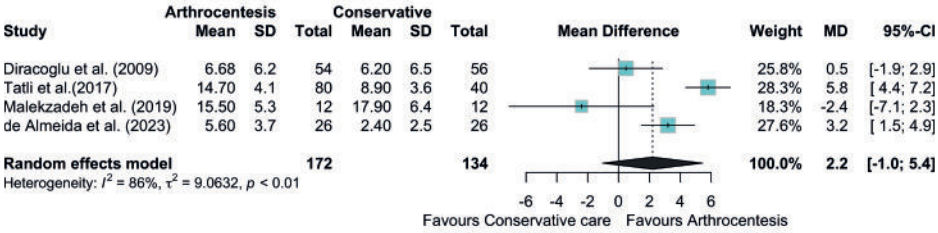


D



Appendix H. Forest plots of studies involving patients with disc displacement without reduction. (A) Pain reduction (visual analog scale, 0-100) at short-term and (B) intermediate-term follow-up. (C) Maximum mouth opening (mm) at short-term and (D) intermediate-term follow-up. Abbr.: SD standard deviation; MD mean difference; 95%-CI 95% Confidence interval.

Appendix I.a. Clinical diversity in meta-analysis tool for heterogeneity assessment of outcome pain improvement at short- and intermediate-term follow-up.

		Diracoglu et al. (2009)[16]	Vos et al. (2014)[30]	Hosgor et al. (2017)[20]	Tatli et al. (2017)[21]	Malekzadeh et al. (2019)[23]	Abbasgholi-zadeh et al. (2020)[25]	de Almeida et al. (2023)[29]	Correa-Silva et al. (2024)[33]	Li et al. (2024)[34]	Score
Setting											
1.	Years reported (A), in developed vs developing country (B), unit type (C)	2009 (A); developed, Turkey (B); University hospital (C)	2014 (A); developed, Netherlands (B); university hospital (C)	2017 (A); developed, Turkey (B); University hospital (C)	2017 (A); developed, Turkey (B); University hospital (C)	2019 (A); developed, Sweden (B); University hospital (C)	2020 (A); developed, Turkey (B); University hospital (C)	2023 (A); developed, Portugal (B); Large outpatient clinic (C)	2024 (A); developed, Brazil (B); University hospital (C)	2024 (A); developed; Hong Kong (B); University hospital (C)	1
Population											
2.	Mean age in years	34.1	29.5	30.4	35.9	29.6	29.9	48.0	32.8	44.9	1
3.	% female	90.1	76.2	90	87.5	79.2	84.4	73.1	79.2	86.5	0
4.	Inclusion criteria and baseline disease severity	DDwoR; pain VAS 59.6	DDwoR/ DDwR/ DJD; pain VAS 53,9	DDwR / DDwoR; pain VAS 67.0	DDwoR; pain VAS 66,3	DDwoR; pain VAS 53,6	DDwR / DDwoR; pain VAS 72,6	DDwoR and DJD; pain VAS 67,5	DDwR/ DDwoR; pain VAS 70.2	DDwoR/ DDwR/ DJD ; pain VAS 59.7	1
5.	Co-morbidities	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	0

Appendix I.a. Clinical diversity in meta-analysis tool for heterogeneity assessment of outcome pain improvement at short- and intermediate-term follow-up. *Continued*

		Diracoglu et al. (2009)[16]	Vos et al. (2014)[30]	Hosgor et al. (2017)[20]	Tatli et al. (2017)[21]	Malekzadeh et al. (2019)[23]	Abbasgholi-zadeh et al. (2020)[25]	de Almeida et al. (2023)[29]	Correa-Silva et al. (2024)[33]	Li et al. (2024)[34]	Score
Intervention											
6.	Intensity, strengths, or duration of intervention	AC Double needle, 60ml Ringer's Lactate. Post-op: none	AC Double needle, 300ml NaCl. Post-op: none	AC Double needle, 100ml Ringer's Lactate. Post-op: soft diet + exercises	AC Double needle, 120ml NaCl or AC + SS. Post-op: NSAID if needed	AC Double needle, 40-60ml NaCl + NSAID. Post-op: NSAID + exercises	AC ultrasound guided, 100-120ml NaCl + SS Post-op: none	AC single needle, 25ml NaCl Post-op: one physical therapy session	AC double needle, 100-200ml Ringer's Lactate. Post op: soft diet + physical therapy	AC double needle, 100ml NaCL. Post-op: none.	1
7.	Timing	Symptom duration 3 weeks	Symptom duration 2 weeks	Not reported	Symptom duration 2 weeks	Symptom duration 3,8 months	Not reported	Symptom duration 6 months	Not reported	Initial treatment	2
8.	Control intervention	SS + hot packs + exercises	Soft diet + SS (pain) + physical therapy (MMO)	SS or NSAID or LLLT	SS + NSAID	CBT + exercises + NSAID (pain) + SS (bruxism)	SS or LLLT + SS	Physical therapy	SS	SS	2
9.	Co-interventions	None	None	None	2ml HA	None	2ml HA	1ml HA	1ml CS	none	1

Appendix I.a. Clinical diversity in meta-analysis tool for heterogeneity assessment of outcome pain improvement at short- and intermediate-term follow-up. *Continued*

		Diracoglu et al. (2009)[16]	Vos et al. (2014)[30]	Hosgor et al. (2017)[20]	Tatli et al. (2017)[21]	Malekzadeh et al. (2019)[23]	Abbasgholi-zadeh et al. (2020)[25]	de Almeida et al. (2023)[29]	Correa-Silva et al. (2024)[33]	Li et al. (2024)[34]	**Score**
Outcome											
10.	Definition of the outcome	VAS (0-10)	VAS (0-100) at movement	VAS (0-10)	VAS (0-10)	VAS (0-100)	VAS (0-10)	VAS (0-10)	VAS (0-100)	VAS (0-10)	0
11.	Timing of follow-up										
a)	Short-term	3 months	3 months	3 months	3 months	3 months	3 months	1 month	3 months	3 months	1
b)	Intermediate-term	6 months	6 months	6 months	6 months	12 months	6 months	12 months	6 months	12 months	2
	Total short-term:										10
	Total intermediate-term:										11

Abbr.: DDwoR Disc displacement without reduction, DDwR Disc displacement with reduction, DJD degenerative joint disease, VAS visual analog scale, AC arthrocentesis, SS stabilization splint, NSAID non-steroidal anti-inflammatory drugs, MMO maximum mouth opening, LLLT low-level laser therapy, CBT cognitive behavioral therapy, HA hyaluronic acid; CS corticosteroids.

Appendix I.b. Clinical diversity in meta-analysis tool for heterogeneity assessment of outcome maximum mouth opening improvement at short- and intermediate-term follow-up.

		Diracoglu et al. (2009)[16]	Vos et al. (2014)[30]	Hosgor et al. (2017)[20]	Tatli et al. (2017)[21]	Malekzadeh et al. (2019)[23]	Abbasgholi-zadeh et al. (2020)[25]	de Almeida et al. (2023)[29]	Correa-Silva et al. (2024)[33]	**Score**
Setting										
1.	Years reported (A), in developed vs developing country (B), unit type (C)	2009 (A); developed, Turkey (B); University hospital (C)	2014 (A); developed, Netherlands (B); university hospital (C)	2017 (A); developed, Turkey (B); University hospital (C)	2017 (A); developed, Turkey (B); University hospital (C)	2019 (A); developed, Sweden (B); University hospital (C)	2020 (A); developed, Turkey (B); University hospital (C)	2023 (A); developed, Portugal (B); large outpatient clinic (C)	2024 (A); developed, Brazil (B); University hospital (C)	1
Population										
2.	Mean age in years	34.1	29.5	30.4	35.9	29.6	29.9	48.0	32.8	1
3.	% female	90.1	76.2	90	87.5	79.2	84.4	73.1	79.2	0
4.	Inclusion criteria and baseline disease severity	DDwoR; MMO 30.5mm	DDwoR/ DDwR/ DJD; MMO 36.7mm	DDwR / DDwoR; MMO 35.4mm	DDwoR; MMO 28.4mm	DDwoR; MMO 27.8mm	DDwR / DDwoR; MMO 32.1mm	DDwoR and DJD; MMO 36.6mm	DDwR/ DDwoR; MMO 32.4mm	1
5.	Co-morbidities	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	0

Appendix I.b. Clinical diversity in meta-analysis tool for heterogeneity assessment of outcome maximum mouth opening improvement at short- and intermediate-term follow-up. *Continued*

		Diracoglu et al. (2009)[16]	Vos et al. (2014)[30]	Hosgor et al. (2017)[20]	Tatli et al. (2017)[21]	Malekzadeh et al. (2019)[23]	Abbasgholi-zadeh et al. (2020)[25]	de Almeida et al. (2023)[29]	Correa-Silva et al. (2024)[33]	**Score**
Intervention										
6.	Intensity, strengths, or duration of intervention	AC Double needle, 60ml Ringer's Lactate; Post-op: none	AC Double needle, 300ml NaCl; Post-op: none	AC Double needle, 100ml Ringer's Lactate; Post-op: soft diet + exercises	AC Double needle, 120ml NaCl or AC + SS; Post-op: NSAID if needed	AC Double needle, 40-60ml NaCl + NSAID. Post-op: NSAID + exercises	AC ultrasound guided, 100-120ml NaCl + SS Post-op: none	AC single needle, 25ml NaCl Post-op: one physical therapy session	AC double needle, 100-200ml Ringer's Lactate. Post op: soft diet + physical therapy	1
7.	Timing	Symptom duration 3 weeks	Symptom duration 2 weeks	Not reported	Symptom duration 2 weeks	Symptom duration 3,8 months	Not reported	Symptom duration 6 months	Not reported	2
8.	Control intervention	SS + hot packs + exercises	Soft diet + SS (pain) + physical therapy (MMO)	SS or NSAID or LLLT	SS + NSAID	CBT + exercises + NSAID (pain) + SS (bruxism)	SS or LLLT + SS	Physical therapy	SS	2
9.	Co-interventions	None	None	None	2ml HA	None	2ml HA	1ml HA	1ml CS	1

Appendix I.b. Clinical diversity in meta-analysis tool for heterogeneity assessment of outcome maximum mouth opening improvement at short- and intermediate-term follow-up. *Continued*

		Diracoglu et al. (2009)[16]	Vos et al. (2014)[30]	Hosgor et al. (2017)[20]	Tatli et al. (2017)[21]	Malekzadeh et al. (2019)[23]	Abbasgholi-zadeh et al. (2020)[25]	de Almeida et al. (2023)[29]	Correa-Silva et al. (2024)[33]	**Score**
Outcome										
10.	Definition of the outcome	MMO in mm	MMO in mm	MMO in mm	MMO in mm	MMO in mm	MMO in mm	MMO in mm	MMO in mm	0
11.	Timing of follow-up									
a)	Short-term	3 months	3 months	3 months	3 months	3 months	3 months	1 month	3 months	1
b)	Intermediate-term	6 months	6 months	6 months	6 months	12 months	6 months	12 months	6 months	2
	Total short-term:									10
	Total intermediate-term:									11

Abbr.: DDwoR Disc displacement without reduction, DDwR Disc displacement with reduction, DJD degenerative joint disease MMO maximum mouth opening, AC arthrocentesis, SS stabilization splint, NSAID non-steroidal anti-inflammatory drugs, LLLT low-level laser therapy, CBT cognitive behavioral therapy, HA hyaluronic acid, CS corticosteroids.

Appendix J. Trial sequential analyses of the primary meta-analyses.

Outcome	Total N/RIS	Crossed conventional boundary	Crossed O'Brien-Fleming boundary	Crossed futility boundary	Interpretation
Pain improvement at short-term follow-up	545/471	Yes	Yes	NA	Arthrocentesis is superior to conservative care
Pain improvement at intermediate-term follow-up	547/287	Yes	Yes	NA	Arthrocentesis is superior to conservative care
Maximum mouth opening improvement at short-term follow-up	472/239	Yes	Yes	NA	Arthrocentesis is superior to conservative care
Maximum mouth opening improvement at intermediate-term follow-up	468/440	Yes	Yes	NA	Arthrocentesis is superior to conservative care

Abbr.: N number of patients; RIS required information size (sample size needed); NA not available.

References of appendices

1. Al-Rifae I, Akram Z, Oraibi Q. Impact of Arthrocentesis in Treatment of Temporomandibular Joint Problems. *Int J Drug Deliv Technol.* 2021;11(1):166-169.
2. Bilici I, Emes Y, Aybar B, Yalcin S. Evaluation of the effects of occlusal splint, trigger point injection and arthrocentesis in the treatment of internal derangement patients with myofascial pain disorders. *J Cranio-Maxillofacial Surg.* 2018;46:916-922.
3. Diracoglu D, Bayraktar Saral I, Keklik B, et al. Arthrocentesis vs conventional methods in the pain and functional status of the patients with temporomandibular disc displacement without reduction. *Pain Pract.* 2008;9:47. https://www.embase.com/search/results?subaction=viewrecord&id=L70207047&from=export%0Ahttp://dx.doi.org/10.1111/j.1533-2500.2009.00266.x
4. Hasson O, Levy Y, Nahlieli O. Arthrocentesis and lavage of the temporomandibular joint: treatment of closed lock. *Harefuah.* 2000;139(5-6):226-229.
5. Isik G, Kenc S, Koyuncu BO, Gunbay S, Gunbay T. Does the Use of Injectable Platelet-Rich Fibrin After Arthrocentesis for Disc Displacement Without Reduction Improve Clinical Outcomes? *J Oral Maxillofac Surg.* 2023;81:689-697.
6. Kholakiya Y, Roychodhury A, Bhutia O, Pandey R. Comparative evaluation of treatment outcome after arthrocentesis versus class IV laser therapy in the internal derangement of temporomandibular joint: a randomized controlled trial. *Int J Oral Maxillofac Surg.* 2015;44:e89-e90. doi:10.1016/j.ijom.2015.08.631
7. Moreno-Sánchez M, Monje Gil F. Lysis and Lavage: What Else in Temporomandibular Joint Surgery? *Atlas Oral Maxillofac Surg Clin North Am.* 2022;30(2):159-164. doi:10.1016/j.cxom.2022.06.002
8. Ritto F, Cueto A, dos Santos Canellas J, et al. Arthrocentesis versus nonsurgical methods in the management of temporomandibular joint closed lock and pain: a double-blind randomized controlled trial. *Oral Surgery, Oral Med Oral Pathol Oral Radiol.* 2022;133(4):369-376.
9. Rodrigues ALP, Cardoso HJ, Ângelo DF. Patient experience and satisfaction with different temporomandibular joint treatments: A retrospective study. *J Cranio-Maxillofacial Surg.* 2023;51(1):44-51. doi:10.1016/j.jcms.2023.01.006
10. Sato S, Ohta M, Ohki H, Kawamura H, Motegi K. Effect of lavage with injection of sodium hyaluronate for patients with nonreducing disk displacement of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1997;84(3):241-244. doi:10.1016/S1079-2104(97)90337-1
11. Vos L, Stant A, Quik E, Slater J, Stegenga B. Cost effectiveness of arthrocentesis as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial. *Int J Oral Maxillofac Surg.* 2013;42(10):1369. doi:10.1016/j.ijom.2013.07.710
12. Yucel M, Gozneli R, Alkumru H, Kulak-Ozkan Y. Evaluating the additional effects of arthrocentesis on the condylar pathways of temporomandibular joint in patients with internal derangement treated with stabilizing splint. *J Cranio-Maxillofacial Surg.* 2014;42(5):e86-e90. doi:10.1016/j.jcms.2013.07.002

13. Cueto A. RBR-24y9dd: Arthrocentesis vs nonsurgical methods in the treatment of temporomandibular joint pain and closed lock. A randomized controlled trial. ReBEC. 2020. https://trialsearch.who.int/Trial2.aspx?TrialID=RBR-24y9dd

14. Murakami K, Hosaka H, Moriya Y, Segami N, Iizuka T. Short-term treatment outcome study for the management of temporomandibular joint closed lock. A comparison of arthrocentesis to nonsurgical therapy and arthroscopic lysis and lavage. *Oral Surgery, Oral Med Oral Pathol Oral Radiol.* 1995;80(3):253-257. doi:10.1016/S1079-2104(05)80379-8

15. Guarda-Nardini L, Masiero S, Marioni G. Conservative treatment of temporomandibular joint osteoarthrosis: Intra-articular injection of sodium hyaluronate. *J Oral Rehabil.* 2005;32(10):729-734. doi:10.1111/j.1365-2842.2005.01505.x

16. Diracoglu D, Saral I, Keklik B, et al. Arthrocentesis versus nonsurgical methods in the treatment of temporomandibular disc displacement without reduction. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology.* 2009;108(1):3-8. doi:10.1016/j.tripleo.2009.01.005

17. Onder M, Tuz H, Kocygit D, Kisnisci R. Long-term results of arthrocentesis in degenerative temporomandibular disorders. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology.* 2009;107:1-5.

18. Machon V, Hirjak D, Lukas J. Therapy of the osteoarthritis of the temporomandibular joint. *J Cranio-Maxillofacial Surg.* 2011;39(2):127-130. doi:10.1016/j.jcms.2010.04.010

19. Lee H, Baek H, Song D, et al. Effect of simultaneous therapy of arthrocentesis and occlusal splints on temporomandibular disorders: anterior disc displacement without reduction. *J Korean Assoc Oral Maxillofac Surg.* 2013;39(1):14. doi:10.5125/jkaoms.2013.39.1.14

20. Hosgor H, Bas B, Celenk C. A comparison of the outcomes of four minimally invasive treatment methods for anterior disc displacement of the temporomandibular joint. *Int J Oral Maxillofac Surg.* 2017;46(11):1403-1410. doi:10.1016/j.ijom.2017.05.010

21. Tatli U, Benlidayi M, Ekren O, Salimov F. Comparison of the effectiveness of three different treatment methods for temporomandibular joint disc displacement without reduction. *Int J Oral Maxillofac Surg.* 2017;46:603-609.

22. Malachovsky I, Statelova D, Stasko J, Mikuskova K, Smatanova M, Janíčková M. Therapeutic effects of arthrocentesis in treatment of temporomandibular joint disorders. *Bratislava Med J.* 2019;120(3):235-239. doi:10.4149/BLL_2019_052

23. Malekzadeh B, Cahlin B, Widmark G. Conservative therapy versus arthrocentesis for the treatment of symptomatic disk displacement without reduction: a prospective randomized controlled study. *Oral Surgery, Oral Med Oral Pathol Oral Radiol.* 2019;128:18-24.

24. Yilmaz O, Korkmaz Y, Tuzumer T. Comparison of treatment efficacy between hyaluronic acid and arthrocentesis plus hyaluronic acid in internal derangements of temporomandibular joint. *J Cranio-Maxillofacial Surg.* 2019;47:1720-1727.

25. Abbasgholizadeh Z, Evren B, Ozkan Y. Evaluation of the efficacy of different treatment modalities for painful temporomandibular disorders. *Int J Oral Maxillofac Surg*. 2020;49:628-635.

26. Goyal P, Singh R, Gangwar S, Mohammad S, Pal U, Singh G. Effect of duloxetine in temporomandibular joint disorders: A comparison with arthrocentesis. *Natl J Maxillofac Surg*. 2020;11(2):219-223.

27. Altaweel A, Ismail H, Fayad M. Effect of simultaneous application of arthrocentesis and occlusal splint versus splint in management of non-reducing TMJ disc displacement. *J Dent Sci*. 2021;16:732-737.

28. Helal M, Agou S, Bayoumi A, Imam A, Hassan A. Management of internal derangement of temporomandibular joint disc displacement with reduction using two different lines of treatment. *Brazilian Dent Sci*. 2021;24(2):1-8. doi:10.14295/bds.2021.v24i2.2080

29. de Almeida A, Botelho J, Machado V, Mendes J, Manso C, Gonzalez-Lopez S. Comparison of the Efficacy of Two Protocol Treatments in Patients with Symptomatic Disc Displacement without Reduction: A Randomized Controlled Trial. *J Clin Med*. 2023;12(3228).

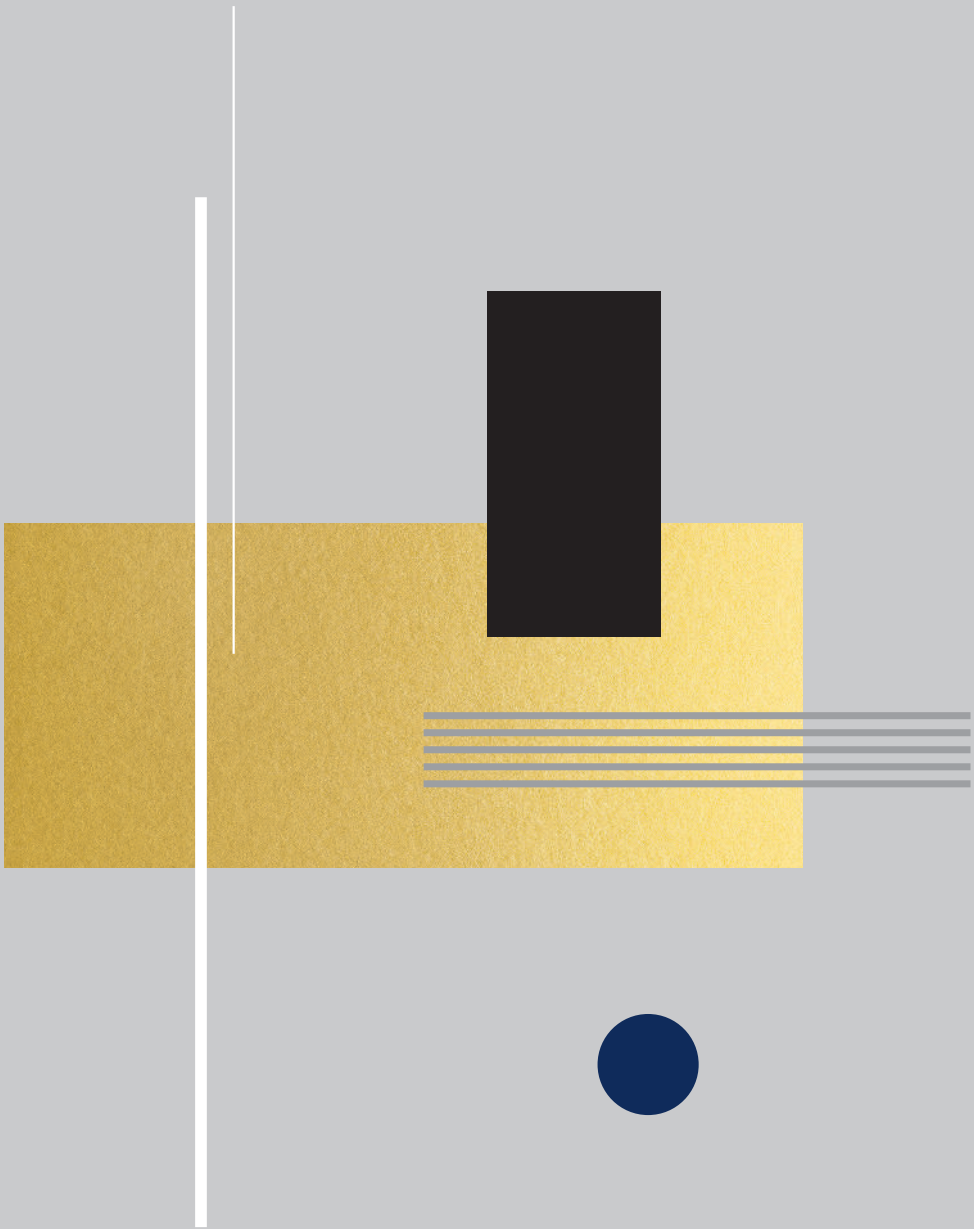
30. Vos L, Huddleston Slater J, Stegenga B. Arthrocentesis as initial treatment for temporomandibular joint arthropathy: A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2014;42(5):e134-e139. doi:10.1016/j.jcms.2013.07.010

31. Vos L, Stegenga B, Stant A, Quik E, Huddleston Slater J. Cost Effectiveness of Arthrocentesis Compared to Conservative Therapy for Arthralgia of the Temporomandibular Joint: A Randomized Controlled Trial. *J Oral Facial Pain Headache*. 2018;32(2):198-207. doi:10.11607/ofph.1457

32. Tang Y, Vos L, Tuin A, et al. Arthrocentesis versus non- surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. *Int J Oral Maxillofac Surg*. 2023;52:595-603.

33. Corrêa-Silva M, de Carvalho T, Zambon C, Peres M, Machado G. Is there a superiority between arthrocentesis and stabilizing occlusal splint for the treatment of anterior disc displacement with reduction and intermittent block and anterior disc displacement without reduction in TMJ? Randomized clinical trial. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2024;138(2):244-254. doi:10.1016/j.oooo.2024.04.001

34. Li D, Luo L, Li K, Su Y, Durham J, Leung Y. Early Arthrocentesis for Temporomandibular Joint Arthralgia: A Superiority Trial. *Int Dent J*. Published online 2024. doi:10.1016/j.identj.2024.04.015



CHAPTER 3

ARTHROCENTESIS VERSUS NON-SURGICAL INTERVENTION AS INITIAL TREATMENT FOR TEMPOROMANDIBULAR JOINT ARTHRALGIA

A randomized controlled trial with long-term follow-up

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Abstract

Arthrocentesis for arthralgia of the temporomandibular joint (TMJ) is often only indicated when conservative, non-surgical interventions have failed. However, performing arthrocentesis as initial therapy may facilitate earlier and better recuperation of the joint. The aim of this study was to assess the efficacy of this therapy with a long-term follow-up. Eighty-four patients were randomly allocated to receive either arthrocentesis as initial treatment (n = 41) or non-surgical intervention (n = 43). Pain (100-mm visual analog scale, VAS) and mandibular function impairment questionnaire scores (MFIQ, 0–100) were recorded at 3, 12, and 26 weeks, and ≥ 5 years (median 6.2, interquartile range 5.6–7.4 years). Univariable analyses were performed and linear mixed-effect models were constructed. Patients in the arthrocentesis group experienced significantly lower TMJ arthralgia compared to those treated non-surgically (pain during movement: −10.23 mm (95% confidence interval −17.86; −2.60); pain at rest: − 8.39 mm (95% confidence interval −13.70; −3.08)), while mandibular function remained similar in the two groups (MFIQ −2.41 (95% confidence interval −8.61; 3.78)). Of the final sample, 10 patients (10/39, 26%) in the non-surgical intervention group and two patients (2/34, 6%) in the arthrocentesis group received additional treatment during follow-up. Thus, initial treatment with arthrocentesis reduced TMJ arthralgia more efficaciously than non-surgical intervention in the long term, while maintaining similar mandibular function.

Introduction

Arthralgia of the temporomandibular joint (TMJ) is a frequently occurring and debilitating problem, affecting an estimated 8% of the population[1]. Although a multitude of causes may give rise to TMJ arthralgia, degenerative joint disease (DJD; i.e., osteoarthritis) and internal derangement (ID) are amongst the leading causes[2]. About 75% of patients with symptomatic DJD have some type of ID, while approximately 50% of all patients with symptomatic ID experience DJD to some degree[3]. Despite often being observed simultaneously, the two conditions are different entities and do not necessarily precede each other[4].

In both DJD and ID, the manifestation of symptoms often indicates a disturbance in the homeostasis of the articular tissue, where degenerative processes exceed the joint's adaptive capability for tissue synthesis and rehabilitation[2,4]. Here, the synovial fluid of the TMJ contains elevated levels of proinflammatory cytokines, matrix degradation enzymes, and breakdown products that cannot easily be cleared from the synovial cavity[4–6]. A secondary inflammatory response may arise subsequently, which is often accountable for most symptoms such as arthralgia, restricted mouth opening, blockages, and joint noise[4,7].

Arthrocentesis may be performed to remove the inflammatory mediators and degradation products that are thought to be responsible for the clinical symptoms; this involves lavage of the upper TMJ compartment[8–10]. However, current management regimens often only indicate arthrocentesis if conservative, non-surgical interventions, based primarily on load reduction and the prescription of non-steroidal anti-inflammatory drugs (NSAIDs), prove to be insufficient in reducing symptoms[2,11]. Previous studies performed at the authors' institution (University Medical Center Groningen) showed that arthrocentesis as the initial treatment for TMJ arthralgia was more efficacious in reducing clinical symptoms[8] and was more cost-effective[12] than conservative, non-surgical intervention after 6 months of follow-up. However, limited evidence exists regarding the long-term efficacy of the immediate performance of arthrocentesis, particularly when compared to other therapies.

Therefore, the aim of this study was to determine the efficacy of arthrocentesis as the initial treatment modality in reducing TMJ arthralgia, compared to non-surgical intervention, during long-term follow-up of ≥ 5 years.

Materials and methods

The 2010 CONSORT guidelines were followed in the reporting of this study. The study was conducted in accordance with the principles of the Declaration of Helsinki (adapted version 2013, Fortaleza, Brazil) and the Dutch 'Medical Research Involving Human Subjects Act' (WMO).

Clinical trial design

This single-center randomized controlled trial was performed in the Department of Oral and Maxillofacial Surgery of the University Medical Center Groningen (UMCG), the Netherlands. Study subjects were recruited between January 2009 and July 2012. Approval was given by the Institutional Review Board of UMCG (METc 2008/197) and signed informed consent was obtained from all of the study participants prior to the commencement of any study-related procedures.

Study population

The study patients were recruited from the outpatient clinic of the Department of Oral and Maxillofacial Surgery of UMCG. A sample size calculation was performed for the primary outcome measure for the initial follow-up period of the study, as described previously[8]. The inclusion criteria were age ≥ 16 years, pain in the TMJ region aggravated by mandibular movement (i.e., protrusion, maximal mouth opening, and/or lateral excursions) and/or during function, the presence of TMJ arthralgia after 2 weeks of 600 mg ibuprofen three times daily (to exclude acute inflammatory pain), and the disappearance of TMJ arthralgia after a diagnostic intra-articular injection with a local anesthetic in the TMJ (Ultracain D-S Forte; Sanofi, Amsterdam, the Netherlands; to exclude myogenous pain)[13].

The exclusion criteria were systemic rheumatic disease, bony ankylosis of the TMJ, prior open TMJ surgery, pregnancy, concurrent use of anti-inflammatory drugs, muscle relaxants, anti-depressants, and/or steroids, other medical contraindications, unwillingness to receive either study treatment, and the inability to speak Dutch or English.

Study procedures

The study patients were randomly allocated (1:1 ratio) to either the treatment group (arthrocentesis) or the control group (non-surgical intervention, NS) for initial treatment, by an independent colleague, using randomization software (StatsDirect version 2.7.7; StatsDirect Ltd, Birkenhead, United Kingdom). Patient allocation to the

initial treatment modality was concealed from the physicians and researchers using opaque, sequentially numbered, sealed envelopes. An independent nurse revealed the group allocation once the patient had agreed to participate in the study.

The patients allocated to arthrocentesis underwent lavage of the upper TMJ space with at least 300 ml isotonic saline, while the patients allocated to the NS group had to follow a strict soft diet protocol for at least 6 weeks. Patients in the NS group who received additional physical therapy and/or splint therapy were carefully selected during a critical interim evaluation, 2 weeks after the start of the soft diet protocol. Physical therapy was provided if the maximum mouth opening did not improve, while splint therapy was provided if the pain did not subside.

All of the arthrocentesis procedures were performed under local anesthesia by a single oral and maxillofacial surgeon (B. Stegenga). Further details of the procedure have been reported previously[8]. Prior to treatment, panoramic radiographs, transcranial radiographs (Schüller projection), and transpharyngeal radiographs (Parma projection) of the TMJ were obtained and examined to evaluate the degree of osseous degeneration. The evaluation of the radiographic images and DJD diagnosis were done according to the criteria described by Ahmad et al.[14]. The ID diagnostic categories were determined according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)[15], based on patient history and clinical examination.

Outcome measures

The main outcome parameter of the study was the extent of TMJ pain, according to a visual analog scale (VAS), during mandibular movement (and/or function) (VASm; 0–100 mm, with 0 indicating no pain). The secondary outcome measures were TMJ pain at rest (VASr; 0–100 mm, with 0 indicating no pain), mandibular function impairment as determined using the validated Mandibular Function Impairment Questionnaire (MFIQ; 0–100)[16], and the number of patients who needed additional treatment during follow-up. A higher MFIQ score indicates worse mandibular function. The outcome measures were recorded at baseline and at four follow-up time points: 3, 12, and 26 weeks (in the outpatient clinic) and ≥ 5 years (via telephone interview). The patients who received additional treatment during follow-up due to insufficient symptom reduction after the primary treatment were registered.

Statistical analysis

Normally distributed variables were presented as the mean and standard deviation (SD) values. Non-normally distributed continuous variables were presented as the median with the first and third quartiles (interquartile range, IQR) and compared using the Mann–Whitney *U*-test. The assumption of a normal distribution of continuous data was assessed by visually examining the Q–Q plot and the Shapiro–Wilk test. All categorical variables were described as frequencies with percentages and compared using Fisher's exact test.

The analyses were performed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA). Graphs were drawn using Prism, version 9 (GraphPad Software Inc., San Diego, CA, USA). Linear mixed-effect models (LMM) were fitted to assess the effect of the interventions on repeated measurements of VASm, VASr, and MFIQ. Simple multivariable models included the fixed effects of the type of intervention and follow-up in weeks. The full multivariable models included the fixed effects of the baseline score, type of intervention, follow-up in weeks, sex, age, presence and type of ID, degree of DJD seen on radiographic imaging, and any additional treatments. These variables were selected because of their prognostic nature and based on model improvement[17]. Additional treatments were included as time-varying variables by taking into account at which point during follow-up the additional treatments were performed. The included random effects were the participants. Additionally, the fixed interaction between the intervention and time and/or the random effect of time were only included if the term significantly improved the multivariable model. Between models, model improvement was tested using likelihood ratio tests. Participants were only included in the analysis if the baseline and at least one follow-up measurement of one or more outcome variables were recorded. All models yielded an estimated regression coefficient (β) with corresponding 95% confidence interval (95% CI). $P \leq 0.05$ (two-tailed) was considered statistically significant. All of the LMM analyses were performed in R, version 4.0.5 (R Core team; R Foundation for Statistical Computing, Vienna, Austria), using the lme4 package[18].

Results

A total of 84 patients were initially enrolled in the study (**Figure 1**). Of these, 41 were allocated to receive arthrocentesis and 43 to receive NS (**Figure 1**). After randomization, 11 patients were excluded from the statistical analysis: seven (17%) from the arthrocentesis group and four (9%) from the NS group. The reasons for exclusion are presented in **Figure 1**.

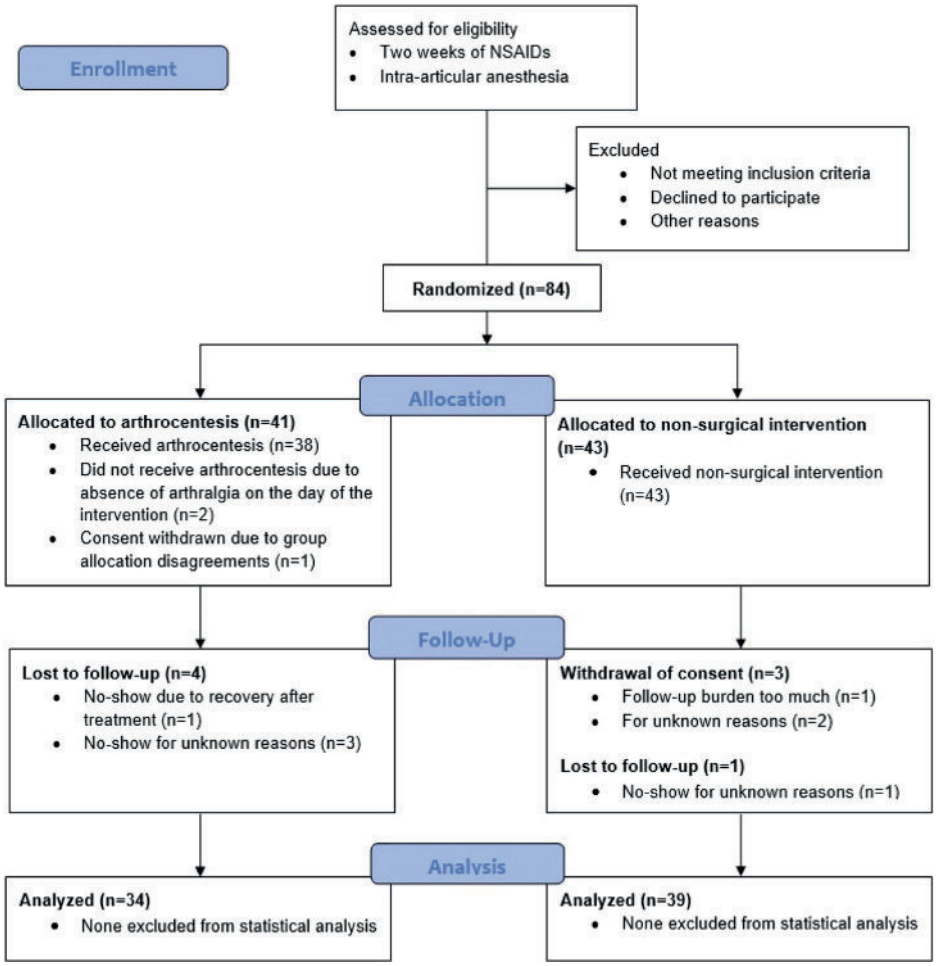

Figure 1. CONSORT flow diagram (version 2010) of subject enrolment, allocation, and follow-up. In the arthrocentesis group, two patients did not receive treatment due to the absence of arthralgia on the day of the intervention. These two patients did not meet the inclusion criteria in the first place and were therefore mistakenly randomized. The outcome measurements of the patients in both groups who were excluded after treatment were not registered at any of the follow-up moments, rendering linear mixed model analyses of these subjects impossible.

Table 1. Baseline characteristics of the study population after randomization, and the final study sample.

Predictors	After randomization		Final study sample	
	Arthrocentesis	*Non-surgical intervention*	*Arthrocentesis*	*Non-surgical intervention*
Sample size, *n*	41	43	34	39
Female, *n (%)*	30 (73)	34 (79)	25 (73)	32 (82)
Age in years, *median (Q1-Q3)*	28 (23-55)	31 (21-49)	27 (23-50)	29 (21-41)
VASm in mm, *mean (SD)*	51.60 (18.88)	54.80 (24.46)	53.16 (17.82)	54.45 (23.96)
VASr in mm, *median (Q1-Q3)*	15.00 (00.0-34.00)	17.00 (0.00-44.75)	17.50 (0.00-34.75)	17.00 (0.00-44.25)
MFIQ, *mean (SD)*	49.43 (14.51)	47.79 (19.10)	49.16 (14.79)	48.98 (18.10)
ID, *n (%)*				
No ID	6 (16)	6 (14)	6 (18)	6 (15)
ID (A)	9 (24)	12 (29)	8 (24)	11 (28)
ID (B)	11 (29)	10 (24)	10 (29)	9 (23)
ID (C)	12 (32)	13 (31)	10 (29)	12 (31)
ID (D)	0 (0)	1 (2)	0 (0)	1 (3)
ID, missing*	3	1	0	0
DJD, *n (%)*				
No DJD	19 (48)	24 (57)	16 (47)	22 (56)
DJD (A)	12 (30)	10 (24)	9 (27)	9 (23)
DJD (B)	9 (23)	8 (19)	9 (27)	8 (21)
DJD, missing*	1	1	0	0

Abbr.: Q1-Q3 First and third quartile; SD standard deviation; VASm pain visual analog scale during mandibular movement (and/or function); VASr pain visual analog scale at rest; MFIQ mandibular function impairment questionnaire; ID internal derangement; ID (A) anterior disc displacement with reduction; ID (B) anterior disc displacement with reduction and intermittent locking; ID (C) anterior disc displacement without reduction and with limited mouth opening; ID (D) anterior disc displacement without reduction and without limited mouth opening; DJD Degenerative Joint disease; DJD (A) indeterminate for DJD; DJD (B) evidence of DJD. *Missing indicates unregistered diagnoses of the drop-outs. The missing subjects are not included in the depiction of the percentages.

The final arthrocentesis group included 25 female patients (74%) and nine male patients (26%); median age was 27 years (IQR 23–50 years). The final NS group included 32 female patients (82%) and seven male patients (18%); median age was 29 years (21–41 years). The median time interval between the baseline and the latest follow-up (≥5 years) was 6.2 years (IQR 5.6–7.4 years).

All of the NS patients adhered to the strict soft diet protocol. Ten patients (26%) in the NS group received additional physical therapy, 15 (38%) received additional splint therapy, and two (5%) received both additional physical and splint therapy. Also, 10 patients in the NS group (26%) underwent additional arthrocentesis during follow-up (at a median of 41 weeks (IQR 30–80 weeks)); the study outcomes of six of these patients (15%) were recorded after the additional procedure (at a median 41 weeks (IQR 25–104 weeks)).

In the arthrocentesis group, two patients (6%) received additional treatment: one patient underwent another arthrocentesis (after 75 weeks) and subsequently diagnostic arthroscopy (after 136 weeks); one patient received a methylprednisolone injection against the joint capsule (after 8 weeks). No serious adverse events were recorded; four patients experienced mild temporary swelling around the TMJ directly after arthrocentesis.

The median scores of the outcome variables VASm, VASr, and MFIQ over time are presented in **Figure 2**; the scores at the latest follow-up are reported in **Table 2**. The simple multivariable LMM analysis indicated a significantly lower VASm in the arthrocentesis group compared to the NS group (−11.13 mm (95% CI −20.04; −2.21)), as shown in **Table 3** Of the secondary outcome measures, VASr was significantly lower in the arthrocentesis group (−8.72 mm (95% CI −16.23; −1.21)), whereas the MFIQ score did not differ significantly between the treatment groups (−3.89 (95% CI −11.16; 3.37)) (**Table 3**).

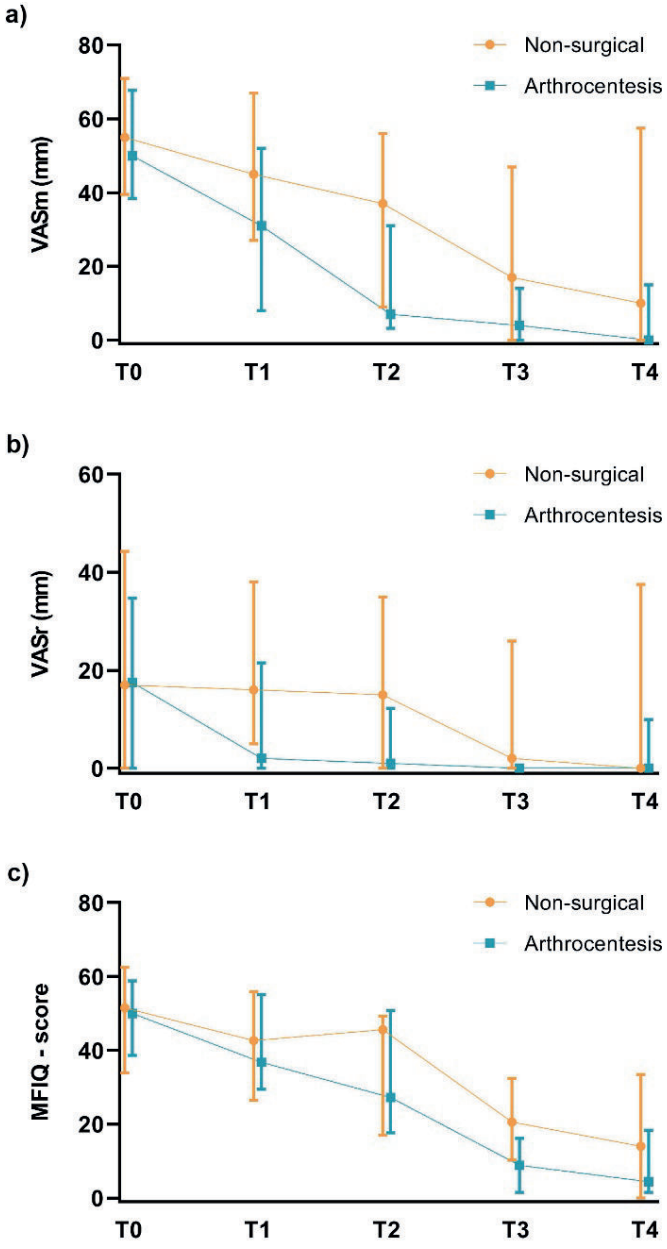

Figure 2. Progression of (a) pain during movement (VASm), (b) pain at rest (VASr), and (c) perceived mandibular function (MFIQ score) over time for non-surgical intervention and arthrocentesis. The graphs are based on the raw data (not the linear mixed models), presented as the median and first and third quartile range error bars. Abbr.: VASm pain visual analog scale during mandibular movement (and/or function); VASr pain visual analog scale at rest; MFIQ mandibular function impairment questionnaire; T0, baseline; T1, 3-week follow-up; T2, 12-week follow-up; T3, 26-week follow-up; T4, ≥ 5-year follow-up.

Table 2. Results of study outcomes registered at latest follow-up (T4, ≥5 years).

Study outcome	Treatment group		*P-value*
	Arthrocentesis	Non-surgical intervention	
VASm (mm), *median (Q1-Q3)*	0.00 (0.00-15.00)	1.00 (0.00-57.5)	0.097
VASr (mm), *median (Q1-Q3)*	0.00 (0.00-10.00)	0.00 (0.00-37.5)	0.154
MFIQ, *median (Q1-Q3)*	4.41 (1.47-18.38)	13.97 (0.00-33.46)	0.360

Abbr.: Q1-Q3 First and third quartile; SD standard deviation; VASm pain visual analog scale during mandibular movement (and/or function); VASr pain visual analog scale at rest; MFIQ mandibular function impairment questionnaire.

In the full multivariable model, there was no fixed interaction between intervention and time and/or the random effect of time did not significantly improve the model (VASm ($P = 0.971$); VASr ($P = 0.888$); MFIQ ($P = 0.298$)). In this model, VASm was significantly lower in the arthrocentesis group compared to the NS group over the entire follow-up (−10.23 mm (95% CI −17.86; −2.60)) (**Table 3**). Of the secondary outcome measures, VASr was significantly lower in the arthrocentesis group (−8.39 mm (95% CI −13.70; −3.08)). However, the MFIQ score did not differ significantly between the treatment groups (−2.41 (95% CI −8.61; 3.78)) after adjustment for confounders (**Table 3**).

In the full multivariable model, the overall presence of ID or DJD had no significant influence on the outcome measures when compared to patients with, respectively, no clinical signs of ID or radiological signs of DJD (**Table 3**).

Table 3. Simple and full multivariable linear mixed model analyses results.

	VASm		VASr		MFIQ	
Predictors	β *(95% CI)*	*p*	β *(95% CI)*	*p*	β *(95% CI)*	*p*
Simple multivariable						
Treatment (ref. = NS)	-11.13 (-20.04;-2.21)	**0.014**	-8.72 (-16.23;-1.21)	**0.023**	-3.89 (-11.16;3.37)	0.293
Follow-up in weeks	-0.07 (-0.09;-0.04)	**<0.001**	-0.02 (-0.04;-0.00)	**0.023**	-0.08 (-0.10;-0.06)	**<0.001**
Full multivariable						
Treatment (ref. = NS)	-10.23 (-17.86;-2.60)	**0.009**	-8.39 (-13.70;-3.08)	**0.002**	-2.41 (-8.61;3.78)	0.445
Follow-up in weeks	-0.07 (-0.09;-0.05)	**<0.001**	-0.02 (-0.03;0.00)	0.063	-0.09 (-0.11;-0.07)	**<0.001**
Baseline (in mm for VASm/VASr)	0.58 (0.39;0.77)	**<0.001**	0.56 (0.45;0.67)	**<0.001**	0.57 (0.37;0.76)	**<0.001**
Gender (ref. = female)	-0.68 (-10.42;9.06)	0.891	-3.30 (-9.93;3.33)	0.330	-2.05 (-9.83;5.72)	0.605
Age in years	0.02 (-0.26;0.30)	0.884	-0.00 (-0.19;0.18)	0.975	-0.05 (-0.26;0.17)	0.678
Additional treatment (A)*	6.77 (-10.71;24.26)	0.448	-10.88 (-22.99;1.23)	0.078	11.02 (-2.81;24.86)	0.118
Additional treatment (B)**	-1.45 (-28.95;26.06)	0.918	-2.15 (-21.12;16.82)	0.824	-11.48 (-47.73;24.76)	0.535
No ID (= ref.)	0	0.133	0	0.170	0	0.261
ID (A)	-14.28 (-26.28;-2.27)		-9.76 (-18.20;-1.33)		-6.91 (-16.39;2.57)	
ID (B)	-10.93 (-23.29;1.43)		-4.76 (-13.43;3.90)		-6.17 (-15.55;3.20)	
ID (C)	-6.90 (-18.44;4.65)		-4.53 (-12.43;3.37)		-1.74 (-10.72;7.25)	
ID (D)	-19.49 (-61.23;22.25)		-13.07 (-41.60;15.47)		N.A.	

Table 3. Simple and full multivariable linear mixed model analyses results. *Continued*

	VASm		VASr		MFIQ	
Predictors	β *(95% CI)*	*p*	β *(95% CI)*	*p*	β *(95% CI)*	*p*
Full multivariable						
No DJD (= ref.)	0	0.547	0	0.769	0	0.785
DJD (A)	-4.62 (-13.68;4.44)		0.77 (-5.47;7.02)		-2.34 (-9.42;4.75)	
DJD (B)	-0.65 (-10.30;9.01)		-1.57 (-8.13;5.00)		-1.09 (-9.33;7.15)	

Abbr.: VASm pain visual analog scale during mandibular movement (and/or function); VASr pain visual analog scale at rest; MFIQ mandibular function impairment questionnaire; β regression coefficient; CI confidence interval; ref. reference; NS non-surgical intervention; ID internal derangement; ID (A) anterior disc displacement with reduction; ID (B) anterior disc displacement with reduction and intermittent locking; ID (C) anterior disc displacement without reduction and with limited mouth opening; ID (D) anterior disc displacement without reduction and without limited mouth opening; DJD Degenerative Joint disease; DJD (A) indeterminate for DJD; DJD (B) evidence of DJD. *Additional treatment in the conservative, non-surgical intervention group with arthrocentesis during the follow-up (n=6); **Additional treatment in the arthrocentesis group during the follow-up (n=2).

Discussion

The aim of this study was to evaluate the efficacy of arthrocentesis as the initial treatment for TMJ arthralgia compared to non-surgical intervention during long-term follow-up (≥5 years). In addition to the previous report[8], where promising results were reported for the 6-month follow-up, the findings of the present study demonstrate that arthrocentesis as the initial treatment is more efficacious in reducing TMJ arthralgia over a period of ≥ 5 years than conservative, non-surgical intervention.

LMM analyses in this study allowed the accurate longitudinal evaluation of treatment efficacy. Results from these analyses are a better representation of treatment efficacy than results from comparing solely the outcome variables of the individual follow-up moments (**Figure 2**; **Table 2**). This is because the LMM allowed the inclusion of the time of latest follow-up (which differed between subjects) and the baseline scores as predictors in the statistical model. Comparison of the outcome variables at the latest follow-up, however, showed a smaller spread in the arthrocentesis group, indicating a more predictable treatment outcome compared to NS (**Table 2**).

The study findings support current evidence that arthrocentesis may be beneficial for patients with ID and/or DJD[19,20]. More importantly, the timing of arthrocentesis is paramount to optimize the treatment outcome. Performing interventions as soon as possible enhances the immediate joint recovery process. The response to arthrocentesis is more evident in acute cases of TMJ arthralgia compared to chronic ones[21]. However, traditional conservative care encompasses a prolonged treatment period, putting patients more at risk of developing chronic pain in the event that those treatment methods are insufficient in reducing symptoms. Therefore, a reconsideration of the current therapeutic strategies in favor of arthrocentesis could potentially be beneficial for patients.

The important role of performing minimally invasive treatment procedures early is supported by a recent systematic review, in which the authors concluded that such procedures are more beneficial than conservative care in the short term (≤5 months) and intermediate term (6 months–4 years)[22]. The current study provides further evidence that arthrocentesis is superior in improving patient-reported outcomes in the long term. On the other hand, another recent systematic review investigating the influence of the timing of arthrocentesis on patient outcomes, in relation to conservative care, concluded that in addition to the favorable outcomes of

arthrocentesis in general, the optimal results were obtained when arthrocentesis was performed within 3 months after conservative care[23]. The authors noted, however, that the evidence was of low to moderate quality due to the low availability of well-designed studies and the heterogeneity between studies in diagnoses, treatment modalities, and techniques used. Definitive conclusions regarding the optimal timing of arthrocentesis may be drawn once different timings are compared in a single clinical trial in the future.

Interestingly, mandibular function, expressed as the MFIQ score, did not differ significantly between the two treatment groups in the specific study model. Seemingly, the patients who underwent arthrocentesis did not experience an improvement in performing daily activities related to their jaw compared to the patients who received NS, despite having less pain. It is hypothesized that factors other than pain may also play a role in the patients' perception of mandibular function, such as mouth opening restrictions due to mechanical obstructions, or the psychosocial profile (i.e., pain-avoiding behavior and fear).

Additional treatment during the follow-up was not associated with better treatment outcomes in the full multivariable model. Remarkably, 10 (26%) patients who were allocated to the NS group required additional treatment, six of whose outcome measurements were recorded afterwards, whereas only two (6%) patients allocated to the arthrocentesis group received additional treatment. These findings are in line with the results of Tatli et al.[24], who reported the superiority of arthrocentesis over splint therapy after 6 months for the treatment of anterior disc displacement (ADD) without reduction (success rate of 93% for arthrocentesis versus 60% for splint therapy).

Neither age nor sex was associated with the degree of TMJ arthralgia or functional impairment in the current full multivariable model. Furthermore, the degree of DJD seen on radiographic imaging was not significantly associated with TMJ arthralgia, which is consistent with previous findings[25,26]. This is because observed radiographic changes in bony structures may have also been the result of remodeling in the context of joint recuperation, indicating a return to a homeostatic state of the articular structures.[4] The presence of ID was not statistically associated with TMJ arthralgia in the multivariable model, which is also consistent with the literature[27].

The main strength of this study is that it is one of only a few randomized controlled trials that have been performed on the efficacy of arthrocentesis compared to non-

surgical intervention, specifically with a long-term follow-up. Other strengths of the study include a thorough study design, using the intra-articular injection procedure as a diagnostic tool, and the relatively large number of study patients. Furthermore, appropriate statistical models for longitudinal analyses were constructed.

This study has some limitations. No magnetic resonance imaging (MRI) scans were performed, which may have affected the diagnostic testing of ID. According to the DC/TMD[15], definitive diagnosis of ID, with the exception of ADD without reduction with limited mouth opening, requires an MRI to achieve adequate diagnostic sensitivity (i.e., ≥70%) and specificity (i.e., ≥95%). However, the participants were included in this study several years before the general consensus regarding optimal diagnostic testing using imaging was described in the current DC/TMD. More importantly, an MRI-confirmed displaced disc is not exclusive to a pathological condition; it is present in approximately 30% of asymptomatic patients[4] and does not influence the treatment choice or outcome[28,29]. In the present study, the psychosocial profiles of the study patients over time were not recorded. This could have distorted the results, since psychosocial factors are known to be associated with temporomandibular pain[27,30]. However, due to the duration of follow-up, answering additional extensive questionnaires on the phone many years post-treatment could have resulted in an excessive burden for the study participants. Furthermore, the trial may be limited in its generalizability to other clinics and general populations with temporomandibular disorders. Patient inclusion through a diagnostic intra-articular injection allowed the accurate selection of patients suffering from pain that primarily originated from the joint[13]. However, since many patients often experience myogenous symptoms concurrently with arthralgia, some arthralgia patients with more prominent myogenous symptoms may have been excluded from the study. Moreover, in the non-surgical intervention group, any additional physical or splinting therapy was given based on the response to the initial soft diet advice, which resulted in treatment heterogeneity within the control group. The authors chose to design the study in such a manner, as this is believed to be an accurate representation of the clinical reality, where conservative therapies are mostly patient-tailored and given based on clinical presentation.

In conclusion, arthrocentesis was found to be more efficacious as an initial treatment in reducing TMJ arthralgia than non-surgical intervention over follow-up of ≥ 5 years, although mandibular function was similar after both treatments. Performing arthrocentesis at an earlier stage to treat TMJ arthralgia allows immediate initiation

of joint recuperation, which is sustained over the long term. Verification of the current study results is mandatory to substantiate this conclusion.

Ethical approval

Approval to conduct this study was given by the Institutional Review Board of UMCG (METc 2008/197).

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Competing interests

None.

Patient consent

Signed informed consent was obtained from all study patients prior to the commencement of any study-related procedures.

Trial registration

This trial is registered in the Netherlands Trial Register (NL1444).

References

1. Marklund S, Wanman A. Incidence and prevalence of temporomandibular joint pain and dysfunction. A one-year prospective study of university students. *Acta Odontol Scand*. 2007;65:119-127.
2. Tanaka E, Detamore MS, Mercuri LG. Degenerative disorders of the Temporomandibular joint: etiology, diagnosis, and treatment. *J Dent Res*. 2008;87(4):296-307. doi:10.1177/154405910808700406
3. Bertram S, Rudisch A, Innerhofer K, Pümpel E, Grubwieser G, Emshoff R. Diagnosing TMJ internal derangement and osteoarthritis with magnetic resonance imaging. *J Am Dent Assoc*. 2001;132(6):753-761. doi:10.14219/jada.archive.2001.0272
4. Stegenga B. Osteoarthritis of the Temporomandibular Joint Organ and Its Relationship to Disc Displacement. *J Orofac Pain*. 2001;15(3):193-205.
5. Kim YK, Kim SG, Kim BS, et al. Analysis of the cytokine profiles of the synovial fluid in a normal temporomandibular joint: Preliminary study. *J Cranio-Maxillofacial Surg*. 2012;40(8):337-341. doi:10.1016/j.jcms.2012.02.002
6. Wang XD, Zhang JN, Gan YH, Zhou YH. Current understanding of pathogenesis and treatment of TMJ osteoarthritis. *J Dent Res*. 2015;94(5):666-673. doi:10.1177/0022034515574770
7. Hamada Y, Kondoh T, Holmlund AB, et al. Inflammatory cytokines correlated with clinical outcome of temporomandibular joint irrigation in patients with chronic closed lock. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2006;102(5):596-601. doi:10.1016/j.tripleo.2005.11.010
8. Vos L, Huddleston Slater J, Stegenga B. Arthrocentesis as initial treatment for temporomandibular joint arthropathy: A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2014;42(5):e134-e139. doi:10.1016/j.jcms.2013.07.010
9. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006
10. Nitzan D, Svidovsky J, Zini A, Zadik Y. Effect of arthrocentesis on symptomatic osteoarthritis of the temporomandibular joint and analysis of the effect of preoperative clinical and radiological features. *J Oral Maxillofac Surg*. 2017;75:260-267. doi:10.1080/00016350601083554
11. Murphy MK, MacBarb RF, Wong ME, Athanasiou KA. Temporomandibular Disorders: A Review of Etiology, Clinical Management, and Tissue Engineering Strategies. *Int J Oral Maxillofac Implants*. 2013;28(6):e393-e414. doi:10.11607/jomi.te20
12. Vos L, Stegenga B, Stant A, Quik E, Huddleston Slater J. Cost Effectiveness of Arthrocentesis Compared to Conservative Therapy for Arthralgia of the Temporomandibular Joint: A Randomized Controlled Trial. *J Oral Facial Pain Headache*. 2018;32(2):198-207. doi:10.11607/ofph.1457

13. Tjakkes GHE, TenVergert EM, De Bont LGM, Stegenga B. The effect of intra-articular injection of ultracain in the temporomandibular joint in patients with preauricular pain: A randomized prospective double-blind placebo-controlled crossover study. *Clin J Pain*. 2007;23(3):233-236. doi:10.1097/AJP.0b013e31802f0950

14. Ahmad M, Hollender L, Anderson Q, et al. Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD): Development of Image Analysis Criteria and Examiner Reliability for Image Analysis. 2009;107(6):844-860. doi:10.1016/j.tripleo. 2009.02.023.

15. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *J oral facial pain headache*. 2014;38(1):6-27.

16. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*. 1993;7(2):183-195. http://www.ncbi.nlm.nih.gov/pubmed/8358365

17. Kahan BC, Morris TP. Adjusting for multiple prognostic factors in the analysis of randomised trials. *BMC Med Res Methodol*. 2013;13(1). doi:10.1186/1471-2288-13-99

18. Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4 | Bates | Journal of Statistical Software. *J Stat Softw*. 2015;67(1):1-48.

19. Guarda-Nardini L, de Almeida A, Manfredini D. Arthrocentesis of the temporomandibular joint: systematic review and clinical implications of research findings. *J oral facial pain headache*. 2021;35:17-29. doi:10.11607/ofph.2606

20. Monje-Gil F, Nitzan D, González-Garcia R. Temporomandibular joint arthrocentesis. Review of the literature. *Med Oral Patol Oral Cir Bucal*. 2012;17(4). doi:10.4317/medoral.17670

21. Emshoff R, Rudisch A. Determining predictor variables for treatment outcomes of arthrocentesis and hydraulic distention of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62(7):816-823. doi:10.1016/j.joms.2003.12.020

22. Al-Moraissi E, Wolford L, Ellis E, Neff A. The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *J Cranio-Maxillofacial Surg*. 2020;48(1):9-23. doi:10.1016/j.jcms.2019.10.004

23. Li D, Wong N, Li S, McGrath C, Leung Y. Timing of arthrocentesis in the management of temporomandibular disorders: an integrative review and meta-analysis. *Int J Oral Maxillofac Surg*. 2021;50:1078-1088.

24. Tatli U, Benlidayi M, Ekren O, Salimov F. Comparison of the effectiveness of three different treatment methods for temporomandibular joint disc displacement without reduction. *Int J Oral Maxillofac Surg*. 2017;46:603-609.

25. Leeuw R de, Boering G, Kuijl B van der, Stegenga B. Hard and soft tissue imaging of the temporomandibular joint 30 years after diagnosis of osteoarthrosis and internal derangement. *J Oral Maxillofac Surg*. 1996;54:1270-1280.

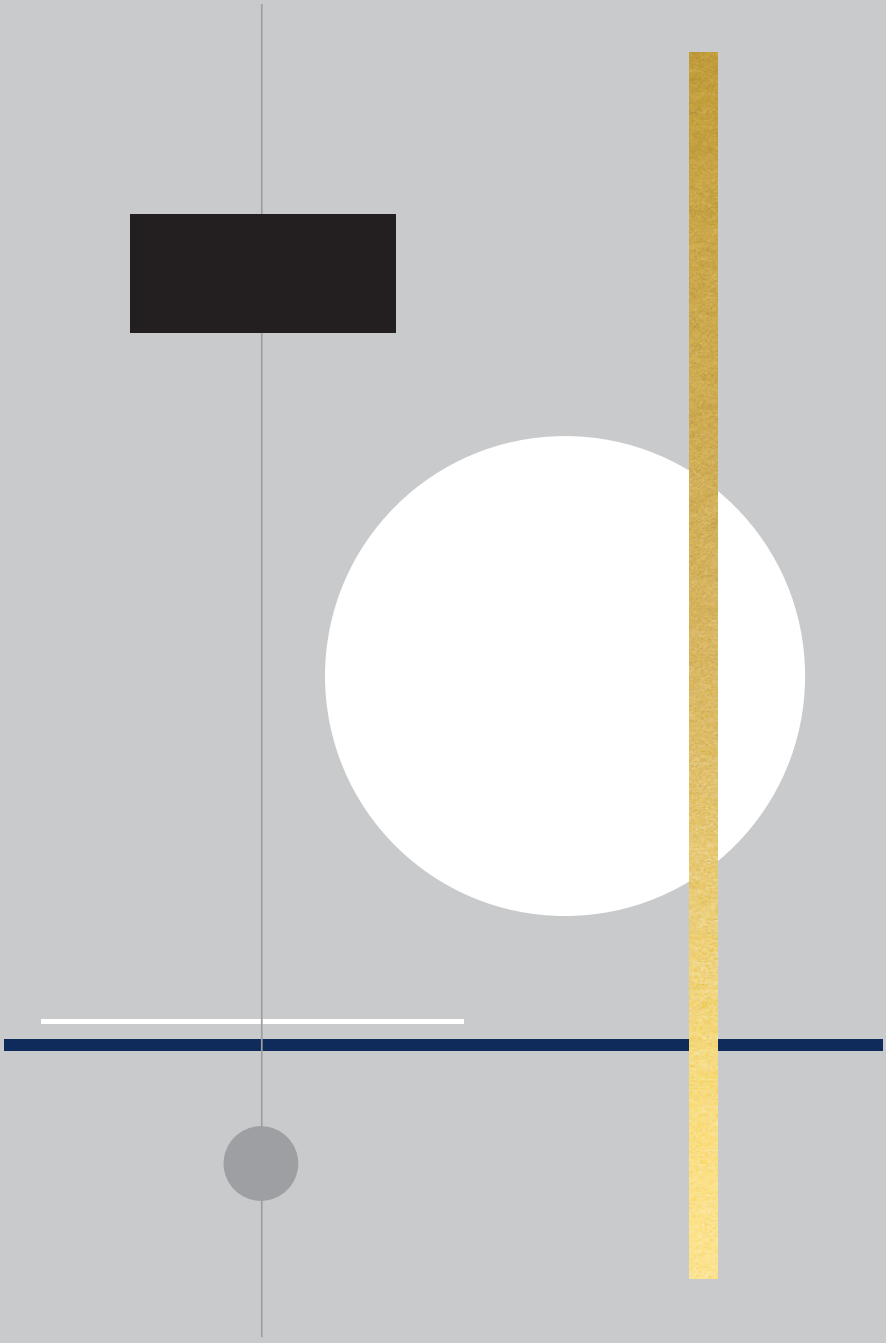
26. Leeuw R de, Boering G, Stegenga B, Bont L de. Radiographic signs of temporomandibular joint osteoarthrosis and internal derangement 30 years after nonsurgical treatment. *Oral Surgery, Oral Med Oral Pathol Oral Radiol*. 1995;79(3):382-392. doi:10.1016/S1079-2104(05)80233-1

27. Ohlmann B, Rammelsberg P, Henschel V, Kress B, Gabbert O, Schmitter M. Prediction of TMJ arthralgia according to clinical diagnosis and MRI findings. *Int J Prosthodont*. 2006;19(4):333-338.

28. Honda K, Yasukawa Y, Fujiwara M, Abe T, Urade M. Causes of persistent joint pain after arthrocentesis of temporomandibular joint. *J Oral Maxillofac Surg*. 2011;69:2311-2315. doi:10.1016/j.joms.2011.02.025

29. Emshoff R, Rudisch A. Are internal derangement and osteoarthrosis linked to changes in clinical outcome measures of arthrocentesis of the temporomandibular joint? *J Oral Maxillofac Surg*. 2003;61(10):1162-1167. doi:10.1016/S0278-2391(03)00676-1

30. Rollman GB, Gillespie JM. The role of psychosocial factors in temporomandibular disorders. *Curr Rev Pain*. 2000;4(1):71-81. doi:10.1007/s11916-000-0012-8



CHAPTER 4

TIMING OF ARTHROCENTESIS AND ITS ASSOCIATION WITH TREATMENT SUCCESS IN PAINFUL TEMPOROMANDIBULAR JOINT DISORDERS

A two-decade cohort study

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Abstract

Arthrocentesis is commonly employed for symptomatic temporomandibular joint (TMJ) disorders when conservative treatments are unsuccessful. To date, the optimal timing for initiating arthrocentesis remains unclear. This retrospective study of a two-decade cohort at a tertiary center aimed to evaluate the association between symptom duration and treatment success of initial arthrocentesis. Adults with painful TMJ disorders were included. Exclusion criteria were prior TMJ surgery, systemic rheumatic or connective tissue diseases, bony ankylosis, dentofacial deformities or significant TMJ trauma. The primary study outcome was patient-reported treatment success over a period of 5 years. Generalized estimating equations (GEE) models were performed to evaluate the association between symptom duration and treatment success and included the prognostic factors age, gender, diagnosis, preoperative conservative treatments, and adjuvant therapy during arthrocentesis. A total of 438 subjects were included in the study. GEE models indicated that a longer duration of symptoms was significantly associated with lower odds of patient-reported treatment success over a follow-up period of 5 years (OR 0.974 per month [95% CI 0.966-0.983]; $p<0.001$). Within its limitations, this study indicates that performing arthrocentesis at an earlier stage may increase the chances of reaching adequate symptom reduction in the management of painful TMJ disorders.

Introduction

Temporomandibular joint (TMJ) disorders are a group of disorders that affect approximately one-third of the general population[1]. Management strategies for symptomatic cases typically follow a stepwise approach based on treatment response. Here, first-line treatment often involves conservative interventions such as splint application, physiotherapy and pharmacological therapy. Minimally invasive surgical procedures, such as arthrocentesis, are effective treatment modalities and often only performed if conservative treatments fail in adequate symptom relief[2].

A major challenge in the current clinical practice is determining the optimal timing for transitioning to subsequent treatments when initial interventions have failed. The absence of a consensus on defining treatment failure and timing for treatment escalation often leads to variability in clinical decision-making. Hence, some patients undergo prolonged conservative treatments without any significant symptom resolution. Understanding the timely use of subsequent, more-invasive treatments is critical, as prolonged ineffective treatments may contribute to chronic disease progression, which may lead to resistance to future treatments[3]. Thus, identifying the ideal timing for initial arthrocentesis could aid clinicians in the decision-making process within the stepwise treatment framework for TMJ disorders following unsuccessful conservative treatment.

Currently, the evidence regarding the optimal timing of arthrocentesis remains scarce. Some evidence suggests that performing arthrocentesis in an earlier stage may be beneficial[4,5]. A recent systematic review assessing the ideal timing of arthrocentesis concluded that early arthrocentesis (i.e., within 3 months of failing conservative treatment) may be more effective in symptom reduction compared to late arthrocentesis (i.e., after at least 3 months of conservative treatment).[6] However, direct evidence from studies examining the relationship between symptom duration and treatment success remains inconclusive[3,7].

The current study aims to assess whether the timing of initial arthrocentesis for painful TMJ disorders affects treatment outcomes. Specifically, the primary study goal is to evaluate the association between the duration of symptoms prior to initial arthrocentesis and the patient-reported success of the procedure over a 5-year follow-up period.

Methods

Study design

A retrospective cohort study was performed at the University Medical Center Groningen (UMCG), the Netherlands, a tertiary referral center and expertise center for TMJ surgery. A pre-specified protocol was finalized before trial initiation. Patient records of individuals who underwent TMJ arthrocentesis at least five years ago were retrospectively and consecutively analyzed, beginning with the most recent cases and progressing chronologically backwards.

Study population

All study subjects were treated at the outpatient clinic of the Department of Oral and Maxillofacial Surgery of the UMCG. The inclusion criteria were subjects of 18 years and older that underwent arthrocentesis under local anesthesia and that suffered from TMJ-arthralgia, proven with a diagnostic intra-articular injection with articaine (4%) and epinephrine (1:100,000)[8]. Subjects were excluded if they suffered from systemic rheumatic diseases, connective tissue diseases, bony ankylosis, congenital or acquired dentofacial deformities or had a history of trauma that resulted in jaw or TMJ pain, bony changes or growth restrictions. Furthermore, subjects were excluded if they had previous surgical treatment of the same TMJ or when no duration of symptoms or follow-ups was reported in the patient files.

Outcome measures

Since standardized outcomes such as the pain scores were not expected to be routinely reported in the patient files, the primary study outcome involved the patient-reported success of primary arthrocentesis over time. This outcome was assessed at 1 year and 5 years follow-up. For this binary study outcome, patient-reported success was defined as the subjective feeling of adequate treatment effect and if additional treatment was not required. The secondary binary outcomes involved the pain-related success ($\geq$30%[11] or $\geq$12mm[12] improvement on a visual analog scale (VAS) 0-100mm) assessed at 1 and 5 years, maximum mouth opening (MMO)-related success ($\geq$6mm[13] improvement in subjects with a restricted mouth opening) assessed at 1 and 5 years and the combined success of pain and MMO (postoperative $\leq$30mm VAS and $\geq$35mm MMO). Furthermore, continuous secondary outcomes involved pain reduction (VAS) and MMO improvement assessed at 1 and 5 years. Finally, the number of retreatments in the follow-up period following initial arthrocentesis was registered.

Statistical analysis

Normality of continuous data was evaluated through visual examination of Q-Q plots and the Shapiro-Wilk test. Normally distributed data were reported as means and standard deviations (SD), while non-normally distributed variables were presented as medians with first and third quartiles (Q1-Q3).

To evaluate the association between symptom duration and repeated measurements of treatment success, GEE models were employed for the primary study outcome (patient-reported success). Because the outcome variable was binary, a binomial distribution with a logit link function was fitted. GEE models were selected to account for repeated measures within subjects and the inclusion of time-dependent covariates. Predictors included in the GEE model were selected based on their potential prognostic relevance. These variables comprised the duration of symptoms before initial arthrocentesis in months, follow-up duration in months, age, sex, previous conservative treatments (i.e., physiotherapy, splints and nonsteroidal anti-inflammatory drugs), adjuvant therapy during arthrocentesis (i.e., corticosteroids and hyaluronic acid) and underlying diagnosis (i.e., disc displacement with reduction, disc displacement without reduction and degenerative joint disease). Since subjects could have more than one diagnosis, each diagnostic category was modelled as a separate binary predictor. An exchangeable correlation structure was applied in all models to account for intra-subject correlation. A secondary analysis was performed to further investigate the association between symptom duration and patient-reported success, using a dichotomized predictor of symptom duration instead of the continuous variable. In this analysis, symptom duration was classified into timely (≤6 months) and delayed (>6 months) treatment. This approach enabled the estimation of the relative odds of treatment success across both symptom duration intervals. The threshold was selected based on the author's clinical judgment. The concordance index (C-index) for each GEE model was calculated using predicted probabilities to assess its discriminatory capabilities. In order to assess whether diagnostic heterogeneity influenced results, a sensitivity analysis was performed where the cohort was stratified into pre- and post-implementation periods of the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)[14]. GEE models were then employed for each subgroup to assess the robustness of the associations between the diagnostic periods and with the primary analysis.

All models yielded odds ratios with corresponding 95% confidence intervals (95% CI). GEE were performed in R, version 4.5.0 (R Core Team; R Foundation for Statistical Computing, Vienna, Austria), using the geepack package[15]. Descriptive

statistics and two-grouped comparison tests were performed in SPSS (version 28; IBM Corp., Armonk, NY, USA). A p-value of ≤0.05 (two-tailed) was considered statistically significant.

Table 1. Baseline characteristics of study population.

Predictors	Baseline values	Total *n*
Male, *n* (%)	65 (14.8)	438
Age in years, median (Q1-Q3)	38.5 (24.0 – 54.0)	438
Duration of symptoms in months, median (Q1-Q3)	13 (7.8 – 25.0)	438
Duration of symptoms ≤6 months, *n* (%)	80 (18.3)	438
Pain 0-100mm, median (Q1-Q3)	70.0 (50.0 – 80.0)	98
MMO in mm, mean (SD)	31.6 (8.9)	364
Diagnosis		
ADDwR, *n* (%)	111 (25.3)	438
ADDwoR, *n* (%)	167 (38.1)	438
DJD, *n* (%)	166 (37.9)	438
Pre-operative conservative treatment		
Physiotherapy, *n* (%)	162 (37.0)	438
Splint, *n* (%)	106 (24.2)	438
NSAID, *n* (%)	251 (57.3)	438
Adjuvant therapy during arthrocentesis		
Corticosteroids, *n* (%)	321 (73.3)	438
Hyaluronic acid, *n* (%)	45 (10.3)	438

Abbr.: n number of subjects; Q1-Q3 first to third quartile; MMO maximum mouth opening; SD standard deviation; ADDwR anterior disc displacement with reduction; ADDwoR anterior disc displacement without reduction; DJD degenerative joint disease; NSAID nonsteroidal anti-inflammatory drugs.

Results

A total of 691 patient files from between March 2000 and March 2020 were analyzed in order to include 438 subjects. The primary reasons for exclusion were previous surgical treatment or trauma of the joint, a history of rheumatic disease or Ehlers-Danlos syndrome, age of under 18 and missing data regarding symptom duration or follow-up. Of the study population, the median age was 38.5 (24.0-54.0), with primarily women (85.2%). The median duration of symptoms was 13 (7.8-25.0) months. All the baseline characteristics are displayed in ***table 1***.

Patient-reported success was reported in all subjects (*n = 438*) and was 70.3% at 1-year follow-up and 65.5% at 5-year follow-up. Regarding pain, success rates were 92.1% at 1 year (*n* = 63) and 92.3% at 5-year follow-up (*n* = 13). Here, an average reduction of 51.0 (24.8) mm at 1 year (*n* = 63) and 58.1 (27.6) mm at 5 years (*n* = 13) was seen. For MMO, success rates were 60.8% at 1 year (*n* = 176) and 59.1% at 5-year follow-up (*n* = 66). Here, an average improvement of 5.8 (8.3) mm at 1 year (*n* = 223) and 6.0 (9.3) mm at 5 years (*n* = 79) was seen. Pain and MMO combined success rates were 59.0% at 1 year (*n* = 39) and 71.4% at 5 years (*n* = 28) follow-up **(Table 2)**. A total of 136 subjects (31.1%) received an additional treatment within 5-year follow-up after initial arthrocentesis.

Table 2. Results of study outcomes at each follow-up.

Outcomes	1-year follow-up		5-year follow-up	
	Events (%)	***n***	**Events (%)**	***n***
Patient-reported success	308 (70.3)	438	287 (65.5)	438
Pain-related success*	58 (92.1)	63	12 (92.3)	13
MMO-related success#	107 (60.8)	176	39 (59.1)	66
Combined success^	23 (59.0)	39	20 (71.4)	28
	Mean (SD)	***n***	**Mean (SD)**	***n***
Pain reduction	51.0 (24.8)	63	58.1 (27.6)	13
MMO improvement	5.8 (8.3)	223	6.0 (9.3)	79

Abbr.: n number of subjects; MMO maximum mouth opening; SD standard deviation.* ≥30% or ≥12mm improvement on visual analog scale (0-100), # ≥6mm improvement in subjects with a restricted mouth opening, only in subjects with a restricted mouth opening, ^ post-operative ≤30mm (visual analog scale (0-100) and ≥35mm MMO.

For patient-reported success, GEE indicated that a longer duration of symptoms was significantly associated with a lower odds of treatment success over a period of 5 years (OR 0.974 per month [95% CI 0.966-0.983]; *p*<0.001) **(Table 3)**. The model showed a good discriminative ability, with a C-index of 0.719. Furthermore, the use of adjuvant corticosteroids or hyaluronic acid was significantly associated with lower odds of patient-reported success. Age, gender, diagnosis and the performance of preoperative conservative treatments were not prognostic factors for success. Secondary GEE analysis indicates that subjects treated within 6 months of symptom initiation had 2.7 times higher odds of experiencing treatment success than those treated later (OR 2.71 [95% CI 1.40-5.26]; *p* = 0.003). Here, a C-index of 0.676 indicated moderate discriminative ability of the model.

Table 3. Results of generalized estimating equations on patient-reported success.

Predictors	OR	95% CI	*p*
Duration of symptoms in months	0.974	0.966 – 0.983	**<0.001**
Follow-up duration in months	0.996	0.994 – 0.998	**<0.001**
Age in years	0.999	0.984 – 1.010	0.884
Gender (ref. = male)	0.624	0.313 – 1.250	0.181
Diagnosis			
ADDwR	1.020	0.542 – 1.930	0.942
ADDwoR	1.070	0.611 – 1.880	0.809
DJD	0.937	0.546 – 1.610	0.815
Pre-operative conservative treatment			
Physiotherapy	0.762	0.463 – 1.250	0.286
Splint	0.852	0.478 – 1.420	0.489
NSAID	0.865	0.526 – 1.420	0.568
Adjuvant therapy during arthrocentesis			
Corticosteroids	0.389	0.209 – 0.723	**0.003**
Hyaluronic acid	0.358	0.153 – 0.835	**0.018**

Abbr.: OR odds ratio; 95% CI 95% confidence interval; ADDwR anterior disc displacement with reduction; ADDwoR anterior disc displacement without reduction; DJD degenerative joint disease; NSAID nonsteroidal anti-inflammatory drugs.

The sensitivity analysis stratifying the cohort between pre- (n = 312) and post-implementation (n = 126) of the DC/TMD yielded results consistent with the primary GEE model **(Appendix A & B)**. Differences in diagnostic cohort did not substantially influence study results, as associations were comparable across the stratified and primary models.

Discussion

The current study aimed to evaluate the association between duration of symptoms prior to initial arthrocentesis and treatment success of the treatment for painful TMJ disorders over a 5-year follow-up period in a cohort of 438 subjects, treated in a tertiary referral institution over two decades. Results of this study demonstrate a significant negative association between the duration of symptoms and patient-reported success (OR 0.974 per month [95% CI 0.966-0.983]; p<0.001). Specifically, each additional month of symptoms prior to treatment was associated with a 2.6% decrease in odds of treatment success. Furthermore, initial arthrocentesis within 6 months of symptom onset drastically improved odds of treatment success

compared to treatment employed after 6 months of symptoms (OR 2.71 [95% CI 1.40-5.26]; $p = 0.003$). In other words, patients treated within 6 months of symptom onset had 2.7 times higher odds of experiencing success compared to those treated after 6 months. These findings suggest that prolonged symptom duration may diminish the likelihood of achieving satisfactory outcomes from arthrocentesis, highlighting the importance of timely referral and early arthrocentesis initiation in patients with painful TMJ disorders.

The rationale for symptom reduction following arthrocentesis is currently hypothesized to be attributed to the washing out of pro-inflammatory cytokines, matrix-degrading enzymes and metabolic waste products from the joint[16], which contribute to synovitis and consequently pain[17]. However, this mechanism does not explain the reduced efficacy of arthrocentesis observed in patients with prolonged symptom duration. The association between symptom duration and treatment outcome observed in this study may, therefore, be partly attributed to the involvement of a distinct pathophysiological system in certain patients with chronic symptoms. For instance, in individuals with prolonged and intense pain, continuous activation of nociceptors may lead to peripheral sensitization, in which increased excitability of these nociceptors result in intensified pain responses[18,19]. This chronic pain may persist if the underlying pathology remains active. In some subjects, ongoing peripheral input may progress to central sensitization[20,21], a condition in which persistent peripheral pain signals lead to changes in the central nervous system, resulting in lower pain thresholds and intensified pain responses such as allodynia and hyperalgesia, even after removal of the stimulus[18,19]. In such cases, the central nervous system may be triggered by persistent inflammatory activity in the joint, but may maintain symptoms independently from damage from the peripheral tissue[22]. This mechanism could explain why some patients continue to experience symptoms despite the washing out of symptom-inducing products from the joint. Consequently, this group of patients may benefit from additional therapeutic modalities other than arthrocentesis, such as interventions based on a more centrally modulated approach[19,21,22]. Alternatively, persistent pain after arthrocentesis could also result from concomitant pain from the masticatory muscles[23], a secondary reactive response to arthrogenous pain that does not fully resolve with joint-focused interventions.

In the present study, the primary GEE model indicated that predictors such as age, gender, diagnosis and preoperative conservative treatments did not significantly influence patient-reported success. The finding that age and gender are not prognostic factors for treatment success has been established before in previous

studies[3,24]. This may be due to treatment outcomes being more likely driven by the underlying pathophysiology (for example, inflammatory, mechanical and pain-processing factors), rather than demographic factors.

Although arthrocentesis has been shown to be effective for anterior disc displacement and degenerative joint disease, evidence suggests that it is most effective for symptomatic anterior disc displacement without reduction[25,26]. In the current results, the underlying diagnosis concurrently occurring with arthralgia did not significantly impact patient-reported success. Sensitivity analyses yielded similar results as the primary analysis, indicating that the discrepancy from previous reports is less likely to be explained by diagnostic heterogeneity, but rather underlying factors not explored in the present study. Furthermore, preoperative treatment with physiotherapy, splint and/ or nonsteroidal anti-inflammatory drugs were not associated with improved patient-reported success. This may be due to the fact that patients who proceed to arthrocentesis represent a more treatment-resistant subgroup, in whom conservative options have already failed, minimizing their predictive value for postoperative success. Additionally, such conservative treatments may not target intra-articular pathologies, such as adhesion formation, as adequately as arthrocentesis. In the GEE model, the use of adjuvant hyaluronic acid or corticosteroids during arthrocentesis was associated with lower odds of patient-reported success. Although the effectiveness of these adjuvant therapies remains debated at least[27,28], current evidence does not suggest that they worsen outcomes. Therefore, the current finding is likely attributable to confounding by indication, where subjects with more severe symptoms were more likely to receive adjuvant treatment. The observed association between the use of adjuvant treatment and lower treatment success is thus more likely to reflect the use of these therapies in patients with more severe symptoms, rather than a detrimental effect of these therapies themselves.

Within the limitations of the substantial amount of missing data for the secondary success criteria (i.e., pain scores and MMO), patient-reported success appeared to show similar rates of improvement as success based on MMO. In contrast, pain-related success was higher than patient-reported success, potentially indicating that a reduction of 12mm on the VAS or a 30% decrease in pain intensity may not be sufficient for patients to perceive the treatment as successful. When considering continuous outcomes, joint pain demonstrated an improvement over time, with mean VAS reduction of 51.0 (SD 24.8) at one year and 58.1 (SD 27.6) at five years of follow-up. These findings are consistent with the current evidence[5,29], supporting the notion that arthrocentesis is primarily effective in alleviating joint

pain, while contributing only modestly to improvements in MMO. Nonetheless, the substantial proportion of missing data for the secondary outcomes pain and MMO improvement introduces a risk of attrition bias. Since only a proportion of the subjects reported these outcomes, observed results may disproportionately reflect outcomes of subjects with a specific disease severity. This may limit the internal validity and generalizability of the findings. As such, these secondary results should be interpreted with caution and regarded as exploratory.

This study has several limitations. The retrospective design limited the ability to control for confounding variables and may have introduced selection and attrition bias inherent to this study design. Furthermore, the study population was treated at a tertiary referral center, potentially limiting the generalizability to a broader population. The strengths of the current study include the long-term follow-up, providing insights into the sustained effects of arthrocentesis over time. Additionally, using patient-reported success as the outcome represents a significant strength, as it involves the patient's perspective and represents an individualized, patient-centered measure. However, it is not based on a quantitative metric and is inherently subjective, potentially influenced by factors such as individual expectations or satisfaction. Past studies focused on quantifiable success criteria such as pain reduction and MMO improvement, which neglect what treatment is about in the end: patient-reported success.

This retrospective study may serve as a hypothesis-generating study for future prospective research. Future studies, ideally prospective cohort studies or randomized controlled trials, should aim to standardize the use of a comprehensive set of outcome measures based on both the pre- and postoperative change scores. Establishing uniform and clear definitions of treatment success is crucial for allowing meaningful comparisons across studies and improving the interpretation of study results. Importantly, upcoming studies should not be limited to outcomes such as pain and MMO, but should also incorporate validated, quantifiable patient-reported outcomes, such as the validated Mandibular Function Impairment Questionnaire (MFIQ)[30]. Only through standardized and comprehensive evaluation in well-designed prospective studies can definitive conclusions be drawn regarding the relationship between symptom duration and treatment success.

In conclusion, the current study indicates that longer symptom duration is negatively associated with the patient-reported success of initial arthrocentesis as therapy for painful TMJ disorders. Each additional month of symptoms prior to initial

arthrocentesis is associated with a 2.6 % decrease in odds of treatment success and patients treated within 6 months of symptom onset have 2.7 times higher odds of experiencing success compared to those treated after 6 months. Within the limitations of the study, results indicate that performing arthrocentesis at an earlier stage may increase the chances of achieving adequate symptom reduction from arthrocentesis.

Ethical Approval

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References

1. Valesan L, Da-Cas C, Réus J, et al. Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. *Clin Oral Investig*. 2021;25(2):441-453. doi:10.1007/s00784-020-03710-w
2. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain*. 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5
3. Emshoff R, Rudisch A. Determining predictor variables for treatment outcomes of arthrocentesis and hydraulic distention of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62(7):816-823. doi:10.1016/j.joms.2003.12.020
4. Tang Y, Vos L, Tuin A, et al. Arthrocentesis versus non- surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. *Int J Oral Maxillofac Surg*. 2023;52:595-603.
5. Al-Moraissi E, Wolford L, Ellis E, Neff A. The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *J Cranio-Maxillofacial Surg*. 2020;48(1):9-23. doi:10.1016/j.jcms.2019.10.004
6. Li D, Wong N, Li S, McGrath C, Leung Y. Timing of arthrocentesis in the management of temporomandibular disorders: an integrative review and meta-analysis. *Int J Oral Maxillofac Surg*. 2021;50:1078-1088.
7. Alpaslan C, Dolwick MF, Heft MW. Five-year retrospective evaluation of temporomandibular joint arthrocentesis. *Int J Oral Maxillofac Surg*. 2003;32(3):263-267. doi:10.1054/ijom.2003.0371
8. Tjakkes GHE, TenVergert EM, De Bont LGM, Stegenga B. The effect of intra-articular injection of ultracain in the temporomandibular joint in patients with preauricular pain: A randomized prospective double-blind placebo-controlled crossover study. *Clin J Pain*. 2007;23(3):233-236. doi:10.1097/AJP.0b013e31802f0950
9. Haeffs TH, D'Amato LN, Khawaja SN, Keith DA, Scrivani SJ. What Variables Are Associated With the Outcome of Arthroscopic Lysis and Lavage Surgery for Internal Derangement of the Temporomandibular Joint? *J Oral Maxillofac Surg*. 2018;76(10):2081-2088. doi:10.1016/j.joms.2018.04.018
10. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. 2007;39(2):175-191. doi:10.3758/BF03193146
11. Dworkin R, Turk D, Wyrwich K, et al. Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. *J pain*. 2008;9(2):105-121.
12. Calixtre L, Oliveira A, Alburquerque-Sendin F, Armijo-Olivo S. What is the minimal important difference of pain intensity, mandibular function, and headache impact in patients with temporomandibular disorders? Clinical significance analysis of a randomized controlled trial. *Musculoskelet Sci Pract*. 2020;46:2020.

13. Kropmans T, Dijkstra P, Stegenga B, Stewart R, Bont L de. Smallest detectable difference of maximal mouth opening in patients with painfully restricted temporomandibular joint function. *Eur J Oral Sci*. 2000;108:9-13.

14. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *J oral facial pain headache*. 2014;38(1):6-27.

15. Højsgaard S, Halekoh U, Yan J. The R package geepack for generalized estimating equations. *J Stat Softw*. 2006;15(2):1-11. doi:10.18637/jss.v015.i02

16. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006

17. Celotti C, Martin-Granizo R, De La Sen O. Correlation of arthroscopic findings with clinical–radiological signs and symptoms of temporomandibular joint dysfunction: retrospective study of 829 joints. *Int J Oral Maxillofac Surg*. 2022;51:1069-1073.

18. Furquim BD, Flamengui LMSP, Conti PCR. TMD and chronic pain: A current view. *Dental Press J Orthod*. 2015;20(1):127-133. doi:10.1590/2176-9451.20.1.127-133.sar

19. Merrill RL. Central Mechanisms of Orofacial Pain. *Dent Clin North Am*. 2007;51(1):45-59. doi:10.1016/j.cden.2006.09.010

20. Cayrol T, Van Den Broeke EN, Gerard E, et al. Chronic temporomandibular disorders are associated with higher propensity to develop central sensitization: A case-control study. *Pain*. 2023;164(5):E251-E258. doi:10.1097/j.pain.0000000000002803

21. La Touche R, Paris-Alemany A, Hidalgo-Pérez A, López-de-Uralde-Villanueva I, Angulo-Diaz-Parreño S, Muñoz-García D. Evidence for Central Sensitization in Patients with Temporomandibular Disorders: A Systematic Review and Meta-analysis of Observational Studies. *Pain Pract*. 2018;18(3):388-409. doi:10.1111/papr.12604

22. Monaco A, Cattaneo R, Marci MC, Pietropaoli D, Ortu E. Central Sensitization-Based Classification for Temporomandibular Disorders: A Pathogenetic Hypothesis. *Pain Res Manag*. 2017;5:1-13. doi:doi: 10.1155/2017/5957076

23. Manfredini D, Arveda N, Guarda-Nardini L, Segù M, Collesano V. Distribution of diagnoses in a population of patients with temporomandibular disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012;114(5):e35-e41. doi:10.1016/j.oooo.2012.03.023

24. Grossmann E, Poluha RL, Iwaki LCV, Santana RG, Filho LI. Predictors of arthrocentesis outcome on joint effusion in patients with disk displacement without reduction. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2018;125(4):382-388. doi:10.1016/j.oooo.2017.12.021

25. Polat M, Yanik S. Efficiency of arthrocentesis treatment for different temporomandibular joint disorders. *Int J Oral Maxillofac Surg*. 2020;49(5):621-627. doi:10.1016/j.ijom.2019.08.017

26. Nitzan D, Naaman H. Athrocentesis: What, When, and Why? *Atlas Oral Maxillofac Surg Clin North Am.* 2022;30(2):137-145. doi:10.1016/j.cxom.2022.06.008

27. Bouloux G, Chou J, Krishnan D, et al. Is Hyaluronic Acid or Corticosteroid Superior to Lactated Ringer Solution in the Short Term for Improving Function and Quality of Life After Arthrocentesis? Part 2. *J Oral Maxillofac Surg.* 2017;*75*(1):63-72. doi:10.1016/j.joms.2016.08.008

28. Bouloux G, Chou J, Krishnan D, et al. Is Hyaluronic Acid or Corticosteroid Superior to Lactated Ringer Solution in the Short-Term Reduction of Temporomandibular Joint Pain After Arthrocentesis? Part 1. *J Oral Maxillofac Surg.* 2017;*75*(1):52-62.

29. Tang Y, Bakelen N van, Gareb B, Spijkervet F. Arthrocentesis versus conservative treatments for temporomandibular joint disorders: A systematic review with meta-analyses and trial sequential analyses. *J Craniomaxillofac Surg.* 2025;53:250-261.

30. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain.* 1993;*7*(2):183-195. http://www.ncbi.nlm.nih.gov/pubmed/8358365

Appendix A. Results of generalized estimating equations on patient reported success in Pre-DC/TMD subgroup (n = 312).

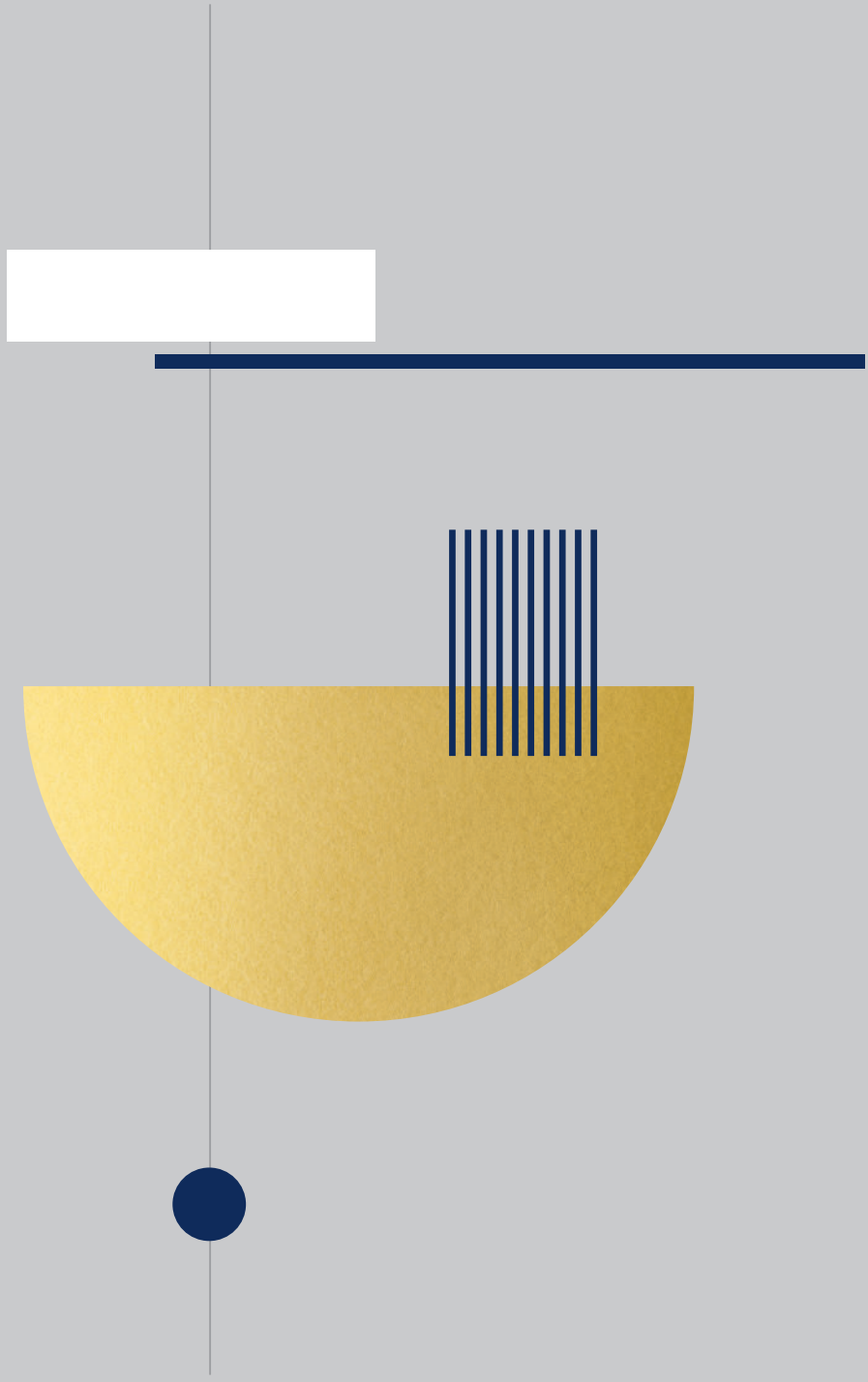
Predictors	OR	95% CI	*p*
Duration of symptoms in months	0.971	0.959 – 0.982	**<0.001**
Follow-up duration in months	0.996	0.994 – 0.999	**0.002**
Age in years	1.00	0.984 – 1.02	0.686
Gender (ref. = male)	1.10	0.486 – 2.51	0.813
Diagnosis			
ADDwR	1.88	0.825 – 4.28	0.133
ADDwoR	1.38	0.697 – 2.73	0.356
DJD	1.01	0.516 – 1.98	0.977
Pre-operative conservative treatment			
Physiotherapy	0.550	0.293 – 1.03	0.063
Splint	1.15	0.576 – 2.30	0.692
NSAID	0.625	0.330 – 1.19	0.150
Adjuvant therapy during arthrocentesis			
Corticosteroids	0.429	0.211 – 0.872	**0.019**
Hyaluronic acid	0.211	0.0615 – 0.725	**0.016**

Abbr.: OR odds ratio; 95% CI 95% confidence interval; ADDwR anterior disc displacement with reduction; ADDwoR anterior disc displacement without reduction; DJD degenerative joint disease; NSAID nonsteroidal anti-inflammatory drugs.

Appendix B. Results of generalized estimating equations on patient reported success in Post-DC/TMD subgroup (n = 126).

Predictors	OR	95% CI	*p*
Duration of symptoms in months	0.984	0.971 – 0.996	**<0.001**
Follow-up duration in months	0.996	0.991 – 1.00	0.069
Age in years	0.989	0.965 – 1.01	0.383
Gender (ref. = male)	0.360	0.081 – 1.60	0.179
Diagnosis			
ADDwR	0.317	0.090 – 1.12	0.0739
ADDwoR	0.877	0.283 – 2.72	0.820
DJD	0.736	0.257 – 2.11	0.568
Pre-operative conservative treatment			
Physiotherapy	1.13	0.478 – 2.69	0.777
Splint	0.671	0.256 – 1.76	0.419
NSAID	1.09	0.443 – 2.66	0.856
Adjuvant therapy during arthrocentesis			
Corticosteroids	0.390	0.102 – 1.49	0.168
Hyaluronic acid	0.786	0.207 – 2.98	0.723

Abbr.: OR odds ratio; 95% CI 95% confidence interval; ADDwR anterior disc displacement with reduction; ADDwoR anterior disc displacement without reduction; DJD degenerative joint disease; NSAID nonsteroidal anti-inflammatory drugs.



CHAPTER 5

ARTHROSCOPY VERSUS ARTHROCENTESIS AND VERSUS CONSERVATIVE TREATMENTS FOR TEMPOROMANDIBULAR JOINT DISORDERS

A systematic review with meta-analysis and trial sequential analysis

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Abstract

The aim of this systematic review was to assess the efficacy of arthroscopy compared to arthrocentesis and to conservative treatments for temporomandibular joint disorders. Thirteen controlled studies on various patient outcomes were included after a systematic search in seven electronic databases. Meta-analyses were conducted separately for arthroscopic surgery (AS) and arthroscopic lysis and lavage (ALL), and short-term (<6 months), intermediate-term (6 months to 5 years), and long-term (≥5 years) follow-up periods were considered. No significant differences in pain reduction and complication rates were found between AS or ALL and arthrocentesis. Regarding improvement in maximum mouth opening (MMO), both AS at intermediate-term and ALL at short-term follow-up were equally efficient when compared to arthrocentesis. However, at intermediate-term follow-up, ALL was superior to arthrocentesis for MMO improvement (mean difference 4.9 mm, 95% confidence interval 2.7-7.1 mm). Trial sequential analysis supported the conclusion of the meta-analysis for MMO improvement for ALL versus arthrocentesis studies at intermediate-term follow-up, but not for the other meta-analyses. Insufficient evidence exists to draw conclusions regarding other patient outcomes or about comparisons between arthroscopy and conservative treatments. Due to the low quality of the primary studies, further research is warranted before final conclusions can be drawn regarding the management of temporomandibular joint disorders.

Introduction

Disorders of the temporomandibular joint (TMJ) occur in approximately 30% of the adult population and encompass primarily, but not exclusively, the conditions internal derangement (ID) and degenerative joint disease (DJD)[1]. Due to their often debilitating nature, TMJ disorders have a significant impact on the quality of life of patients[2].

Treatment options for TMJ disorders vary from conservative non-surgical approaches to minimally invasive and open joint surgeries. Typically, conservative treatment modalities are the first choice for initial therapy and consist primarily of counselling, splints, physiotherapy, and medications (i.e., non-steroidal anti-inflammatory drugs (NSAIDs) and muscle relaxants). Minimally invasive surgical treatments, such as arthroscopy and arthrocentesis, are only considered if conservative treatment modalities have failed to adequately reduce pain or improve function[3]. However, there is growing evidence that using minimally invasive therapies as an initial treatment may be more efficient at reducing clinical symptoms when compared to conservative treatments[4–6]

TMJ arthroscopy allows the visualization of the inner tissues of the upper TMJ compartment for diagnostic purposes and subsequent targeted treatment of the visualized tissues, i.e., the lysis of adhesions, injection of medication into the inflamed tissue, and electrocauterization/coblation of redundant and hyperaemic tissue. Technical advancements over the years have resulted in the differentiation of arthroscopy according to its complexity and level of invasiveness. The different modalities of arthroscopy vary in their therapeutic maneuvers, ranging from simple diagnostic arthroscopy (level I) or arthroscopic lysis and lavage (ALL) to more advanced arthroscopic surgery (AS), without (level II) or with (level III) disc repositioning and fixation procedures[7].

Despite its widespread application in the treatment of TMJ disorders, arthroscopy has received minor attention regarding its efficacy in comparison to other treatment modalities, such as arthrocentesis or conservative non-surgical treatments. A systematic review with meta-analysis published in 2015 compared the efficacy of arthroscopy with arthrocentesis in the management of ID of the TMJ, and concluded that arthroscopy resulted in more favorable outcomes than arthrocentesis with regard to pain reduction and improvement in mouth opening, while having similar complication rates[8]. However, that review also noted that more high-quality studies

would be needed before final conclusions could be drawn. Since then, several new studies comparing the two treatment modalities have been conducted[9–11]. Additionally, no pair-wise systematic review has been performed to date that presents direct evidence of the efficacy of arthroscopy versus conservative treatments, and no review has included outcome variables other than pain reduction, improvement in maximum mouth opening (MMO), and complication rates. An updated systematic review, complying with the highest review standards, is therefore needed to provide a more comprehensive overview of the current evidence regarding the efficacy of TMJ arthroscopy.

Hence, the aim of the current systematic review was to assess the efficacy and feasibility of AS and ALL as treatment modalities for TMJ disorders versus arthrocentesis and versus conservative treatments, by analyzing joint pain, MMO, mandibular function, joint blocks and noises, mandibular range of motion, quality of life, safety, and costs/cost-effectiveness.

Methods

This systematic review was performed and reported in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (version 6.3)[12] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[13]. The research protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO; CRD42022324103) prior to the initial literature search.

Eligibility criteria and data items

The PICOTS format was used to formulate the inclusion and exclusion criteria and the subsequent selection of articles, as outlined below.

Population (P): studies were eligible for inclusion if the study population encompassed patients diagnosed with the following temporomandibular disorders (TMD) as classified by the Diagnostic Criteria for Temporomandibular Disorders[14]: TMJ arthralgia, ID of the TMJ (i.e., disc displacement with or without reduction, and any synonyms such as closed lock and anchored disc phenomenon), and DJD of the TMJ (i.e., osteoarthritis or osteoarthrosis). Furthermore, studies involving participants with more general TMJ disorders (i.e., TMJ arthropathy, intra-articular or capsular disorder of the TMJ, TMJ synovitis, and craniomandibular disorder) were also eligible for inclusion. The exclusion criteria were studies involving

patients younger than 16 years of age and those with patients who suffered from congenital or acquired dentofacial deformities, rheumatic disorders, connective tissue disorders, or bony ankylosis of the TMJ.

Intervention (I): the intervention group in the study had undergone TMJ arthroscopy (i.e., diagnostic arthroscopy, arthroscopic lysis and lavage, arthroscopic surgery, level I–III arthroscopy). Due to the differences in the therapeutic maneuvers performed between arthroscopic interventions, the pooling of all arthroscopy types was considered inappropriate. The intervention group was, therefore, stratified into ALL and AS for all of the analyses. ALL was defined in accordance with the technique described by Sanders[15] and with level I arthroscopy[7], where visualization of the upper joint compartment is established in combination with joint lavage and an instrument sweep for lysis of any present adhesions. AS was defined as the procedure where any additional surgical maneuvers on top of ALL were performed, as also described for level II or level III arthroscopy[7]. This often encompasses the introduction of additional portals and includes techniques such as anterolateral capsular release, (electro)coagulation of hypervascular (retrodiscal) tissues, and/or manipulation/fixation of the articular disc[7].

Control (C): the control group consisted either of (1) arthrocentesis with lavage of the TMJ using any technique (i.e., single/double needle use) or (2) conservative non-surgical treatments of any modality or a combination of these modalities; i.e., soft diet advice, medications such as NSAIDs and muscle relaxants, physiotherapy, and/or splints/oral appliances.

Outcomes (O): the primary study outcome was pain during mandibular movement and/or function, assessed using a visual analog scale (VAS) or another continuous numerical scale. Secondary study outcomes included pain at rest assessed using a VAS or another continuous numerical scale, MMO in millimeters, mandibular function (assessed for instance using the Mandibular Function Impairment Questionnaire (MFIQ)[16] or with regard to chewing ability), joint blocks and noises, mandibular range of motion (i.e., lateral and protrusive movements), quality of life, safety (i.e., complication rates), and costs/cost-effectiveness.

Time points (T): the outcome measures were stratified into three follow-up time ranges for the analyses: short-term (<6 months), intermediate-term (6 months to 5 years), and long-term (≥5 years). If multiple measurements were reported from the

same study population that were within a single follow-up range, the latest reported outcome measurement in that range was used for the quantitative analyses.

Study design (S): the study types that were eligible for inclusion were randomized controlled trials (RCTs), prospective non-randomized controlled clinical trials (CCTs), and retrospective cohort studies with a control group. Case reports, conference abstracts, reviews, letters to the editor, and expert opinions were excluded. Furthermore, the studies had to have included at least 10 participants and been published in a peer-reviewed journal. No restriction was placed on language or publication date.

Search strategy and information sources

With the help of a biomedical literature specialist, a sensitive electronic literature search was performed in seven electronic databases and trial registers using controlled vocabulary (medical subject heading, MeSH) and free text terms **(Appendix A)**. The electronic databases and registers were PubMed, Embase, Web of Science, Cochrane Library, Scopus, Clinicaltrials.gov, and the International Clinical Trials Registry Platform (ICTRP). The latest search date was February 15, 2023. No language or publication date restrictions were applied. In addition, the grey literature was searched. The reference lists of relevant trials and systematic reviews on the same topic were screened, and experts on the study subject (NBvB and FKLS) were asked about relevant articles.

Study selection process

After de-duplication following the method of Bramer et al.[17], two reviewers (YHT and NBvB) independently assessed the titles and abstracts of the records found in the literature search to identify those eligible for full-text assessment. Records that lacked sufficient information in the title and abstract were also selected for full-text assessment. The full-text assessment was performed by the same two independent reviewers. After each stage, the assessments were de-blinded and a consensus meeting was held between the two reviewers to resolve any disagreements. If there was a lack of consensus, a third reviewer (FKLS) would be asked to aid in the decision-making. The inter-observer agreement (Cohen's kappa and percentage of agreement) was calculated for both stages.

Data collection process

A predefined standardized form was used to collect the data from the eligible studies. One reviewer (YHT) collected the data from all of the reports, while the second reviewer (NBvB) reviewed 15% of the reports independently. The agreement between the reviewers regarding the data collection was required to be ≥90%. If this was not the case, the second reviewer had to evaluate all of the remaining reports, followed by a consensus meeting.

The following data were collected from each study: authors and publication date, primary and secondary outcome measures, baseline patient characteristics (age, sex, and number of patients), study design, specifications of the treatments in each study arm (i.e., type, technique, additional intraoperative injections, anesthesia modality, and pre- and postoperative treatment regimens), and the type of disorder treated. If multiple outcome measures from different follow-up periods were reported in a single study, all of the outcome measures from each follow-up time-point were collected. If multiple reports were published for a single study, the outcome measures were checked for duplication and, if present, the duplicates were removed. All of the reported continuous pain scores were recalculated to a numerical VAS scale of 0–100 mm (the higher the value the greater the pain) to allow between-study comparisons and quantitative analyses.

An attempt was made to contact the corresponding authors of included articles in the event that additional study data were required for both the qualitative and quantitative analyses. The additional data were only included in the current study if the authors could provide the necessary data.

Quality assessment

The assessment of methodological and clinical heterogeneity of the included studies was conducted independently by two reviewers (YHT and NBvB). Any inconsistencies were resolved through discussion in a consensus meeting. The methodological heterogeneity assessment was performed for all of the included studies, while the clinical and statistical heterogeneity assessments were only performed for the studies included in the quantitative analyses, by meta-analysis.

The risk of bias in the RCTs was assessed using the Cochrane Risk of Bias Tool for Randomized Trials, version 2 (RoB 2)[18]. Five domains were assessed to obtain an indication of whether the study had either a low risk of bias, some concerns of bias, or a high risk of bias. The validated Methodological Index for Non-Randomized

Studies (MINORS) was used to assess the risk of bias in the non-randomized studies[19]. Using this tool, the studies were assessed for 12 items that were then scored as either 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate).

The assessment of the certainty of the body of evidence for outcomes was performed using the Grading of Recommendations Assessment, Development and Evaluations (GRADE) approach[20] by two independent reviewers (YHT and NBvB. The quality of the evidence was rated high, moderate, low, or very low for each quantitatively analyzed study outcome, after being potentially up- or downgraded based on factors as described by the GRADE working group system (e.g., downgrading quality of evidence due to inconsistency or inaccuracy of the results).

The clinical heterogeneity between the studies included in the quantitative analyses was systematically evaluated using the Clinical Diversity In Meta-analyses (CDIM) tool[21]. The clinical heterogeneity of each meta-analysis was measured on an ordinal scale based on four domains, i.e., setting diversity, population diversity, intervention diversity, and outcome diversity, with a total of 11 items. Each item was scored 0 (low diversity), 1 (moderate diversity or unknown), or 2 (high diversity) and assigned an equal weight, resulting in a total score of 0–22. A total score of 0–11 indicated low clinical heterogeneity, 12–18 indicated moderate clinical heterogeneity, and 19–22 indicated high clinical heterogeneity between the studies.

Effect measures and data synthesis

Inter-observer agreement, examined by Cohen's kappa statistic and the percentage of agreement, was calculated using IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA).

A summary effect estimate was calculated if two or more studies reported similar study outcomes[12]. If study subjects had been excluded from an analysis in the original study for reasons other than the exclusion criteria set by the current review (i.e., the excluded subjects would fit within the scope of the current review), and the outcome data were available for the excluded subjects, these subjects were included in the effect measures calculation.

Dichotomous variables were presented as events and totals, from which the odds ratio (OR) and 95% confidence interval (CI) were calculated. The Mantel–Haenszel fixed-effects method was used due to the limited number of events[12]. Studies with

zero events in both arms were included in the main meta-analysis with a reciprocal continuity correction of the opposite arm (i.e., correction = 1/(sample size of opposite arm))[22,23]. A sensitivity analysis using conventional methods, where studies with zero events in both arms were excluded, was also performed. Regarding the continuous variables suitable for quantitative analysis, the mean difference (MD) and corresponding 95% CI were calculated as effect measures[12]. If studies only reported the standard deviations (SDs) of the baseline and postoperative outcome scores, the SDs of the changes were estimated from the baseline measurements, with a correlation coefficient of 0.5[12,24]. The meta-analyses and forest plots were synthesized in R version 4.2.2 (R Core team; R Foundation for Statistical Computing, Vienna, Austria), using the *meta* package, version 6.1–0[25]. A random-effects model with the DerSimonian–Laird estimator[26] was used, based on the assumption that there was a high likelihood of clinical heterogeneity between the studies[27]. Sensitivity analyses were performed based on the study design (inclusion of only RCTs) and per diagnosis of the study participants (i.e., ID, DJD, or arthralgia).

As traditional meta-analyses are prone to type I errors (i.e., false-positive findings), additional trial sequential analyses (TSA) were performed[28]. The TSA, with a random-effects model (DerSimonian–Laird estimator), was performed using Trial Sequential Analysis Viewer version 0.9.5.10 Beta (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark)[29]. TSA was used to determine the required information size (RIS) (i.e., the sample size needed for the meta-analysis) of each outcome to provide an indication of the robustness of the conclusion from the meta-analysis. Statistical heterogeneity was considered substantial if I^2 was ≥50%[12]. A *P*-value <0.05 was considered statistically significant in all of the analyses.

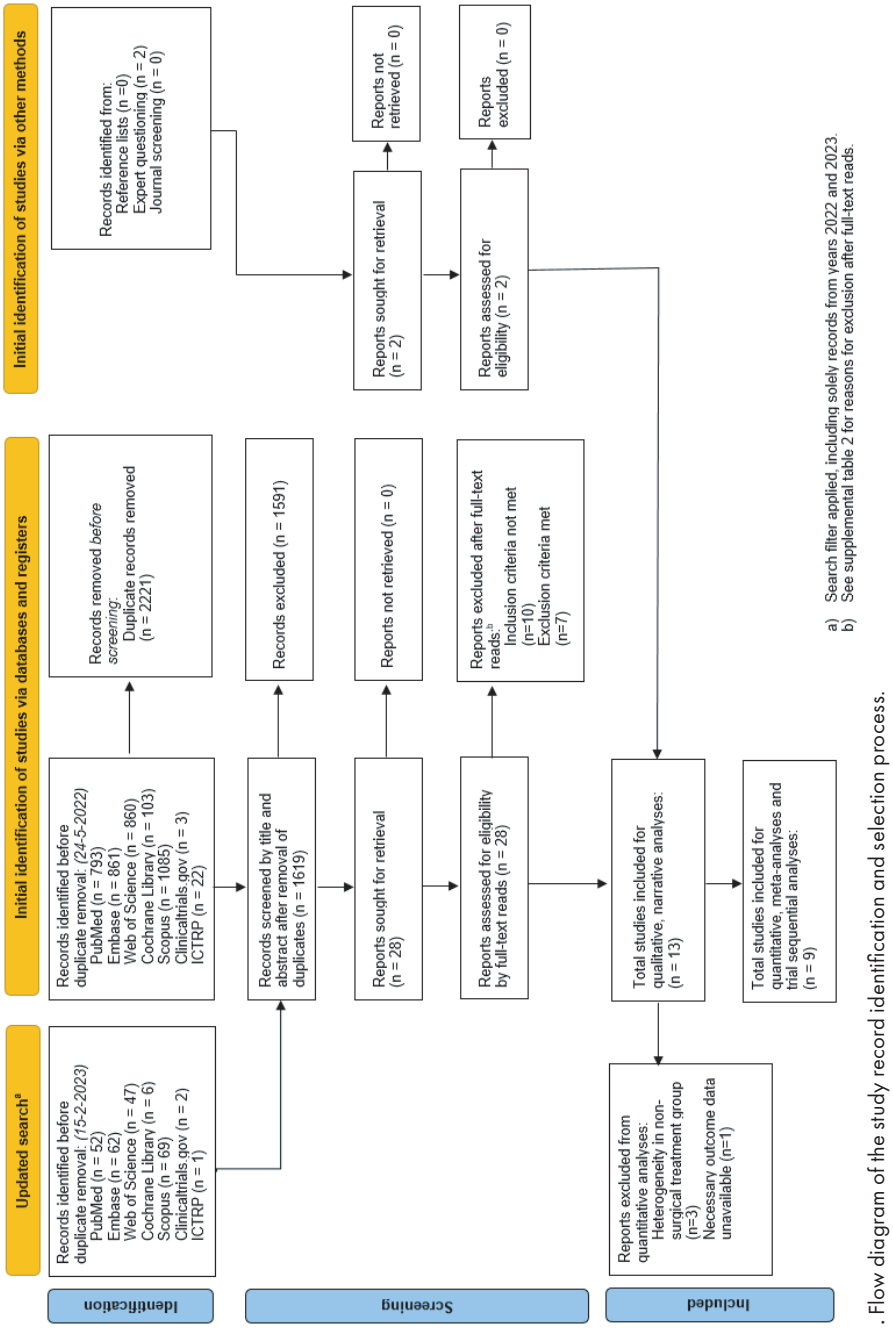

Figure 1. Flow diagram of the study record identification and selection process.

Results

Study selection

After the initial and updated search, a total of 1619 unique records were identified for title and abstract screening (**Figure 1**). Based on this screening, 28 records were selected for full-text reading. The inter-observer agreement was high (Cohen's kappa coefficient (κ) = 0.88; percentage of agreement = 99.6%). After the full-text assessment, 11 records were selected for inclusion[10,30–39] (κ = 1.00; percentage of agreement = 100%). Two additional records were identified after questioning the experts on the subject[9,11] ultimately leading to the inclusion of 13 studies in the qualitative review. Finally, nine studies were included in the quantitative analyses[9–11,30,33–37]. The third reviewer was not consulted in the study screening and selection process. **Appendix B** provides an overview of the records that were excluded after full-text reading, including the reasons. The agreement between the two reviewers regarding the data collection was 100%.

Study characteristics

From the 13 included studies, a total of 609 study participants were included in this review. One study compared arthroscopy with both arthrocentesis and conservative treatment[30], while the remaining studies compared arthroscopy with either arthrocentesis or conservative treatment.

Studies involving arthroscopy versus arthrocentesis

Ten studies compared arthroscopy and arthrocentesis[9–11,30,32–37], and of these, three were RCTs[11,34,35], two were CCTs[10,32] (one study reported two groups without statistically comparing them[32]), and five were retrospective cohort studies with a control group[9,30,33,36,37] (**Table 1a**). The studies were published between 1995 and 2023 and included a total of 430 patients, the majority of whom were female. Four studies involved AS[11,30,32,33] and six studies reported ALL[9,10,34–37] as the intervention. None of the studies reported the use of level III AS. The studies reported results for one or several postoperative follow-up time-points, ranging from 1 day to 5 years. One study included patients diagnosed with either ID or DJD[9], while the other studies included patients with a diagnosis of ID. Among the studies, the arthroscopic procedures varied to a greater extent than the arthrocentesis procedures (**Table 1a**). The preoperative and postoperative treatment regimens varied considerably between the studies (**Table 2a**).

Studies involving arthroscopy versus conservative treatments

Four studies involved conservative non-surgical treatment regimens as the control group[30,31,38,39], of which three studies were RCTs[31,38,39] and one study was a retrospective cohort study with a control group (**Table 1b**)[30]. The studies, published between 1993 and 2014, included a total of 204 patients, the majority of whom were female. Three studies reported on AS [30,38,39] and one study on ALL[31] as the intervention. One study reported the use of level III AS[39]. The studies recorded one or several postoperative follow-up time-points, ranging from 1 month to 5 years. One study included patients with movement restricting arthralgia[38], while the other studies included patients with a diagnosis of ID. There was a high heterogeneity in the conservative treatment procedures between the studies (**Table 1b**). The preoperative and postoperative treatment regimens varied considerably between the studies (**Table 2b**).

Table 1a. Characteristics of included studies involving arthroscopy versus arthrocentesis.

Studies involving arthroscopy versus arthrocentesis											
						Intervention			Control		
Author (year)	Study design	Nº of patients intervention/ control	% of females intervention/ control	Mean age (SD) intervention/ control	Study population	Therapy type (lavage fluid)	Co-interventions	Anesthesia	Therapy type (lavage fluid)	Co-interventions	Anesthesia
Arthroscopic surgery as intervention											
Murakami et al. (1995)[30]	Retro.	25/20	92/85	33(17)/ 31(14)	ID (Wilkes 3 closed lock)	ALL + ALCR (NA)[a]	C	GA	Arthrocentesis (Ringer)[a]	C	LA
Sanroman (2004)[32]	CCT	16/8	NA	NA	ID (Closed lock)	ALL + coagulation (NA)[a]	SH	GA	Arthrocentesis (Ringer)[a]	SH	LA
Hobeich et al. (2017)[33]	Retro.	28/20	NA	31(7)/31(8)	ID (ADDwoR)	ALL + coagulation (Ringer)[a]	SH	GA	Arthrocentesis (Ringer)[a]	SH	LA + IVS
Atteya et al. (2020)[11]	RCT	20/20	95/80	38(11)/ 32(9)	ID (Wilkes 2-3)	ALL + ALCR + coagulation (Ringer)[a]	SH	GA	Arthrocentesis (Ringer)[a]	SH	LA
Arthroscopic lysis and lavage as intervention											
Fridrich et al. (1996)[34]	RCT	11/8	100/100	32(11)/ 28(9)	ID (ADDwR + ADDwoR)	ALL (Ringer)[a]	C	GA	Arthrocentesis (Ringer)[a]	C	IVS
Goudot et al. (2000)[35]	RCT	33/29	NA	NA	ID (ADDwR + ADDwoR)	ALL (Ringer)[b]	-	GA	Arthrocentesis (Saline)[a]	-	LA

Table 1a. Characteristics of included studies involving arthroscopy versus arthrocentesis. *Continued*

Studies involving arthroscopy versus arthrocentesis											
						Intervention			Control		
Author (year)	Study design	N° of patients intervention/ control	% of females intervention/ control	Mean age (SD) intervention/ control	Study population	Therapy type (lavage fluid)	Co-interventions	Anesthesia	Therapy type (lavage fluid)	Co-interventions	Anesthesia
Tan et al. (2012)[36]	Retro.	11/9	73/78	40(15)/ 28(9)	ID (Closed lock + painful click)	ALL (Saline)[b]	-	GA	Arthrocentesis (Saline)[a]	-	LA
Xu et al. (2013)[37]	Retro.	37/41	78/73	36(NA/ 38(NA)	ID (ADD)	ALL (Ringer)[a]	SH	LA	Arthrocentesis (Ringer)[a]	SH	LA
Rajpoot et al. (2021)[10]	CCT	15/15	67/80	NA	ID (Wilkes 2-5)	ALL (Ringer)[b]	-	GA	Arthrocentesis (Ringer)[b]	-	LA
Talaat et al. (2022)[9]	Retro.	32/32	75/59	NA	ID (ADDwoR w/ lim. MO) + DJD	ALL (Saline)[b]	SH	GA	Arthrocentesis (Saline)[b]	SH	LA

Abbr.: Retro. Retrospective cohort study with control group; CCT Prospective non-randomized controlled trial; RCT Randomized controlled trial; SD standard deviation; ID internal derangement; ADDwoR anterior disc displacement without reduction; ADDwR anterior disc displacement with reduction; ADD anterior disc displacement; ADDwoR w/lim. MO anterior disc displacement without reduction with limited mouth opening; DJD degenerative joint disease; ALL arthroscopic lysis and lavage; ALCR anterolateral capsular release; C corticosteroids, SH sodium hyaluronate; GA general anesthesia, LA local anesthesia, IVS intravenous sedation; NA not available. [a] Dual portal (arthroscopy) or dual puncture (arthrocentesis) technique. [b]Single portal (arthroscopy) or single puncture (arthrocentesis) technique.

Table 1b. Characteristics of included studies involving arthroscopy versus conservative treatment.

Studies involving arthroscopy versus conservative treatment										
						Intervention			Control	
Author (year)	Study design	Nº of patients intervention/ control	% of females intervention/ control	Mean age (SD) intervention/ control	Study population	Therapy type (lavage fluid)	Co-interventions	Anesthesia	Conservative treatment technique	
Arthroscopic surgery as intervention										
Stegenga et al. (1993)[38]	RCT	9/12	NA	NA	Arthralgia	ALL + ALCR + coagulation (saline)[a]	C + AB	GA	Self-exercise + physiotherapy	
Murakami et al. (1995)[30]	Retro.	25/63	92/76	33(17)/30(16)	ID (Wilkes 3 closed lock)	ALL + ALCR (NA)[a]	C	GA	1-2 weeks NSAIDs and muscle relaxants + physiotherapy + 12 weeks splint	
McNamara et al. (1996)[39]	RCT	10/10	NA	NA	ID (ADD)	ALL + ALCR + coagulation + discopexy (NA)[a]	NA	GA	Physiotherapy + splint	
Arthroscopic lysis and lavage as intervention										
Schiffman et al. (2014)[31]	RCT	23/29	85/90	32(2)/34(2)	ID (ADDwoR)	ALL (Ringer)[b]	C	GA	Self-exercise + 6 days methylprednisolone + 6 weeks NSAIDs and muscle relaxants	
		23/23	85/100	32(2)/30(2)					Abovementioned management + physiotherapy + cognitive behavioral-therapy + splint	

Abbr.: Retro. Retrospective cohort study with control group; RCT Randomized controlled trial; SD standard deviation; ID internal derangement; ADDwoR anterior disc displacement without reduction; ALL arthroscopic lysis and lavage; ALCR anterolateral capsular release; C corticosteroids, AB antibiotics; GA general anesthesia; NSAIDs non-steroidal anti-inflammatory drugs; NA not available. [a] Dual portal (arthroscopy) or dual puncture (arthrocentesis) technique. [b] Single portal (arthroscopy) or single puncture (arthrocentesis) technique.

Table 2a. Pre- and post-operative treatment regimens of included studies involving arthroscopy versus arthrocentesis.

Author (year)	Study design	Pre-operative treatment	Post-operative treatment
Arthroscopic surgery as intervention			
Murakami et al. (1995)[30]	Retro.	Arthroscopy group: none or after 1-2 weeks of NSAIDs and muscle relaxants, physiotherapy and up to 12 weeks splint. Arthrocentesis group: none	Self-exercise
Sanroman (2004)[32]	CCT	4-6 months of soft diet advice, NSAIDs, physiotherapy and splint	Self-exercise, 2 weeks of NSAIDs and splint
Hobeich et al. (2017)[33]	Retro.	Splint	Self-exercise, 2 weeks of NSAIDs and muscle relaxants
Atteya et al. (2020)[11]	RCT	6 months of conservative treatment (non-specified).	Self-exercise, 2 months of soft diet advice, 3 days of NSAIDs and antibiotics
Arthroscopic lysis and lavage as intervention			
Fridrich et al. (1996)[34]	RCT	Soft diet advice, NSAIDs, ice therapy, physiotherapy and splint	1 week of soft diet advice, 4 weeks of NSAIDs, physiotherapy and splints
Goudot et al. (2000)[35]	RCT	6 months of self-exercise, psychologic support, physiotherapy and splint	Self-exercise, 2 weeks of soft diet advice and physiotherapy
Tan et al. (2012)[36]	Retro.	3-8 weeks of NSAIDs and muscle relaxants and splint	Soft diet advice, NSAIDs, physiotherapy and splint
Xu et al. (2013)[37]	Retro.	NA	NA
Rajpoot et al. (2021)[10]	CCT	NA	Self-exercise, 2 weeks of soft diet advice, analgesics, antibiotics
Talaat et al. (2022)[9]	Retro.	2 months of soft diet advice, NSAIDs, physiotherapy and splint.	Self-exercise, 3 days of NSAIDs and splint

Abbr.: Retro. Retrospective cohort study with control group; CCT Prospective non-randomized controlled trial; RCT Randomized controlled trial; NSAIDs non-steroidal anti-inflammatory drugs; NA not available.

Table 2b. Pre- and post-operative treatment regimens of included studies involving arthroscopy versus conservative treatment.

Author (year)	Study design	Pre-operative treatment	Post-operative treatment
Arthroscopic surgery as intervention			
Stegenga et al. (1993)[38]	RCT	Explanation, self-exercise, soft diet advice	Arthroscopy group: physiotherapy, ice massage and self-exercises
Murakami et al. (1995)[30]	Retro.	Arthroscopy group: none or after 1-2 weeks of NSAIDs and muscle relaxants, physiotherapy and up to 12 weeks of splint use	Arthroscopy group: self-exercises
McNamara et al. (1996)[39]	RCT	12 months of explanations, self-exercise, soft diet advice and medication (not further specified)	Arthroscopy group: conservative treatment (physiotherapy and splint)
Arthroscopic lysis and lavage as intervention			
Schiffman et al. (2014)[31]	RCT	Arthroscopy group: physiotherapy and cognitive behavioral therapy	Arthroscopy group: medical management (education, self-exercise, methylprednisolone, NSAIDs, muscle relaxants) and physical rehabilitation (physiotherapy, cognitive behavioral therapy, splint)

Abbr.: Retro. Retrospective cohort study with control group; RCT Randomized controlled trial; NSAIDs non-steroidal anti-inflammatory drugs.

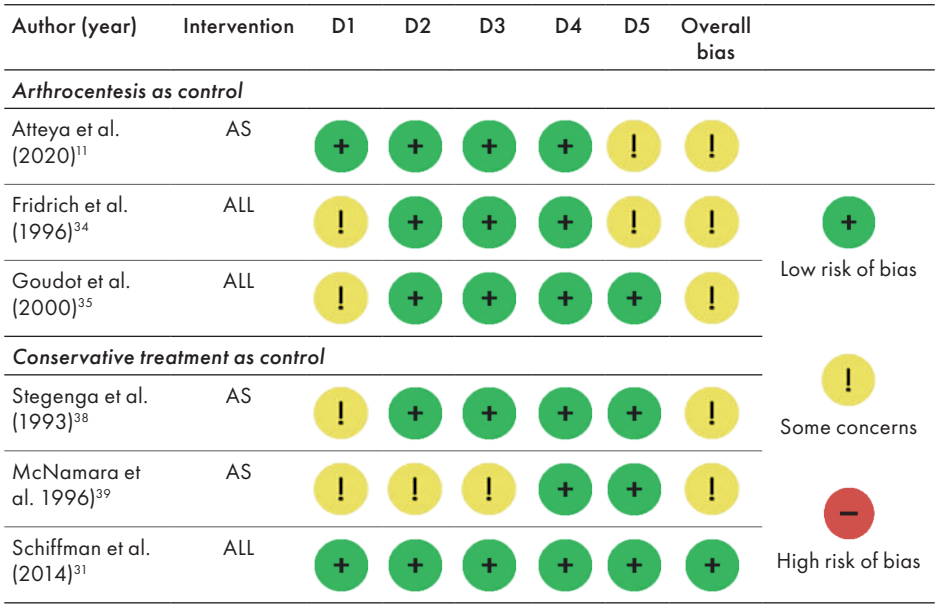

Figure 2. Risk of bias assessment of randomized controlled trials using the Cochrane Risk of Bias Tool 2. D1 Randomization process; D2 Deviations from intended interventions; D3 Missing outcome data; D4 Measurement of the outcome result; D5 Selection of the reported results.

Risk of bias in the studies

The risk of bias assessment for the six RCTs using the RoB 2 tool resulted in 'some concerns' as the overall judgement for five studies[11,34,35,38,39], primarily due to the lack of information regarding concealment of the allocation sequence, deviations from the intended interventions, and the statistical analyses employed. One study had a low risk of bias as the overall judgement[31]. There was no 'high risk of bias' assessment for any of the domains (**Figure 2**). MINORS was used to assess the risk of bias of the seven CCTs and retrospective cohort studies[9,10,30,32,33,36,37]. The score for each study ranged from 13 to 16 on a scale of 0–24 (**Figure 3**).

Author (year)	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the study aim	Unbiased assessment of the study endpoint	Follow-up period appropriate to study aim	Lost to follow-up <5%	Prospective calculation of study size	Adequate control group	Contemporary groups	Baseline equivalence	Adequate statistical analysis	Total
Arthroscopic surgery as intervention													
Murakamiet al. (1995)[30]	2	2	0	2	0	2	2	0	2	0	2	0	14
Sanroman (2004)[32]	2	0	2	2	0	2	2	0	2	2	0	0	14
Hobeich et al. (2007)[33]	2	1	0	2	0	2	1	0	2	2	1	0	13
Arthroscopic lysis and lavage as intervention													
Tan et al. (2012)[36]	2	2	0	2	0	2	2	0	2	2	1	0	15
Xu et al. (2013)[37]	2	2	0	2	0	2	2	0	2	0	1	0	13
Rajpoot et al. (2021)[10]	2	1	2	2	0	2	2	0	2	2	1	0	16
Talaat et al. (2022)[9]	2	2	0	2	0	2	1	0	2	2	1	2	16

Figure 3. Risk of Bias assessment of non-randomized studies using the Methodological Index for Non-randomized Studies. 0 not reported; 1 reported but inadequate; 2 reported and adequate.

Primary outcome — pain

None of the studies made a distinction between the pain score during mandibular movement/function and when at rest, therefore general pain VAS scores were used to represent the main study outcome.

Studies comparing arthroscopy versus arthrocentesis

All 10 studies involving arthroscopy and arthrocentesis investigated the pain VAS scores using a numerical scale (**Appendix C.1**)[9–11,30,32–37]. The pain scores improved significantly at follow-up compared to the scores at baseline, in both groups in all 10 studies.

One study involving AS and arthrocentesis reported an improvement in pain over time for both groups, but the study outcomes were only reported in a graphical manner with no between-group comparisons, therefore not allowing qualitative or quantitative analysis in the context of this study[32]. Of the remaining three studies comparing AS and arthrocentesis, one reported short-term results for pain (1 month), with no statistically significant difference between the two groups[11]. All three studies reported intermediate-term results for pain (range 6–24 months), with no significant difference between the groups after pooling the data (MD 2.2, 95% CI −15.4 to 19.7; I^2 = 87%, very low quality; **Figure 4A**)[11,30,33]. None of the studies comparing AS and arthrocentesis reported long-term results for pain.

Among the six studies comparing ALL and arthrocentesis, three reported short-term results for pain (range 1–3 months), with no significant difference between the groups after pooling the data (MD 2.8, 95% CI −8.9 to 14.6; I^2 = 61%, very low quality; **Figure 4B**)[10,36,37]. Of note, patients who were excluded from one study[36] based on criteria other than those of the current review were included in this meta-analysis. Two studies reported intermediate-term results for pain (range 6–12 months), with no significant difference between the groups after pooling the data (MD −4.4, 95% CI −16.0 to 7.2; I^2 = 31%, very low quality; **Figure 4C**)[10,35]. One study comparing ALL and arthrocentesis reported long-term results for pain (60 months), with no significant difference between the two groups[9].

Sensitivity analyses including only RCTs or based on the diagnosis (only possible for ID) did not yield any differences in outcome when compared to the conventional meta-analyses.

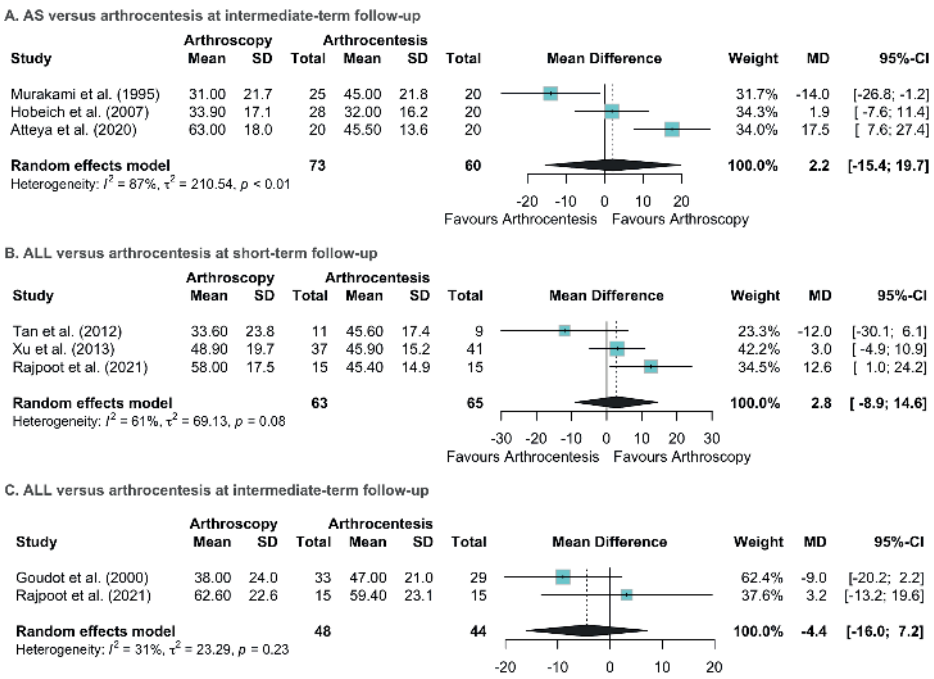

Figure 4. Pooled results for the reduction in VAS pain score in the studies comparing arthroscopy versus arthrocentesis. In all studies, the study participants were treated for a type of internal derangement. Trial sequential analysis did not support the conclusions drawn in each of the three meta-analyses regarding the reduction in pain score, indicating potentially false neutral results. Abbr.: VAS visual analog scale; AS arthroscopic surgery; ALL arthroscopic lysis and lavage; SD standard deviation; MD mean difference; 95% CI 95% confidence interval.

Studies comparing arthroscopy versus conservative treatments

Out of the four studies comparing arthroscopy with conservative treatments, three investigated pain VAS scores using a numerical scale (**Appendix C.2**)[30,38,39]. Quantitative analysis was considered unfeasible due to the limited amount of suitable data.

Among the studies comparing AS and conservative treatment, two investigated pain in the short term (range 1–3 months)[38,39]. Both of these studies reported no statistically significant difference between the groups. Three studies on AS versus conservative treatment reported intermediate-term pain results (range 6–12 months), with no significant difference between the groups[30,38,39]. None of the studies that compared AS and conservative treatments reported any long-term pain results.

Only one study compared ALL with conservative treatments; this study found no statistical difference between ALL and medical management/ non-surgical rehabilitation regarding pain intensity and frequency over the course of 60 months, however the outcomes were measured on a dichotomous scale[31].

All of the studies reported a significant reduction in pain over time for both groups.

Secondary outcomes

Studies comparing arthroscopy versus arthrocentesis

Maximum mouth opening

All 10 studies comparing arthroscopy and arthrocentesis reported the improvement in MMO (**Appendix C.1**)[9–11,30,32–37]. A significant improvement in MMO was seen in both groups in all 10 studies.

One study on AS and arthrocentesis depicted MMO only in a graphical manner without a between-groups comparison, therefore not allowing analysis in the context of this study[32]. None of the AS and arthrocentesis comparative studies reported short-term results for MMO. Three studies reported intermediate-term results for MMO (range 6–24 months), which showed no significant difference between the groups after pooling the data (MD 1.1, 95% CI −1.1 to 3.2; I^2 = 0%, very low quality; **Figure 5A**)[11,30,33]. None of the studies comparing AS and arthrocentesis reported long-term results for MMO.

Of the studies comparing ALL and arthrocentesis, three reported short-term results for MMO (range 1–3 months), with no significant difference between the groups after pooling the data (MD −1.4, 95% CI −8.1 to 5.3; I^2 = 89%, very low quality; **Figure 5B**)[10,36,37]. Of note, patients excluded from one study[36] based on criteria other than those of the current review were included in this meta-analysis. Three studies reported intermediate-term results for MMO (range 6–24 months), with a significant difference favoring arthroscopy after pooling the data (MD 4.9, 95% CI 2.7 to 7.1; I^2 = 18%, low quality; **Figure 5C**)[10,34,35]. One study comparing ALL and arthrocentesis reported long-term results for MMO (60 months), with no significant difference between the two groups[9].

Sensitivity analyses including only RCTs or based on the diagnosis (only possible for ID) did not yield any differences in outcome compared to the conventional meta-analyses.

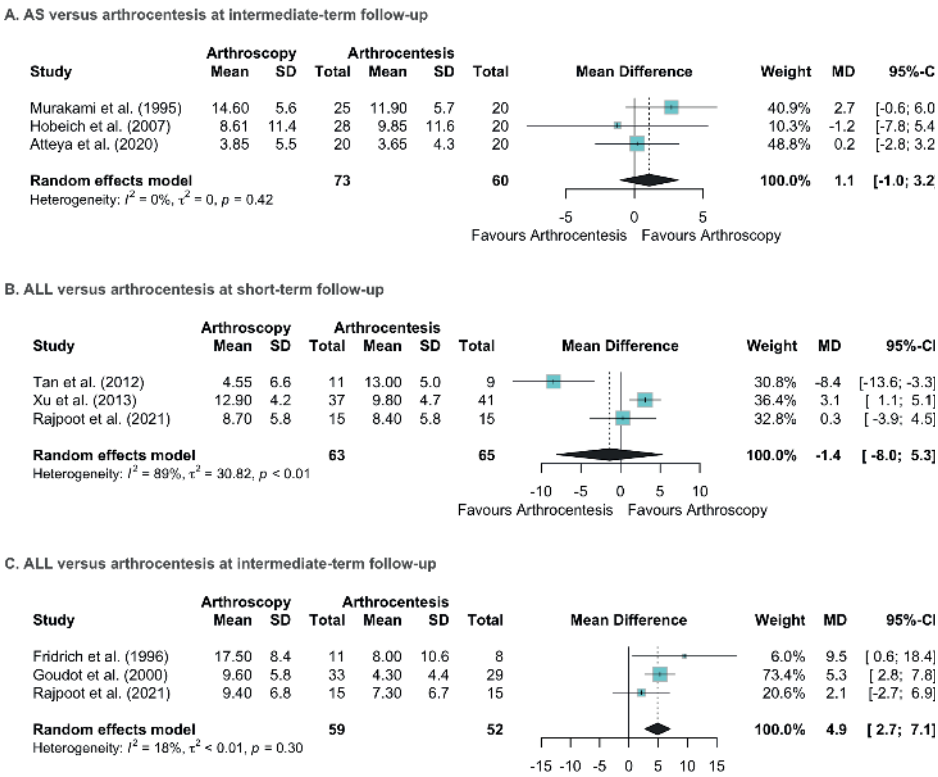

Figure 5. Pooled results for the improvement in MMO in the studies comparing arthroscopy versus arthrocentesis. In all studies, the study participants were treated for a type of internal derangement. Trial sequential analysis did not support the conclusions drawn in the meta-analyses regarding the improvement in MMO for AS versus arthrocentesis at intermediate-term follow-up or ALL versus arthrocentesis at short-term follow-up, indicating potentially false neutral results (A, B). However, trial sequential analysis supported the conclusions drawn in the meta-analysis involving ALL versus arthrocentesis at intermediate-term follow-up (C). Abbr.: MMO maximum mouth opening; AS arthroscopic surgery; ALL arthroscopic lysis and lavage; SD standard deviation; MD mean difference; 95% CI 95% confidence interval.

Mandibular function

Three studies with arthrocentesis as the control group reported on mandibular function, each using a different measurement tool (**Appendix C.1**)[9,30,34]. One study on AS reported the jaw function score (numerical scale of 0–20) and dietary evaluation score (numerical scale of 0–72) at intermediate-term follow-up (6 months)[30]. AS improved the dietary evaluation score significantly, but not the jaw function score. Arthrocentesis, on the other hand, improved both scores at the follow-up. The second study, which was on ALL, scored disability in the long term (5 years) on a categorical scale from 0 to 6[9]. In that study, both treatments improved the disability scores significantly. The third study, also involving ALL, looked at the

intermediate-term chewing ability (6–24 months) using a 0–100 numerical scale and found that both treatments significantly improved chewing ability at the follow-up[34]. All three studies reported no significant difference between arthroscopy and arthrocentesis.

Joint blocks and noises

Regarding joint blocks and noises, only one study comparing ALL and arthrocentesis described the subjective intensity of joint noises at intermediate-term follow-up (6–24 months) based on a 0–100 numerical scale (**Appendix C.1**)[34]. Both treatments decreased the subjective intensity of the joint noises, with no statistically significant difference between them.

Mandibular range of motion

Three studies reported the mandibular range of motion (**Appendix C.1**)[10,32,37]. One study on AS reported maximum contralateral and protrusive mandibular movements solely in a graphical manner, therefore not allowing further analysis[32]. The second study reported superior efficacy of ALL over arthrocentesis (MD 1.1 mm) for the improvement in contralateral movement at short-term follow-up (3 months)[37]. The third study reported a superior effect of ALL over arthrocentesis for the improvement of left lateral (MD 1.0 mm), right lateral (MD 0.7 mm), and protrusive movement (MD 0.3 mm) at intermediate-term follow-up (6 months)[10]. All of the studies reported an improvement in mandibular range of motion over time for both groups.

Safety

The complication rates for both treatments were described in seven studies, one involving AS[11] and six involving ALL[9,10,34–37] as the intervention. One study looked at safety per complication type instead of per study participant[10]. In that study, transient facial nerve paralysis, fluid extravasation, and bleeding occurred in 66.6%, 46.6%, and 26.6%, respectively, of the participants in the arthrocentesis group and 0.0%, 26.6%, and 40.0%, respectively, of those in the ALL group[10]. The other six studies reported the presence of complications per study participant, which ranged between 0% and 6.1% among the treated participants in the arthroscopy group and between 0% and 6.9% in the arthrocentesis group. The study comparing AS and arthrocentesis reported no complications in either of the groups. After pooling the data of the five studies involving ALL versus arthrocentesis, there was no significant difference between the two groups (OR 1.2, 95% CI 0.3 to 4.5; I^2 = 0%, very low quality; **Figure 6A**)[9,34–37]. A sensitivity analysis, in which studies with zero events in both arms were excluded, also resulted in no significant difference between the

groups regarding the complication rate (OR 1.2, 95% CI 0.3 to 4.7; I^2 = 0%, very low quality; **Figure 6B**).

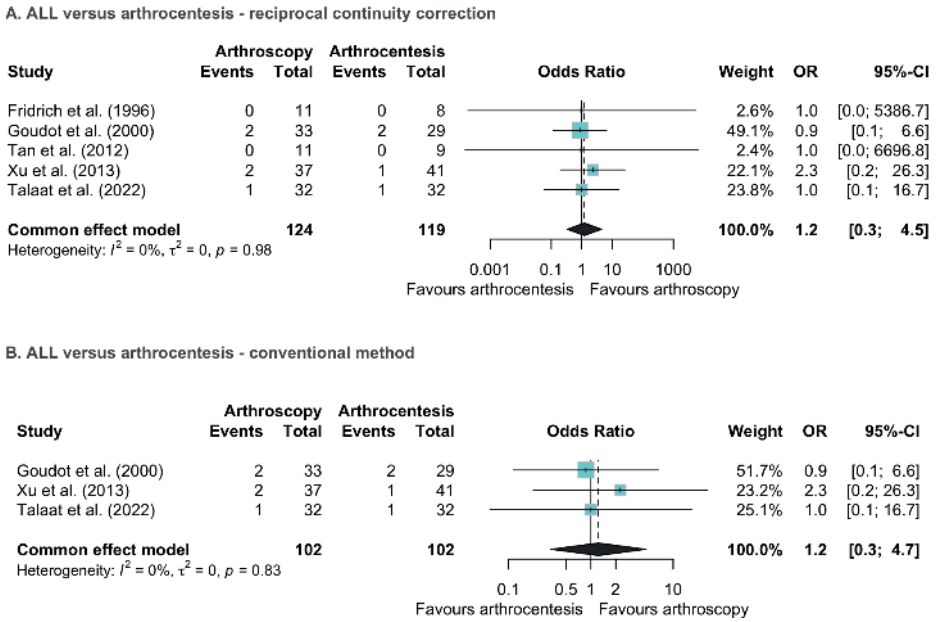

Figure 6. Pooled results for the complication rate in the studies comparing arthroscopy versus arthrocentesis. Study participants were treated for a type of internal derangement in all studies except the study by Talaat et al.[9], in which participants suffering from internal derangement or osteoarthritis were selected. A sensitivity analysis in which this study was excluded showed no influence on the results. Trial sequential analysis did not support the conclusion drawn from the meta-analysis with a reciprocal continuity correction regarding the complication rate, indicating potentially false neutral results (A). Abbr.: ALL, arthroscopic lysis and lavage; OR, odds ratio; 95% CI, 95% confidence interval.

Quality of life and costs/ cost-effectiveness

None of the studies that compared arthroscopy with arthrocentesis reported the effect of either treatment on quality of life or the costs/cost-effectiveness of the treatments.

Studies comparing arthroscopy versus conservative treatments

Maximum mouth opening

A quantitative analysis of the secondary outcomes was not performed for studies using conservative treatments as the control group, due to a lack of suitable data. All four studies comparing arthroscopy versus conservative treatment included MMO as an outcome (**Appendix C.2**)[30,31,38,39]. Among the studies involving AS, one reported a reduced MMO in the AS group and improved MMO in the conservative treatment group at the short-term and intermediate-term follow-ups (3 and 12 months) based

on analysis of variance with repeated measures[39]. The other two studies involving AS and conservative treatment reported an improvement in MMO for both groups, with no between-group difference in the short term (1 month)[38] or intermediate term (6 months)[30,38]. The only study with ALL as the intervention reported a significant improvement in MMO over the long-term follow-up period (60 months) for the ALL, physical rehabilitation, and medical management groups, but with no difference between the three groups[31].

Mandibular function

All four studies comparing arthroscopy with conservative treatments reported mandibular function, but used different measurement tools (**Appendix C.2**). Of the three studies involving AS, one used the Helkimo Clinical Dysfunction Index score[40] (on a numerical scale of 0–25) at the short-term and intermediate-term follow-ups (3 and 12 months)[39]. Another noted the categorical global pain impact scores[41] (range 0–5) and the converted Mandibular Functional Impairment Questionnaire (MFIQ) scores[16] (range 1–3) at short-term and intermediate-term follow-up (1 and 6 months)[38]. The third study reported the Activities of Daily Living scores (range 0–72) and jaw function scores (range 0–20) at intermediate follow-up (6 months)[30]. The study involving ALL reported mandibular function impairment as a dichotomous outcome, over a period of 60 months[31]. In all of the studies, a significant treatment effect was seen over time, with no between-group differences.

Joint blocks and noises

Only one study comparing arthroscopy and conservative treatment reported on joint blocks and noises (**Appendix C.2**). ALL and conservative treatments did not improve joint clicking or joint crepitus over time and there was no between-groups difference over a 60-month period[31]. The same study investigated mandibular range of motion and reported that lateral and protrusive movements improved after both ALL and conservative treatments over a period of 60 months (**Appendix C.2**)[31]. There were no differences between the groups.

Quality of life

One study involving AS reported quality of life using a total well-being score, based on the West Haven–Yale Multidimensional Pain Inventory[42] and the General Health Questionnaire[43], at short-term and intermediate-term follow-ups (1 and 6 months) (**Appendix C.2**)[38]. There was no significant difference between the groups or improvement over time.

Complication rates

None of the studies comparing arthroscopy and conservative treatments reported the safety or complication rates of the procedures (**Appendix C.2**).

Costs/ cost-effectiveness

One study looked at the costs of the treatments based on the average costs incurred per study participant (**Appendix C.2**)[31]. Medical management resulted in the lowest average costs ($1385, range $410–$3555), followed by rehabilitation ($2379, range $1375–$5240) and then by ALL ($7890, range $5830–$15,940)[31].

Certainty of the evidence

Assessment of the certainty of the evidence using the GRADE approach resulted in a very low quality of evidence for the outcomes improvement in pain and complication rates. Regarding the improvement in MMO, a very low quality of evidence judgement was obtained for the outcomes of AS versus arthrocentesis at intermediate-term follow-up and ALL versus arthrocentesis at short-term follow-up. For ALL versus arthrocentesis at intermediate-term follow-up, a low quality of evidence judgement was obtained. All outcomes had an initial assessment of low quality of evidence due to the inclusion of non-randomized studies. Downgrading occurred due to inconsistency or imprecision (**Table 3**).

Table 3. Summary of findings table (GRADE assessment).

Outcome	**Arthroscopy type**	**Follow-up term (months)**	MD (95% CI) between interventions			Nº of participants (studies)	Certainty of the evidence (GRADE)
Pain reduction using VAS (0-100mm, higher is worse)	AS	Intermediate (6-24)	2.2 (-15.4;19.7)			133 (3)	⊕◯◯◯ Very low[a,b]
	ALL	Short (1-3)	2.8 (-8.9;14.6)			128 (3)	⊕◯◯◯ Very low[a,b]
	ALL	Intermediate (6-12)	-4.4 (16.0;7.2)			92 (2)	⊕◯◯◯ Very low[b]
MMO improvement (in mm)	AS	Intermediate (6-24)	1.1 (-1.0;3.2)			133 (3)	⊕◯◯◯ Very low[b]
	ALL	Short (1-3)	-1.4 (-8.0;5.3)			128 (3)	⊕◯◯◯ Very low[a,b]
	ALL	Intermediate (6-12)	4.9 (2.7;7.1)			111 (3)	⊕⊕◯◯ Low
Outcome	**Arthroscopy type**	**Statistical method**	OR (95% CI)	Illustrative comparative risk (95% CI)		Nº of participants (studies)	Certainty of the evidence (GRADE)
				Assumed risk - AC	Comparative risk - ALL		
Complication rates	ALL	Reciprocal Continuity Correction	1.2 (0.3;4.5)	34 per 1000	41 per 1000 (11;137)	243 (5)	⊕◯◯◯ Very low[b]
	ALL	Conventional	1.2 (0.3;4.7)	39 per 1000	47 per 1000 (12;160)	204 (3)	⊕◯◯◯ Very low[b]

Abbr.: VAS visual analog scale; CI confidence interval; MD difference in means; VAS visual analog scale; AS arthroscopic surgery; ALL arthroscopic lysis and lavage; MMO maximum mouth opening; OR odds ratio; AC arthrocentesis. [a] Downgraded one level due to inconsistency: unexplained heterogeneity that were not accounted for in the analyses ($I^2 > 50\%$). [b] Downgraded one level due to imprecision: sample size lower than required/ optimal information size.

The assessment of clinical diversity among the studies, using the CDIM tool[21], resulted in a judgement of low clinical heterogeneity for all of the meta-analyses performed for the outcomes pain by VAS score (CDIM score range 9–11) and MMO (CDIM score range 8–10) (**Appendix D.1-D.6**). The clinical diversity among the studies in the meta-analysis regarding safety (complication rate) was moderate, mainly due to the heterogeneity between the study intervention group treatments and the control group treatments (CDIM score 12) (**Appendix D.7**).

TSA was performed only for the study outcomes with pooled data, hence only for those studies that had compared arthroscopy with arthrocentesis. Regarding pain on a VAS, the RIS (i.e., the sample size needed in the meta-analysis) was not reached and the conventional and O'Brien–Fleming boundaries were not crossed in any of the three meta-analyses (AS vs arthrocentesis at intermediate-term follow-up, ALL versus arthrocentesis at short-term follow-up, and ALL versus arthrocentesis at intermediate-term follow-up) (**Appendix E**). Therefore, TSA indicates that the current available evidence from these meta-analyses may be inconclusive due to potential false neutral outcomes. For MMO, TSA did not support the conclusions from the meta-analyses involving AS versus arthrocentesis at intermediate-term follow-up and ALL versus arthrocentesis at short-term follow-up, since the RIS was not attained and the boundaries were not crossed (**Appendix E**). However, the RIS was attained and the boundaries were crossed for the meta-analysis involving ALL versus arthrocentesis on MMO at intermediate-term follow-up (**Appendix E**). For this analysis, TSA supports the conclusion that ALL may be superior to arthrocentesis in improving MMO. Finally, TSA did not support the conclusions drawn from the meta-analysis regarding safety (complication rates) (**Appendix E**).

Discussion

The aim of this systematic review was to compare the efficacy and feasibility of two arthroscopic techniques (AS and ALL) with arthrocentesis and also with conservative treatment regimens for TMJ disorders. AS at intermediate-term follow-up and ALL at short-term and intermediate-term follow-ups were equally efficient to arthrocentesis at reducing pain. Additionally, AS at intermediate-term follow-up and ALL at short-term follow-up were equally efficient to arthrocentesis at improving MMO, but ALL was superior to arthrocentesis with regard to the improvement in MMO at intermediate-term follow-up. TSA only supported the conclusion that ALL may be superior to arthrocentesis in improving MMO in the intermediate term. There was no difference in complication rates between the procedures. The data regarding

mandibular function, joint blocks and noises, mandibular range of motion, quality of life, and costs/cost-effectiveness were too heterogeneous or scarce to draw any conclusions from. Only a limited number of studies compared arthroscopy with conservative treatment regimens. Due to the high heterogeneity between the conservative treatment methods used in these studies, the performance of meta-analyses was considered inappropriate.

The finding that arthroscopy and arthrocentesis are equally efficient at reducing pain is in accordance with the notion that joint lavage facilitates the removal of the proinflammatory cytokines and degradation products[44,45] that contribute to synovitis[46,47]. Synovitis, in turn, has been found to be associated with the intensity of pain experienced by patients[48]. Hence, the observed similarity in pain reduction between the procedures suggests that both interventions have equal potential in alleviating pain through the removal of inflammatory mediators from the joint space. Two recent studies found that an additional subsynovial corticosteroid injection during TMJ arthroscopy is more effective at alleviating pain when compared to no injection[49,50]. It should be noted that none of the studies included in the current review performed this procedure. Subsynovial injections cannot be performed during arthrocentesis as this requires direct visualization of the inflamed tissues. This highlights the potential advantages of arthroscopy over arthrocentesis in providing additional therapeutic options. Further research is warranted to establish the efficacy of co-interventions during arthroscopy.

In TMJ disorders, limited mouth opening is partly attributed to the formation of intra-articular adhesions[51]. Since arthroscopy allows direct visualization of the joint, a more targeted lysis of any intra-articular adhesions is possible. This could explain why the results indicate a superiority of ALL over arthrocentesis for the improvement in MMO at intermediate-term follow-up. Surprisingly, AS did not lead to a better improvement in MMO, while ALL did at intermediate-term follow-up. It is hypothesized that during electrocautery, a procedure that is only possible during AS, thermal shrinkage of the intra-articular tissue may occur, leading to less improvement or even a reduction in MMO.

The findings of this study present a general tendency that patients with TMJ disorders experience a reduction in clinical symptoms over time regardless of the treatment received. This finding is in line with numerous non-comparative reports in the literature suggesting beneficial effects of arthroscopy[52–54], arthrocentesis[55,56], and conservative treatments[57,58] on symptom reduction based on pre- and post-treatment

differences. However, in a significant proportion of patients, TMD symptoms have a propensity to decrease in severity or to resolve on their own over time[59,60]. This, therefore, emphasizes the need to conduct comparative studies and analyze them systematically, in order to evaluate the 'true' therapeutic effects of the different treatment modalities. The current study focused exclusively on comparative studies involving arthroscopy. Despite the fact that several studies have compared arthrocentesis with conservative treatments[4–6], it was considered beyond the scope of the current review to assess such studies systematically.

The studies included in this review examined populations with various conditions, including function-limiting arthralgia[38], ID and DJD[9], or only ID[10,11,30–37,39]. It should be noted that these conditions are often associated with each other and occur simultaneously[61,62], and that having one condition does not exclude the other, despite the studies making a clear distinction between them. Hence, it could be that a significant proportion of the study participants diagnosed with ID suffered concurrently from DJD and vice versa. Moreover, since all of the studies reported pain scores, it is conceivable that only ID and DJD patients were included who were simultaneously experiencing arthralgia, i.e., painful ID and/or DJD.

The arthroscopy group in the current review was stratified into two techniques based on the complexity of the treatment, instead of the commonly used three-level classification described by McCain[7]. The decision for this approach was based on the notion that the repositioning and/or fixation of the articular disc, which plays a central part in level III arthroscopy, has no influence on clinical symptom severity or treatment outcomes[63–65]. Hence, distinguishing between level II and level III arthroscopy would not have led to additional insights in the current study. Furthermore, since the only study involving level III arthroscopy[39] was not included in any meta-analysis, considering level III arthroscopy as a separate arthroscopic technique would not have affected the study findings.

The findings of the current study do not completely correspond with those of a previous systematic review with meta-analysis published in 2015[8], which concluded that arthroscopy is superior to arthrocentesis in reducing pain and improving mouth opening, while the two have similar complication rates. These differences could be explained by methodological differences between the two reviews. First, the previous review performed fixed-effects meta-analyses for the continuous outcomes, which ignore heterogeneity[12], despite the clear presence of statistical and methodological heterogeneity between studies (e.g., difference in study design,

arthroscopic techniques, setting, and study population). To account for the observed heterogeneity, a random-effects model is preferred[27]. Secondly, the previous systematic review utilized end-point values to synthesize effect measures instead of change-from-baseline scores. The use of end-point values may be appropriate for study designs involving randomization procedures[12], but they do not account for potential baseline imbalances between groups in non-randomized studies. Since most of the studies in that review did not allocate the study participants randomly, biased effect measures may have been used. Therefore, the choice to use end-point values in the previous review may have influenced the accuracy of the data. Additionally, no stratification of postoperative follow-up periods or arthroscopic techniques during the analysis of the outcomes was performed in that specific study. It is important to note that, when applying random-effects models and change-from-baseline scores in the meta-analysis of the previous review, no difference in pain score reduction or MMO improvement is found between arthroscopy and arthrocentesis.

Several limitations need to be acknowledged concerning the quality of the evidence presented in the current review. Only one included study had a low risk of bias judgement, and only a few RCTs on TMJ arthroscopy have been conducted. The inclusion of non-randomized comparative studies may have introduced bias in the results of the individual studies and, consequently, reduced the strength of the evidence provided in this review. Additionally, TSA indicated that the RIS was not reached in any but one of the meta-analyses, implying that the current available evidence may be inconclusive due to insufficient sample sizes. This may also have been caused by the fact that none of the studies included in the meta-analyses performed a prospective sample size calculation. Furthermore, several of the non-randomized studies included in this study implemented a subject inclusion procedure based on factors such as clinical symptom severity or the patients' preference. Hence, these study designs may not have accounted for the effect of time as a factor for symptom reduction, or corrected for the severity of the symptoms at baseline, leading to imbalances between the groups. Consequently, these studies are prone to selection bias by indication. Additionally, in the current quantitative analyses, despite stratification of the data based on arthroscopy type and follow-up period, and a low to medium clinical judgement based on the CDIM tool, a certain degree of heterogeneity persists between studies, mainly regarding the included diagnoses, the preoperative treatment regimens, and co-intervention use. Although sensitivity analyses based on diagnosis did not change the results or conclusions, it cannot be ruled out for certain that the identification of true therapeutic effects may have

been complicated because of this heterogeneity. Finally, the inclusion of AS was not stated in the a priori stated study protocol. During the performance of the study, the authors realized that the scope of the review could be enhanced to provide a more comprehensive overview of the current evidence regarding TMJ arthroscopy. Since the addition of these extra analyses would not interfere or influence the procedures or the results in this study as specified in the protocol, no bias was introduced because of it.

The current systematic review offers the most comprehensive analysis of the efficacy of TMJ arthroscopy compared to arthrocentesis as treatment for TMJ disorders to date. Furthermore, it appears that this review is novel in providing an overview of the available literature comparing TMJ arthroscopy to conservative treatment regimens. The strengths of this study include a pre-registered, robust and transparent methodology, which is in accordance with the latest Cochrane Handbook for Systematic Reviews and the PRISMA guidelines. Furthermore, attempts were made to reach out to authors to retrieve any absent data in order to enhance the completeness of the data collection procedure. An overview of the authors contacted, the reasons for the contact, and the resultant outcome is provided in **Appendix F**. In order to improve the reliability of the conclusions drawn, additional TSA were performed. Finally, the use of the CDIM tool allowed for a comprehensive assessment of the clinical diversity between studies.

Due to the limited availability of high-quality studies, resulting in low to very low quality of evidence, additional research is necessary to establish definitive conclusions. The current heterogeneity between clinics and lack of methodologically robust studies underscore the significance and necessity of adhering to appropriately drafted protocols and standardized guidelines prior to reaching final conclusions. Adhering to internationally accepted guidelines may lead to a more consistent performance of therapies for TMJ disorders regarding technique, timing, the use of co-interventions, and the pre- and postoperative treatment regimens. Although the authors emphasize the importance of uniformity for research purposes, they are aware that it may also be a challenge in daily practice, as TMD treatments are often individualized to fit the specific needs of the patient. Nonetheless, acting in accordance with guidelines allows a more comprehensive and standardized approach to outcome registration, setting follow-up intervals, statistical analysis and data reporting, which in turn can allow proper conclusions to be drawn. Future research should consider reporting outcome measures other than pain scores and MMO in order to gain a better understanding of the therapeutic effects

of different treatments for TMJ disorders. Currently, there is a lack of evidence regarding the impact of treatments on outcomes such as mandibular functioning, quality of life, and costs/cost-effectiveness. Intensifying research efforts and using validated questionnaires such as the MFIQ[16] may address this gap. Additionally, the authors believe that the rate of symptom reduction, rather than only the efficacy at final follow-up, should be considered when evaluating the efficacy of treatment modalities. Proper study designs in future studies, such as following study participants early on and at several follow-up time-points, and the use of regression analyses[66], are essential for evaluating the speed of recovery.

In the context of future research, several topics may be considered as relevant. Although this study did not focus on the use of intra-articular substances such as hyaluronic acid and platelet-rich plasma as additional treatment modalities, the number of studies on this subject is increasing[67–71]. Addressing these subjects in future research would allow further insight into the potential therapeutic benefits of these substances and their roles as adjuvants in relation to arthroscopy and arthrocentesis. Furthermore, advancements in the development of surgical instruments have led to the possibility of performing arthroscopy under local anesthesia, using smaller portals[53,72]. This development presents an interesting focus for further research, as it could lead to a lesser burden for patients by eliminating the need for general anesthesia, as well as to greater efficiency regarding time and costs. Lastly, although many clinics advocate the use of minimally invasive therapies after conservative treatments have been exhausted, an increasing body of evidence suggests that these may be performed at an earlier stage to allow faster joint recuperation[5,6]. The current review did not aim to explore the debate on the timing of minimally invasive procedures, but rather to highlight the existing knowledge gap that should be addressed in future research.

In conclusion, based on qualitative and quantitative analyses of the currently available data, TMJ arthroscopy results in similar pain reduction and complication rates to arthrocentesis. Additionally, arthroscopic lysis and lavage is superior to arthrocentesis in increasing maximum mouth opening at intermediate-term follow-up. However, these conclusions should be interpreted with caution due to the low quality of the primary studies and the low to very low quality of evidence. There is insufficient evidence available to draw any conclusions regarding the effects of arthroscopy versus arthrocentesis on mandibular function, joint blocks and noises, mandibular range of motion, quality of life, and costs/cost-effectiveness. Furthermore, there is insufficient evidence from the comparison of TMJ arthroscopy and conservative

treatment regimens to draw any conclusions regarding their efficacy in clinical symptom reduction.

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Patient consent

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Competing interests

None.

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References

1. Valesan L, Da-Cas C, Réus J, et al. Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. *Clin Oral Investig*. 2021;25(2):441-453. doi:10.1007/s00784-020-03710-w
2. Almoznino G, Zini A, Zakuto A, et al. Oral health-related quality of life in patients with temporomandibular disorders. *J oral facial pain headache*. 2015;29(4):231-241. doi:10.11607/ofph.1413
3. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain*. 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5
4. Diracoglu D, Saral I, Keklik B, et al. Arthrocentesis versus nonsurgical methods in the treatment of temporomandibular disc displacement without reduction. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;108(1):3-8. doi:10.1016/j.tripleo.2009.01.005
5. Tang Y, Vos L, Tuin A, et al. Arthrocentesis versus non- surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. *Int J Oral Maxillofac Surg*. 2023;52:595-603.
6. Tatli U, Benlidayi M, Ekren O, Salimov F. Comparison of the effectiveness of three different treatment methods for temporomandibular joint disc displacement without reduction. *Int J Oral Maxillofac Surg*. 2017;46:603-609.
7. Hakim M, McCain J, Ahn D, Troulis M. Minimally Invasive Endoscopic Oral and Maxillofacial Surgery. *Oral Maxillofac Surg Clin North Am*. 2019;31(4):561-567.
8. Al-Moraissi EA. Arthroscopy versus arthrocentesis in the management of internal derangement of the temporomandibular joint: A systematic review and meta-analysis. *Int J Oral Maxillofac Surg*. 2015;44(1):104-112. doi:10.1016/j.ijom.2014.07.008
9. Talaat W, Hamdoon Z, Ghoneim M. Minimally invasive surgeries for the treatment of temporomandibular disorders: Prognostic indicators and persistence of treatment outcomes over a 5-year follow-up. *Adv Biomed Heal Sci*. 2022;1(1):34-44.
10. Rajpoot D, Anchlia S, Bhatt U, Dhuvad J, Patel H, Mansuri Z. Arthrocentesis versus level 1 arthroscopy in internal derangement of temporomandibular joint. *J Maxillofac Oral Surg*. 2023;22:94-101. doi:https://doi.org/10.1007/s12663-021-01627-9
11. Atteya A, Warda M, Fata M, Medra A, Monje F. Prospective randomized study between arthrocentesis and operative arthroscopy in the management of temporomandibular joint internal derangement. *Alexandria Dent J*. 2020;46(1):58-65. doi:10.21608/adjalexu.2020.25155.1051
12. Higgins J, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions, version 6.3 (updated February 2022). *Cochrane*. Published online 2022.
13. Page M, McKenzie J, Bossuyt P, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;29;372:n71. doi:10.1136/bmj.n71

14. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *J oral facial pain headache*. 2014;38(1):6-27.

15. Sanders B. Arthroscopic surgery of the temporomandibular joint: Treatment of internal derangement with persistent closed lock. *Oral Surgery, Oral Med Oral Pathol*. 1986;62(4):361-372. doi:10.1016/0030-4220(86)90282-3

16. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*. 1993;7(2):183-195. http://www.ncbi.nlm.nih.gov/pubmed/8358365

17. Bramer W, Giustini D, Jonge G de, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. *J Med Libr Assoc*. 2016;104(3):240-243. doi:http://dx.doi.org/10.3163/1536-5050.104.3.014

18. Sterne J, Savovic J, Page M, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *Res Methods Report*. 2019;366(14898).

19. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (Minors): Development and validation of a new instrument. *ANZ J Surg*. 2003;73(9):712-716. doi:10.1046/j.1445-2197.2003.02748.x

20. Atkins D, Best D, Briss P, Eccles M, Falck-Ytter Y, Flottorp S. Grading quality of evidence and strength of recommendations. The GRADE Working Group. *Br Med J (Clin Res Ed)*. 2004;(June):328(7454):1490.

21. Barbateskovic M, Koster T, Eck R, et al. A new tool to assess clinical diversity in meta-analyses (CDIM) of internventions. *J Clin Epidemiol*. 2021;135:29-41. doi:doi:10.1016/j.jclinepi.2021.01.023

22. Sweeting M, Sutton A, Lambert P. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. *Stat Med*. 2004;23:1351-1375. doi:10.1002/sim.1761

23. Cheng J, Pulleneyagum E, Marshall J, Iorio A, Thabane L. Impact of including or excluding both-armed zero-event studies on using standard meta-analysis methods for rare event outcome: a simulation study. *BMJ Open*. 2016;6(e010983). doi:10.1136/bmjopen-2015- 010983

24. Smaïl-Faugeron V, Fron-Chabouis H, Courson F, Durieux P. Comparison of intervention effects in split-mouth and parallel-Arm randomized controlled trials: A meta-epidemiological study. *BMC Med Res Methodol*. 2014;14(1). doi:10.1186/1471-2288-14-64

25. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. *Evid Based Ment Heal*. 2019;22:153-160. doi:10.1136/ebmental-2019-300117

26. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188. doi:10.1016/0197-2456(86)90046-2

27. Borenstein M, Hedges L, Higgins J, HR Rothstein. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1:97-111.

28. Wetterslev J, Jakobsen J, Gluud C. Trial sequential analysis in systematic reviews with meta-analysis. *BMC Med Res Methodol.* 2017;17(39):1-18.

29. Thorlund K, Engstrom J, Wetterslev J, Brok J, Imberger G, Gluud C. *User Manual for Trial Sequential Analysis (TSA).;* 2011.

30. Murakami K, Hosaka H, Moriya Y, Segami N, Iizuka T. Short-term treatment outcome study for the management of temporomandibular joint closed lock. A comparison of arthrocentesis to nonsurgical therapy and arthroscopic lysis and lavage. *Oral Surgery, Oral Med Oral Pathol Oral Radiol.* 1995;80(3):253-257. doi:10.1016/S1079-2104(05)80379-8

31. Schiffman E, Velly A, Look J, et al. Effects of four treatment strategies for temporomandibular joint closed lock. *Int J Oral Maxillofac Surg.* 2014;43:217-226.

32. Sanromán JF. Closed lock (MRI fixed disc): A comparison of arthrocentesis and arthoscopy. *Int J Oral Maxillofac Surg.* 2004;33(4):344-348. doi:10.1016/j.ijom.2003.10.005

33. Hobeich J, Salameh Z, Ismail E, Sadig W, Hokayem N, Almas K. Arthroscopy versus arthrocentesis: A retrospective study of disc displacement management without reduction. *Saudi Med J.* 2007;28(10):1541-1544.

34. Fridrich KL, Wise JM, Zeitler DL. Prospective comparison of arthroscopy and arthrocentesis for temporomandibular joint disorders. *J Oral Maxillofac Surg.* 1996;54(7):816-820. doi:10.1016/S0278-2391(96)90526-1

35. Goudot P, Jaquinet A, Hugonnet S, Haefliger W, Richter M. Improvement of pain and function after arthroscopy and arthrocentesis of the temporomandibular joint : a comparative study. *J Cranio-Maxillofacial Surg.* 2000;28:39-43. doi:10.1054/jcms.1998.0103

36. Tan DBP, Krishnaswamy G. A retrospective study of temporomandibular joint internal derangement treated with arthrocentesis and arthroscopy. *Proc Singapore Healthc.* 2012;21(1):73-78. doi:10.1177/201010581202100112

37. Xu Y, Lin H, Zhu P, et al. A comparative study between use of arthroscopic lavage and arthrocentesis of temporomandibular joint based on computational fluid dynamics analysis. *PLoS One.* 2013;8(11). doi:10.1371/journal.pone.0078953

38. Stegenga B, de Bont LGM, Dijkstra PU, Boering G. Short-term outcome of arthroscopic surgery of temporomandibular joint osteoarthrosis and internal derangement: A randomized controlled clinical trial. *Br J Oral Maxillofac Surg.* 1993;31(1):3-14. doi:10.1016/0266-4356(93)90089-F

39. McNamara DC, Rosenberg I, Jackson PA, Hogben J. Efficacy of arthroscopic surgery and midlaser treatments for chronic temporomandibular joint articular disc derangement following motor vehicle accident. *Aust Dent J.* 1996;41(6):377-387. doi:10.1111/j.1834-7819.1996.tb06023.x

40. Alonso-Royo R, Sánchez-Torrelo CM, Ibáñez-Vera AJ, et al. Validity and reliability of the helkimo clinical dysfunction index for the diagnosis of temporomandibular disorders. *Diagnostics.* 2021;11(3). doi:10.3390/diagnostics11030472

41. Gentile DA, Woodhouse J, Lynch P, Maier J, McJunkin T. Reliability and validity of the global pain scale with chronic pain sufferers. *Pain Physician*. 2011;14(1):61-70. doi:10.36076/ppj.2011/14/61

42. Kerns R, Turk D, Rudy T. The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). *Pain*. 1985;23:345-356.

43. Goldberg D, Hillier V. A scaled version of the GHQ. *Psychol Med*. 1979;9:139-145.

44. Kaneyama K, Segami N, Nishimura M, Sato J, Fujimura K, Yoshimura H. The ideal lavage volume for removing bradykinin, interleukin-6, and protein from the temporomandibular joint by arthrocentesis. *J Oral Maxillofac Surg*. 2004;62(6):657-661. doi:10.1016/j.joms.2003.08.031

45. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006

46. Nishimura M, Segami N, Kaneyama K, Suzuki T, Miyamaru M. Proinflammatory cytokines and arthroscopic findings of patients with internal derangement and osteoarthritis of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2002;40:68-71.

47. Sandler NA, Buckley MJ, Cillo JE, Braun TW. Correlation of inflammatory cytokines with arthroscopic findings in patients with temporomandibular joint internal derangements. *J Oral Maxillofac Surg*. 1998;56(5):534-543. doi:10.1016/S0278-2391(98)90446-3

48. Celotti C, Martin-Granizo R, De La Sen O. Correlation of arthroscopic findings with clinical–radiological signs and symptoms of temporomandibular joint dysfunction: retrospective study of 829 joints. *Int J Oral Maxillofac Surg*. 2022;51:1069-1073.

49. Martins I, Radaic P, Marchi L, Barreto G, Pastore G. Assessment of postoperative pain in patients undergoing temporomandibular joint arthroscopy with infiltration of dexamethasone disodium phosphate in different concentrations. A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2023;51(2):89-97.

50. Oren D, Dror A, Khalil T, et al. Comparisons between lysis and lavage, intra-articular steroid injections, and three-point subsynovial steroid injections using operative single-cannula arthroscopy d A retrospective analysis Daniel. *J Cranio-Maxillofacial Surg*. 2022;50(4):336-342.

51. Murakami K, Nishida M, Bessho K, Iizuka T, Tsuda Y, Konishi J. MRI evidence of high signal intensity and temporomandibular arthralgia and relating pain. Does the high signal correlate to the pain? *Br J Oral Maxillofac Surg*. 1996;34(3):220-224. doi:10.1016/S0266-4356(96)90273-9

52. McCain JP, Sanders B, Koslin MG, Quinn JD, Peters PB, Indresano AT. Temporomandibular joint arthroscopy: A 6-year multicenter retrospective study of 4,831 joints. *J Oral Maxillofac Surg*. 1992;50(9):926-930. doi:10.1016/0278-2391(92)90047-4

53. Hossameldin RH, McCain JP. Outcomes of office-based temporomandibular joint arthroscopy: a 5-year retrospective study. *Int J Oral Maxillofac Surg*. 2018;47(1):90-97. doi:10.1016/j.ijom.2017.06.025

54. Machoň V, Šedý J, Klíma K, Hirjak D, Foltán R. Arthroscopic lysis and lavage in patients with temporomandibular anterior disc displacement without reduction. *Int J Oral Maxillofac Surg*. 2012;41(1):109-113. doi:10.1016/j.ijom.2011.07.907

55. Nitzan D, Svidovsky J, Zini A, Zadik Y. Effect of arthrocentesis on symptomatic osteoarthritis of the temporomandibular joint and analysis of the effect of preoperative clinical and radiological features. *J Oral Maxillofac Surg*. 2017;75:260-267. doi:10.1080/00016350601083554

56. Carvajal W, Laskin D. Long-Term Evaluation of Arthrocentesis for the Treatment of Internal Derangements of the Temporomandibular Joint. *J Oral Maxillofac Surg*. 2000;58:852-855. doi:10.1053/joms.2000.8201

57. Kirk jr. W, Calabrese D. Clinical Evaluation of Physical Therapy in the Management of Internal Derangement of the Temporomandibular Joint. *J Oral Maxillofac Surg*. 1989;47:113-119.

58. Kai S, Kai H, Tabata O, Shiratsuchi Y, Ohishi M. Long-term outcomes of nonsurgical treatment in nonreducing anteriorly displaced disk of the temporomandibular joint. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;85(3):258-267. doi:10.1016/S1079-2104(98)90005-1

59. Kurita K, Westesson P, Yuasa H, Toyama M, Machida J, Ogi N. Natural Course of Untreated Symptomatic Temporomandibular Joint Disc Displacement without Reduction. *J Dent Res*. 1998;77(2):361-365.

60. Sato S, Kawamura H, Nagasaka H, Motegi K. The natural course of anterior disc displacement without reduction in the temporomandibular joint: Follow-up at 6, 12, and 18 months. *J Oral Maxillofac Surg*. 1997;55(3):234-238. doi:10.1016/S0278-2391(97)90531-0

61. Stegenga B. Osteoarthritis of the Temporomandibular Joint Organ and Its Relationship to Disc Displacement. *J Orofac Pain*. 2001;15(3):193-205.

62. Bertram S, Rudisch A, Innerhofer K, Pümpel E, Grubwieser G, Emshoff R. Diagnosing TMJ internal derangement and osteoarthritis with magnetic resonance imaging. *J Am Dent Assoc*. 2001;132(6):753-761. doi:10.14219/jada.archive.2001.0272

63. Dolwick MF. Intra-articular disc displacement part I: Its questionable role in temporomandibular joint pathology. *J Oral Maxillofac Surg*. 1995;53(9):1069-1072. doi:10.1016/0278-2391(95)90126-4

64. Nitzan D, Dolwick M, Heft M. Arthroscopic lavage and lysis of the temporomandibular joint: A change in perspective. *J Oral Maxillofac Surg*. 1990;48(8):798-801. doi:10.1016/0278-2391(90)90335-Y

65. Emshoff R, Rudisch A. Are internal derangement and osteoarthrosis linked to changes in clinical outcome measures of arthrocentesis of the temporomandibular joint? *J Oral Maxillofac Surg*. 2003;61(10):1162-1167. doi:10.1016/S0278-2391(03)00676-1

66. Caruana E, Roman M, Hernandez-Sanchez J, Solli P. Longitudinal studies. *J Thorac Dis*. 2015;7(11):E537-E540. doi:10.3978/j.issn.2072-1439.2015.10.63

67. Hosgor H. Is arthrocentesis plus hyaluronic acid superior to arthrocentesis alone in the treatment of disc displacement without reduction in patients with bruxism? *J Cranio-Maxillofacial Surg*. 2020;48:1023-1027.

68. Marzook H, Abdel Razek A, Yousef E, Attia A. Intra-articular injection of a mixture of hyaluronic acid and corticosteroid versus arthrocentesis in TMJ internal derangement. *J Stomatol oral Maxillofac Surg*. 2020;121:30-34.

69. Sakalys D, Dvylys D, Simuntis R, Leketas M. Comparison of Different Intraarticular Injection Substances Followed by Temporomandibular Joint Arthroscopy. *J Craniofac Surg*. 2020;31(3):637-641. doi:10.1097/SCS.0000000000006098

70. Yilmaz O, Korkmaz Y, Tuzumer T. Comparison of treatment efficacy between hyaluronic acid and arthrocentesis plus hyaluronic acid in internal derangements of temporomandibular joint. *J Cranio-Maxillofacial Surg*. 2019;47:1720-1727.

71. Zotti F, Albanese M, Rodella L, Nocini P. Platelet-Rich Plasma in Treatment of Temporomandibular Joint Dysfunctions: Narrative Review. *Int J Mol Sci*. 2019;20(2):277.

72. Weedon S, Ahmed N, Sidebottom AJ. Prospective assessment of outcomes following disposable arthroscopy of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2013;51(7):625-629. doi:10.1016/j.bjoms.2013.06.004

Appendix A. Search terms used per electronic database for the literature search.

Database	Search terms	Hits (initial search)	Hits (second search)
Pubmed	("Craniomandibular Disorders"[Mesh] OR "Temporomandibular Joint"[Mesh] OR temporomandib*[tiab] OR temporo-mandib*[tiab] OR tmj[tiab] OR craniomandib*[tiab]) AND ("Arthroscopy"[Mesh] OR "Therapeutic Irrigation"[Mesh] OR arthroscop*[tiab] OR irrigat*[tiab] OR lavage*[tiab] OR minimally-invasive[tiab]) NOT (("Animals"[Mesh] NOT "Humans"[Mesh]) OR "Case Reports" [pt] OR "Review" [pt])	793	52
Embase	('jaw disease'/de/mj OR 'temporomandibular joint disorder'/exp OR 'temporomandibular joint'/exp OR (temporomandib* OR 'temporo-mandib*' OR tmj OR craniomandib*):ab,ti,kw) AND ('arthroscopy'/de OR 'arthroscopic surgery'/exp OR 'lavage'/de OR 'arthroscopic lavage'/exp OR (arthroscop* OR irrigat* OR lavage* OR 'minimally invasive'):ab,ti,kw) NOT (('animal'/exp NOT 'human'/exp) OR 'review'/de OR 'case report'/exp OR 'conference abstract'/it)	861	62
Web of Science	TS=(temporomandib* OR temporomandib* OR tmj OR craniomandib*) AND TS=(arthroscop* OR irrigat* OR lavage* OR "minimally-invasive") AND DT=(article)	860	47
Cochrane Library	([mh "Craniomandibular Disorders"] OR [mh "Temporomandibular Joint"] OR temporomandib*:ti,ab OR temporo-mandib*:ti,ab OR tmj:ti,ab OR craniomandib*:ti,ab) AND ([mh Arthroscopy] OR [mh "Therapeutic Irrigation"] OR arthroscop*:ti,ab OR irrigat*:ti,ab OR lavage*:ti,ab OR minimally-invasive:ti,ab)	103	6
Scopus	TITLE-ABS-KEY (temporomandib* OR "temporo-mandib*" OR tmj OR craniomandib*) AND TITLE-ABS-KEY (arthroscop* OR irrigat* OR lavage* OR "minimally-invasive") AND (LIMIT-TO (DOCTYPE , "ar"))	1085	69
Clinicaltrials.gov	(temporomandib* OR temporomandib* OR tmj OR craniomandib*) AND arthroscop* OR irrigat* OR lavage* OR minimally-invasive)	3	2
International Clinical Trials Registry Platform	(temporomandib* OR temporo-mandib* OR tmj OR craniomandib*) AND (arthroscop* OR irrigat* OR lavage* OR minimally-invasive)	22	1

Appendix B. Excluded reports after full-text screening.

Author (year)	Reason for exclusion	Did not meet
Ahmed (2012)[1]	No control group	Inclusion criteria
Bare (1987)[2]	Review paper	Exclusion criteria
Brignardello-Peterson (2018)[3]	Review paper	Exclusion criteria
Brignardello-Peterson (2019)[4]	Review paper	Exclusion criteria
Gonzalez-garcia (2011)[5]	Review paper	Exclusion criteria
Goudot (1998)[6]	Technical note	Exclusion criteria
Hosgor (2017)[7]	Intervention does not fit current review	Inclusion criteria
Indresano (2001)[8]	No control group	Inclusion criteria
Ohnuki (2006)[9]	Arthroscopy performed after arthrocentesis	Inclusion criteria
Polso (2010)[10]	Intervention does not fit current review	Inclusion criteria
Sahlström (2013)[11]	Intervention does not fit current review	Inclusion criteria
Sakamoto (2000)[12]	Intervention does not fit current review	Inclusion criteria
Schiffman (2005)[13]	Conference abstract	Exclusion criteria
Schiffman (2007)[14]	Outcome measures do not fit current review	Inclusion criteria
Stasko (2020)[15]	Control treatment does not fit current review	Inclusion criteria
Tarro (2001)[16]	Letter to the editor	Exclusion criteria
Yoda (1997)[17]	Arthroscopy performed after arthrocentesis	Inclusion criteria

Appendix C.1. Results from individual studies regarding arthroscopy versus arthrocentesis.

Author (year)	Follow-up period (months)	Study arm		Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life improvement	Costs/ cost-effectiveness	Complications
Arthroscopic surgery as intervention												
Murakami et al. (1995)[18]	Intermediate (6)	AS	MD ±SD	31.0 ±21.7*	14.6 ±5.6*	6.9[a] / 3.9[b]						E
			N	25	25	25						N
		AC	MD ±SD	45.0 ±21.8*	11.9 ±5.7*	7.3[a]/ 5.3[b]						E
			N	20	20	20						N
Sanroman (2004)[19]	Short and intermediate (1 to 24)	AS	MD ±SD	ANA	ANA			ANA	ANA			
			N	16	16			16	16			
		AC	MD ±SD	ANA	ANA			ANA	ANA			
			N	8	8			8	8			
Hobeich et al. (2017)[20]	Intermediate (18-24)	AS	MD ±SD	33.9 ±17.1*	8.6 ±11.4*							E
			N	28	28							N
		AC	MD ±SD	32.0 ±16.3*	9.9 ±11.6*							E
			N	20	20							N

* Standard deviations imputed for quantitative analysis using a correlation coefficient of 0.5; [a] Activity Daily Living-score, scale 0-72 (higher is worse); [b] Jaw function score, scale 0-20 (higher is worse). Abbr.: VAS visual analog scale; MMO maximal mouth opening; AS arthroscopic surgery; AC arthrocentesis; MD difference between baseline and follow-up means; SD standard deviation; N number of subjects; E number of events; ANA analyzed in the included study, but data were not available for extraction.

Appendix C.1. Results from individual studies regarding arthroscopy versus arthrocentesis. *Continued.*

Author (year)	Follow-up period (months)	Study arm		Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications	
Atteya et al. (2020)[21]	Short (1)	AS	MD ±SD	18.5 ±17.9*									
			N	20									
		AC	MD ±SD	6.0 ±14.4*									
			N	20									
	Intermediate (6)	AS	MD ±SD	63.0 ±18.2*	3.9 ±5.5*							E	0
			N	20	20							N	20
		AC	MD ±SD	45.5 ±13.6*	3.7 ±4.3*							E	0
			N	20	20							N	20

Appendix C.1. Results from individual studies regarding arthroscopy versus arthrocentesis. *Continued*

Author (year)	Follow-up period (months)	Study arm		Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications	
Arthroscopic lysis and lavage as intervention													
Fridrich et al. (1996)[22]	Intermediate (6-24)	ALL	MD ±SD	47.5	17.5 ±8.4*	45.0[a]	15.0[b]					E	0
			N	11	11	11	11					N	11
		AC	MD ±SD	43.0	8.0 ±10.6*	41.5[a]	27.0[b]					E	0
			N	8	8	8	8					N	8
Goudot et al. (2000)[23]	Intermediate (12)	ALL	MD ±SD	38.0 ±24.0	9.6 ±5.8							E	2
			N	33	33							N	33
		AC	MD ±SD	47.0 ±21.0	4.3 ±4.4							E	2
			N	29	29							N	29

* Standard deviations imputed for quantitative analysis using a correlation coefficient of 0.5; [a] Dietary alterations, scale 0-100 (higher is worse); [b] Subjective intensity of joint noises, scale 0-100 (higher is worse). Abbr.: VAS visual analog scale; MMO maximal mouth opening; AS arthroscopic surgery; AC arthrocentesis; ALL arthroscopic lysis and lavage; MD difference between baseline and follow-up means; SD standard deviation; N number of subjects; E number of events.

Appendix C.1. Results from individual studies regarding arthroscopy versus arthrocentesis. *Continued*

Author (year)	Follow-up period (months)	Study arm		Pain VAS in mm (0-100)	Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement (mm)	Maximum lateral movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications	
Tan et al. (2012)[24]	Short (1)	ALL	MD ±SD	33.6 ±23.8[a]	4.6 ±6.7[a]							E	0
			N	11	11							N	11
		AC	MD ±SD	45.6 ±17.4[a]	13.0 ±5.0[a]							E	0
			N	9	9							N	9
Xu et al. (2013)[25]	Short (3)	ALL	MD ±SD	48.9 ±19.8*	12.9 ±4.2*			5.0 ±2.0[c]				E	2
			N	37	37			37				N	37
		AC	MD ±SD	45.9 ±15.2*	9.8 ±4.7*			3.9 ±1.8[c]				E	1
			N	41	41			41				N	41

Appendix C.1. Results from individual studies regarding arthroscopy versus arthrocentesis. *Continued.*

Author (year)	Follow-up period (months)	Study arm		Pain VAS in mm (0-100)	Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement (mm)	Maximum lateral movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications
Rajpoot et al. (2021)[26]	Short (1)	ALL	MD ±SD	58.0 ±17.5[b]	8.7 ±5.8[b]			1.5 ±1.3[b,l]/ 1.7 ±0.9[b,r]	1.1 ±1.4			
			N	15	15			15	15			
		AC	MD ±SD	45.4 ±14.9[b]	8.4 ±5.8[b]			1.2 ±1.7[b,l]/ 1.4 ±1.7[b,r]	1.6 ±0.9			
			N	15	15			15	15			
	Intermediate (6)	ALL	MD ±SD	62.6 ±22.6[b]	9.4 ±6.8[b]			2.3 ±1.4[b,l]/ 2.4 ±1.1[b,r]	1.8 ±0.9			E
			N	15	15			15	15			N
		AC	MD ±SD	59.4 ±23.0[b]	7.3 ±6.7[b]			1.3 ±1.9[b,l]/ 1.7 ±1.8[b,r]	1.5 ±1.1			E
			N	15	15			15	15			N

* Standard deviations imputed for quantitative analysis using a correlation coefficient of 0.5; [a] Means and standard deviations imputed by current authors for quantitative analysis based on available database from included study; [b] Standard deviations retrieved for quantitative analysis after contact with study authors; [c] To contralateral side; [l] To left side; [r] To right side. Abbr.: VAS visual analog scale; MMO maximal mouth opening; ALL arthroscopic lysis and lavage; AC arthrocentesis; MD difference between baseline and follow-up means; SD standard deviation; N number of subjects; E number of events.

Appendix C.1. Results from individual studies regarding arthroscopy versus arthrocentesis. *Continued.*

Author (year)	Follow-up period (months)	Study arm		Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications	
Talaat et al. (2022)[27]	Short to intermediate (3 to 36)	ALL	MD ±SD	ANA	ANA								
			N	32	32								
		AC	MD ±SD	ANA	ANA								
			N	32	32								
	Long (60)	ALL	MD ±SD	61.2 ±12.7*	13.2 ±3.4*	*cat*						E	0
			N	32	32	32						N	32
		AC	MD ±SD	60.0 ±12.8*	11.7 ±3.7*	*cat*						E	1
			N	32	32	32						N	32

* Standard deviations imputed for quantitative analysis using a correlation coefficient of 0.5; cat: categorical outcome of disability scores not displayed here for the sake of simplicity. Abbr.: VAS visual analog scale; MMO maximal mouth opening; ALL arthroscopic lysis and lavage; AC arthrocentesis; MD difference between baseline and follow-up means; SD standard deviation; N number of subjects; E number of events; ANA analyzed in the included study, but data were not available for extraction

Appendix C.2. Results from individual studies regarding arthroscopy versus conservative treatment.

Author (year)	Follow-up period (months)	Study arm		Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications
Arthroscopic surgery as intervention												
Stegenga et al. (1993)[28]	Short (1)	AS	MD ±SD	33.0 ±23.3*	4.9 ±4.2*	*cat*				3.0[a]		
			N	8	8	8				8		
		C	MD ±SD	16.0 ±20.7*	4.9 ±5.0*	*cat*				0.0[a]		
			N	11	11	11				11		
	Intermediate (6)	AS	MD ±SD	45.0±18.7*	6.6 ±3.9*	*cat*				5.0[a]		E
			N	9	9	9				9		N
		C	MD ±SD	25.0 ±15.8*	8.1 ±4.9*	*cat*				5.0[a]		E
			N	12	12	12				12		N
Murakami et al. (1995)[18]	Intermediate (6)	AS	MD ±SD	31.0 ±21.7*	14.6 ±5.6*	6.9[b] / 3.9[c]						E
			N	25	25	25						N
		C	MD ±SD	29.0 ±25.9*	9.1 ±7.8*	3.9[b] / 2.7[c]						E
			N	63	63	63						N

Appendix C.2. Results from individual studies regarding arthroscopy versus conservative treatment. *Continued*

Author (year)	Follow-up period (months)	Study arm		Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications
McNamara et al. (1996)[29]	Short and intermediate (3 to 12)	AS	MD ±SD	ANA	ANA	ANA						E
			N	10	10	10						N
		C	MD ±SD	ANA	ANA	ANA						E
			N	10	10	10						N

* Standard Deviations imputed using a correlation coefficient of 0.5; [a] Total well-being score based on the West Haven-Yale Multidimensional Health Questionnaire score and the General Health Questionnaire score, scale 0-100 (higher is worse); [b] Activity Daily Living-score, scale 0-72 (higher is worse); [c] Jaw function score, scale 0-20 (higher is worse); cat: categorical outcome of global pain impact score and converted mandibular function impairment questionnaire score not displayed here for the sake of simplicity. Abbr.: VAS visual analog scale; MMO maximal mouth opening; AS arthroscopic surgery; C conservative treatment; MD difference between baseline and follow-up means; SD standard deviation; N number of subjects; E number of events; ANA analyzed in the included study, but data were not available for extraction.

Appendix C.2. Results from individual studies regarding arthroscopy versus conservative treatment. *Continued*

Author (year)	Follow-up period (months)	Study arm	N	Pain VAS reduction (mm, 0-100)	MMO improvement (mm)	Mandibular function improvement	Joint blocks and noises improvement	Maximum lateral movement improvement (mm)	Maximum proal movement improvement (mm)	Quality of Life	Costs/ cost-effectiveness	Complications
Arthroscopic lysis and lavage as intervention												
Schiffman et al. (2014)[30]	Short to Long (3 to 60)	ALL	23	*nd**	*nd**	*nd**	*nd**	*nd**	*nd**		1385[a]	E
												N
		C_{reh}	23	*nd**	*nd**	*nd**	*nd**	*nd**	*nd**		2379[a]	E
												N
		C_{med}	29	*nd**	*nd**	*nd**	*nd**	*nd**	*nd**		7890[a]	E
												N

* Generalized Estimated Equations used for each treatment outcome, which were dichotomized: pain (excessive intensity/ no or mild pain), MMO (<35mm /≥35mm), mandibular function (impaired chewing/ only impaired when chewing most resistant foods or no impairment), joint blocks and noises (yes/no), maximum lateral movement on most limited side (<6mm /≥6mm), maximum proal movement (<6mm /≥6mm); [a] costs per treatment in US dollars. Abbr.: N number of subjects; VAS visual analog scale; MMO maximal mouth opening; AS arthroscopic surgery; C_{reh} conservative treatment rehabilitation; C_{med} conservative treatment medical management; nd no difference between treatment groups; E number of events.

Appendix D.1. Clinical heterogeneity between studies involving arthroscopic surgery versus arthrocentesis for pain scores at intermediate-term follow-up using the CDIM tool.

		Murakami et al. (1995)[18]	Hobeich et al. (2007)[20]	Atteya et al. (2020)[21]	Score
Setting					
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	1995 (A); developed country, Japan (B); outpatient clinic & probably OT hospital (C)	2007 (A); developing country, Lebanon (B); specialized private clinic (C)	2020 (A); developed & developing country, Spain & Egypt (B); OT hospital (C)	2
Population					
2.	Mean age	32.0	31.0	34.9	0
3.	Sex	89% woman	83% woman	88% woman	0
4.	Inclusion criteria and baseline disease severity	Closed Lock Wilkes III; baseline VAS 52.0mm*	ADD w/o R; baseline VAS 57.3mm*	ID, Wilkes II-III; baseline VAS 73.8mm*	2
5.	Comorbidities	Not reported	Not reported	Not reported	0
Intervention					
6.	Intensity, strengths, or duration of intervention	ALL + antero-lateral capsular release; double portal; GA.	ALL + coagulation synovitis + cauterization retrodiscal tissue; double portal; GA	ALL + antero-lateral capsular release; cauterization retrodiscal tissue; double portal; GA	1
7.	Timing	Symptom duration 6.3 mo.; Pre-op: AS group conservative treatment first.**	Symptom duration 12-24 mo.; Pre-op: anterior deprogrammer device	Symptom duration not reported; Pre-op: 6 mo. of conservative treatment	2
8.	Control intervention	Arthrocentesis with 2 needles; LA; 200ml Ringer lactate	Arthrocentesis with 2 needles; LA; 200ml Ringer lactate	Arthrocentesis with 2 needles; LA; Ringer lactate	0
9.	Cointerventions	Betamethasone after procedures; Post-op: jaw exercises	Sodium hyaluronate after procedures; Post-op: jaw exercises, 2 weeks NSAIDs and muscle relaxants	Sodium hyaluronate after procedures; Post op: jaw exercises, 2 mo. soft diet, 3 days antibiotics and NSAIDs	2

Appendix D.1. Clinical heterogeneity between studies involving arthroscopic surgery versus arthrocentesis for pain scores at intermediate-term follow-up using the CDIM tool. *Continued*

	Murakami et al. (1995)[18]	Hobeich et al. (2007)[20]	Atteya et al. (2020)[21]	Score
Outcome				
10. Definition of the outcome	VAS (0-10)	VAS (0-10)	VAS (0-10)	0
11. Timing of outcome	6 mo.	18-24 mo.	6 mo.	2
Total score				11

* VAS-score converted to 0-100 scale. ** Arthroscopic surgery was decided by choice or when subjects were refractory to conservative treatment (1-2 weeks non-steroidal anti-inflammatory drugs and muscle relaxants, then physiotherapy, then pivot splints for up to 12 weeks). Abbr.: OT operating theatre; VAS visual analog scale; ADD w/o R anterior disc displacement without reduction; ID internal derangement; ALL arthroscopic lysis and lavage; GA general anesthesia; mo. months; LA local anesthesia; NSAIDs non-steroidal anti-inflammatory drugs.

Appendix D.2. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for pain scores at short-term follow-up using the CDIM tool.

		Tan et al. (2012)[24]	Xu et al. (2013)[25]	Rajpoot et al. (2021)[26]	Score
Setting					
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	2012 (A); developed country, Singapore (B); OT hospital (C)	2013 (A); developed country, China (B); probably OT hospital (C)	2021 (A); developed country, India (B); OT hospital (C)	0
Population					
2.	2. Mean age	34.6	36.6	34.6	0
3.	Sex	75% woman	75.6% woman	73.3% woman	0
4.	Inclusion criteria and baseline disease severity	Closed lock/ Painful click; baseline VAS 64.5mm*	Anterior disc displacement; baseline VAS 56.8mm*	ID; baseline VAS 81.4mm*	2
5.	Comorbidities	Not reported	Not reported	Not reported	0
Intervention					
6.	Intensity, strengths, or duration of intervention	ALL + blind sweep; single portal; GA; 200ml Saline	Arthroscopic lavage; double portal; LA; 500ml Ringer lactate	Level 1 arthroscopy; single portal; anesthesia not reported; 300ml Ringer lactate	1
Intervention					
7.	Timing	Symptom duration 8.8 mo; Pre-op: 3-8 weeks NSAID/ muscle relaxant + splint for bruxism patients	Symptom duration not reported; Pre-op: not reported	Symptom duration 12.1 mo; Pre-op: not reported	2
8.	Control intervention	Arthrocentesis with 2 needles; LA; 200ml saline	Arthrocentesis with 2 needles; LA; 500ml Ringer lactate	Arthrocentesis with single puncture double needle; LA; 300ml Ringer lactate	1
9.	Cointerventions	Post-op: NSAIDs, physiotherapy and soft diet. Splint continuation.	Sodium hyaluronate after procedure; Post-op: not reported	Post-op: ice, antibiotics, analgesics, physiotherapy from 2nd week and 2 weeks soft diet	2

Appendix D.2. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for pain scores at short-term follow-up using the CDIM tool. *Continued*

	Tan et al. (2012)[24]	Xu et al. (2013)[25]	Rajpoot et al. (2021)[26]	Score
Outcome				
10. Definition of the outcome	VAS (1-10)	VAS (1-100)	VAS	0
11. Timing of outcome	1 mo.	3 mo.	1 mo.	1
Total score				9

* VAS-score converted to 0-100 scale. Abbr.: OT operating theatre; VAS visual analog scale; ID internal derangement; ALL arthroscopic lysis and lavage; GA general anesthesia; LA local anesthesia; mo. months; NSAIDs non-steroidal anti-inflammatory drug.

Appendix D.3. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for pain scores at intermediate follow-up using the CDIM tool.

		Goudot et al. (2000)[23]	Rajpoot et al. (2021)[26]	Score
Setting				
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	2000 (A); developed country, Switzerland (B); probably OT hospital (C)	2021 (A); developed country, India (B); OT hospital (C)	1
Population				
2.	Mean age	Not reported	34.6	1
3.	Sex	Not reported	73.3% woman	1
4.	Inclusion criteria and baseline disease severity	TMJ pain dysfunction syndrome*; baseline VAS 56.5mm**	ID; baseline VAS 81.4mm**	2
5.	Comorbidities	Not reported	Not reported	0
Intervention				
6.	Intensity, strengths, or duration of intervention	ALL; single portal; GA; Ringer lactate	Level 1 arthroscopy; single portal; anesthesia not reported; 300ml Ringer lactate	0
7.	Timing	Symptom duration at least 6 mo., for the rest not reported Pre-op: 6 mo. of consulting, splint and physiotherapy, psychologic support	Symptom duration 12.1 mo.; Pre-op: not reported	2
8.	Control intervention	Arthrocentesis with 2 needles; LA; 100-150ml saline.	Arthrocentesis with single puncture double needle; LA; 300ml Ringer lactate	1
9.	Cointerventions	Post-op: physiotherapy, 2 weeks soft diet,	Post-op: ice, antibiotics, analgesics, physiotherapy from 2nd week and 2 weeks soft diet	1
Outcome				
10.	Definition of the outcome	VAS (0-10)	VAS	0
11.	Timing of outcome	12 mo.	6 mo.	2
Total score				11

* Internal derangement, muscular dysfunction and psycho-affective disorder ** VAS-score converted to 0-100 scale. Abbr.: OT operating theatre; TMJ temporomandibular joint; VAS visual analog scale; ID internal derangement; ALL arthroscopic lysis and lavage; GA general anesthesia; mo. months; LA local anesthesia; NSAIDs non-steroidal anti-inflammatory drugs

Appendix D.4. Clinical heterogeneity between studies involving arthroscopic surgery versus arthrocentesis for maximum mouth opening at intermediate follow-up using the CDIM tool.

		Murakami et al. (1995)[18]	Hobeich et al. (2007)[20]	Atteya et al. (2020)[21]	Score
Setting					
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	1995 (A); developed country, Japan (B); outpatient clinic & probably OT hospital (C)	2007 (A); developing country, Lebanon (B); specialized private clinic (C)	2020 (A); developed & developing country, Spain & Egypt (B); OT hospital (C)	2
Population					
2.	Mean age	32.0	31.0	34.9	0
3.	Sex	89% woman	83% woman	88% woman	0
4.	Inclusion criteria and baseline disease severity	Closed Lock Wilkes III; baseline MMO 28.8mm	ADD w/o R; baseline MMO 34.1mm	ID, Wilkes II-III; baseline MMO 29.9mm	1
5.	Comorbidities	Not reported	Not reported	Not reported	0
Intervention					
6.	Intensity, strengths, or duration of intervention	ALL + antero-lateral capsular release; double portal; GA.	ALL + coagulation synovitis + cauterization retrodiscal tissue; double portal; GA	ALL + antero-lateral capsular release; cauterization retrodiscal tissue; double portal; GA	1
7.	Timing	Symptom duration 6.3 mo.; Pre-op: AS group conservative treatment first.**	Symptom duration 12-24 mo; Pre-op: anterior deprogrammer device	Symptom duration not reported; Pre-op: 6 mo of conservative treatment	2
8.	Control intervention	Arthrocentesis with 2 needles; LA; 200ml Ringer lactate	Arthrocentesis with 2 needles; LA; 200ml Ringer lactate	Arthrocentesis with 2 needles; LA; Ringer lactate	0
9.	Cointerventions	Betamethasone after procedures; Post-op: jaw exercises	Sodium hyaluronate after procedures; Post-op: jaw exercises, 2 weeks NSAIDs and muscle relaxants	Sodium hyaluronate after procedures; Post op: jaw exercises, 2 mo soft diet, 3 days antibiotics and NSAIDs	2

Appendix D.4. Clinical heterogeneity between studies involving arthroscopic surgery versus arthrocentesis for maximum mouth opening at intermediate follow-up using the CDIM tool. *Continued*

	Murakami et al. (1995)[18]	Hobeich et al. (2007)[20]	Atteya et al. (2020)[21]	Score
Outcome				
10. Definition of the outcome	MMO in mm	MMO in mm	MMO in mm	0
11. Timing of outcome	6 mo.	18-24 mo.	6 mo.	2
Total score				10

* Arthroscopic surgery was decided by choice or when the subjects were refractory to conservative treatment (1-2 weeks medication, then physiotherapy, then pivot splints for up to 12 weeks). Abbr.: OT operating theatre; MMO maximum mouth opening; ADD w/o R anterior disc displacement without reduction; ID internal derangement; ALL arthroscopic lysis and lavage; GA general anesthesia; mo. months; LA local anesthesia; NSAIDs non-steroidal anti-inflammatory drugs

Appendix D.5. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for maximum mouth opening at short-term follow-up using the CDIM tool.

		Tan et al. (2012)[24]	Xu et al. (2013)[25]	Rajpoot et al. (2021)[26]	Score
Setting					
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	2012 (A); developed country, Singapore (B); OT hospital (C)	2013 (A); developed country, China (B); probably OT hospital (C)	2021 (A); developed country, India (B); OT hospital (C)	0
Population					
2.	Mean age	34.6	36.6	34.6	0
3.	Sex	75% woman	75.6% woman	73.3% woman	0
4.	Inclusion criteria and baseline disease severity	Closed lock/ Painful click; baseline MMO 30.9mm	Anterior disc displacement; baseline MMO 25.1mm	ID; baseline MMO 25.8mm	1
5.	Comorbidities	Not reported	Not reported	Not reported	0
Intervention					
6.	Intensity, strengths, or duration of intervention	ALL + blind sweep; single portal; GA; 200ml Saline	Arthroscopic lavage; double portal; LA; 500ml Ringer lactate	Level 1 arthroscopy; single portal; anesthesia not reported; 300ml Ringer lactate	1
7.	Timing	Symptom duration 8.8 mo; Pre-op: 3-8 weeks NSAID/ muscle relaxant + splint for bruxism patients	Symptom duration not reported; Pre-op: not reported	Symptom duration 12.1 mo; Pre-op: not reported	2
8.	Control intervention	Arthrocentesis with 2 needles; LA; 200ml saline	Arthrocentesis with 2 needles; LA; 500ml Ringer lactate	Arthrocentesis with single puncture double needle; LA; 300ml Ringer lactate	1
9.	Cointerventions	Post-op: NSAIDs, physiotherapy and soft diet. Splint continuation.	Sodium hyaluronate after procedure; Post-op: not reported	Post-op: ice, antibiotics, analgesics, physiotherapy from 2nd week and 2 weeks soft diet	2

Appendix D.5. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for maximum mouth opening at short-term follow-up using the CDIM tool. *Continued*

		Tan et al. (2012)[24]	Xu et al. (2013)[25]	Rajpoot et al. (2021)[26]	Score
Outcome					
10.	Definition of the outcome	MMO in mm	MMO in mm	MMO in mm	0
11.	Timing of outcome	1 mo.	3 mo.	1 mo.	1
Total score					8

Abbr.: OT operating theatre; MMO maximum mouth opening; ID internal derangement; ALL arthroscopic lysis and lavage; GA general anesthesia; LA local anesthesia; mo. months; NSAIDs non-steroidal anti-inflammatory drugs.

Appendix D.6. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for maximum mouth opening at intermediate-term follow-up using the CDIM tool.

		Fridrich et al. (1996)[22]	Goudot et al. (2000)[23]	Rajpoot et al. (2021)[26]	Score
Setting					
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	1996 (A); developed country, USA (B), OT hospital (C)	2000 (A); developed country, Switzerland (B); probably OT hospital (C)	2021 (A); developed country, India (B); OT hospital (C)	1
Population					
2.	Mean age	31.0	Not reported	34.6	1
3.	Sex	100% woman	Not reported	73.3% woman	1
4.	Inclusion criteria and baseline disease severity	ADD w/ and wo/ R; baseline MMO 31.3mm	TMJ pain dysfunction* syndrome; baseline MMO 29.2mm	ID; baseline MMO 25.8mm	1
5.	Comorbidities	Not reported	Not reported	Not reported	0
Intervention					
6.	Intensity, strengths, or duration of intervention	ALL; dual portal; GA; Ringer lactate	ALL; single portal; GA; Ringer lactate	Level 1 arthroscopy; single portal; anesthesia not reported; 300ml Ringer lactate	0
7.	Timing	Symptom duration not reported. Pre-op: Treatment when refractory to NSAIDs, soft diet, moist heat, ice therapy, habit modification, physical therapy and occlusal appliance therapy	Symptom duration at least 6 mo., for the rest not reported Pre-op: 6 mo. of consulting, splint and physiotherapy, psychologic support	Symptom duration 12.1 mo; Pre-op: not reported	1
8.	Control intervention	Arthrocentesis with dual port; IVS; 120ml Ringer lactate;	Arthrocentesis with 2 needles; LA; 100-150ml saline.	Arthrocentesis with single puncture double needle; LA; 300ml lactated Ringer	1
9.	Cointerventions	Betamethasone flush after procedure; Post-op: full liquid to soft diet, jaw exercises, 4 weeks NSAIDs, splint continuation	Post-op: physiotherapy, 2 weeks soft diet,	Post-op: ice, antibiotics, analgesics, physiotherapy from 2nd week and 2 weeks soft diet	2

Appendix D.6. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for maximum mouth opening at intermediate-term follow-up using the CDIM tool. *Continued*

		Fridrich et al. (1996)[22]	Goudot et al. (2000)[23]	Rajpoot et al. (2021)[26]	Score
Outcome					
10.	Definition of the outcome	MMO in mm	MMO in mm	MMO in mm	0
11.	Timing of outcome	12.9 mo.	12 mo	6 mo.	2
Total score					10

*Internal derangement, muscular dysfunction and psycho-affective disorder Abbr.: OT operating theatre; ADD w/ R anterior disc displacement with reduction; ADD wo/R anterior disc displacement without reduction; MMO maximum mouth opening; TMJ temporomandibular joint; ID internal derangement; ALL arthroscopic lysis and lavage; GA general anesthesia; NSAIDs non-steroidal anti-inflammatory drugs; mo. months; IVS intravenous sedation; LA local anesthesia.

Appendix D.7. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for complication rates using the CDIM tool.

		Fridrich et al. (1996)[22]	Goudot et al. (2000)[23]	Tan et al. (2012)[24]	Xu et al. (2013)[25]	Talaat et al. (2022)[27]	Score
Setting							
1.	Years reported (A), performed in developed vs developing country (B), unit type (C)	1996 (A); developed country, USA (B), OT hospital (C)	2000 (A); developed country, Switzerland (B); probably OT hospital (C)	2012 (A); developed country, Singapore (B); OT hospital (C)	2013 (A); developed country, China (B); probably OT hospital (C)	2022 (A); developing country, Egypt (B); probably OT hospital (C)	1
Population							
2.	Age	31.0	Not reported	34.6	36.6	36.5	1
3.	Sex	100% woman	Not reported	75% woman	75.6% woman	67% woman	2
4.	Inclusion criteria and baseline disease severity	ADD w/ and wo/ R	TMJ pain dysfunction* syndrome;	Closed lock/ Painful click;	Anterior disc displacement;	ADD wo/ R and osteoarthritis;	1
5.	Comorbidities	Not reported	Not reported	Not reported	Not reported	Not reported	0
Intervention							
6.	Intensity, strengths, or duration of intervention	ALL; dual portal; GA; Ringer lactate	ALL; single portal; GA; Ringer lactate	ALL + blind sweep; single portal; GA; 200ml Saline	Arthroscopic lavage; double portal; LA; 500ml Ringer lactate	ALL, single portal; GA; 300ml saline	2
7.	Timing	Symptom duration not reported. Pre-op: Treatment when refractory to NSAIDs, soft diet, moist heat, ice therapy, habit modification, physical therapy and occlusal appliance therapy	Symptom duration at least 6 mo., for the rest not reported Pre-op: 6 mo. of consulting, splint and physiotherapy, psychologic support	Symptom duration 8.8 mo.; Pre-op: 3-8 weeks NSAID/ muscle relaxant + splint for bruxism patients	Symptom duration not reported; Pre-op: not reported	Symptom duration 16.6 mo.; Pre-op: 2 mo. conservative treatment of rest, soft diet, NSAIDS, physiotherapy and splints.	2

Appendix D.7. Clinical heterogeneity between studies involving arthroscopic lysis and lavage versus arthrocentesis for complication rates using the CDIM tool. *Continued*

		Fridrich et al. (1996)[22]	Goudot et al. (2000)[23]	Tan et al. (2012)[24]	Xu et al. (2013)[25]	Talaat et al. (2022)[27]	Score
Intervention							
8.	Control intervention	Arthrocentesis with dual port; IVS; 120ml Ringer lactate;	Arthrocentesis with 2 needles; LA; 100-150ml saline.	Arthrocentesis with 2 needles; LA; 200ml saline	Arthrocentesis with 2 needles; LA; 500ml Ringer lactate	Arthrocentesis with 1 needle; LA; 300ml saline	1
9.	Cointerventions	Betamethasone flush after procedure; Post-op: full liquid to soft diet, jaw exercises, 4 weeks NSAIDs, splint continuation	Post-op: physiotherapy, 2 weeks soft diet,	Post-op: NSAIDs, physiotherapy and soft diet. Splint continuation.	Sodium hyaluronate after procedure; Post-op: not reported	Sodium hyaluronate after procedures; Post-op: 3 days NSAIDs, 4 weeks exercise, splint 6 mo. when myogenous pain.	2
Outcome							
10.	Definition of the outcome	Number of complications	Number of complications	Number of complications	Number of complications	Number of complications	0
11.	Timing of outcome	Entire study**	Entire study**	Entire study**	Entire study**	Entire study**	0
Total score							12

* Internal derangement, muscular dysfunction and/or psycho-affective disorder. ** The latest follow-up difference was not relevant due to the assumption that complications occur during or immediately after treatment. Abbr.: OT operating theatre; ADD w/ R anterior disc displacement with reduction; ADD wo/R anterior disc displacement without reduction; TMJ temporomandibular joint; ALL arthroscopic lysis and lavage; GA general anesthesia; NSAIDs non-steroidal anti-inflammatory drugs; mo. months; IVS intravenous sedation; LA local anesthesia.

Appendix E. Trial sequential analyses involving arthroscopy versus arthrocentesis studies for pain scores, maximum mouth opening and complication rates.

Outcome	Total N/RIS	Crossed conventional boundary	Crossed O'Brien-Fleming boundary	Crossed futility boundary	Interpretation
Pain VAS (AS IFU)	104/15901	No	No	No	Inconclusive, potentially false neutral
Pain VAS (ALL SFU)	128/2897	No	No	No	Inconclusive, potentially false neutral
Pain VAS (ALL IFU)	92/1295	No	No	No	Inconclusive, potentially false neutral
MMO (AS IFU)	133/1061	No	No	No	Inconclusive, potentially false neutral
MMO (ALL SFU)	128/5727	No	No	No	Inconclusive, potentially false neutral
MMO (ALL IFU)	*111/73*	*Yes*	*Yes*	*No*	*Arthroscopy is superior to arthrocentesis*
Complication rates (ALL)	243/31074	No	No	No	Inconclusive, potentially false neutral

Abbr.: N sample size; RIS required information size; VAS visual analog scale; AS arthroscopic surgery; IFU intermediate-term follow-up; ALL arthroscopic lysis and lavage; SFU short-term follow-up; MMO maximum mouth opening.

Appendix F. Study records from which additional data was required and the corresponding contacted authors.

Author (year)	Reason for contact	Date of contact	Outcome of contact
Murakami et al. (1995)[18]	Study design unclear	26-01-2023	Received clarification about the study design
Fridrich et al. (1996)[22]	Standard deviations missing from the study outcomes	13-12-2022	Received relevant data regarding outcomes, but not for the meta-analysis
McNamara et al. (1996)[29]	Study outcomes only depicted in a figure	No contact due to unavailability of contact information	
Sanroman (2004)[19]	Study outcomes only depicted in figure	13-12-2022	No response
Schiffman et al. (2014)[30]	Mean + standard deviation missing from the study outcomes	13-12-2022	Database not available
Rajpoot et al. (2021)[26]	Standard deviations missing from the study outcomes	13-12-2022	Received the requested data with relevant data for the meta-analysis
Talaat et al. (2022)[27]	Short- and intermediate term study outcomes missing	13-12-2022 & 29-12-2022	No response

References of appendices

1. Ahmed N, Sidebottom A, O'Connor M, Kerr H. Prospective outcome assessment of the therapeutic benefits of arthroscopy and arthrocentesis of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2012;50:745-745.
2. Bare V. Temporomandibular joint arthroscopy: a new treatment alternative. *AORN J*. 1987;45(6):1368-1373.
3. Brignardello-Petersen R. Intra-articular injections of platelet-rich plasma may improve pain associated with temporomandibular disorders compared with arthrocentesis and arthroscopy. *J Am Dent Assoc*. 2018;149(2):e52. doi:10.1016/j.adaj.2017.11.012
4. Brignardello-Petersen R. Injection of platelet-rich fibrin probably reduces pain but not trismus when used after arthrocentesis or arthroscopy in patients with temporomandibular joint osteoarthritis. *J Am Dent Assoc*. 2019;150(5):e57.
5. González-García R, Gil-Díez Usandizaga J, Rodríguez-Campo F. Arthroscopic Anatomy and Lysis and Lavage of the Temporomandibular Joint. *Atlas Oral Maxillofac Surg Clin*. 2011;19:131-144.
6. Goudot P. La chirurgie articulaire dans le traitement des dysfonctions temporo-mandibulaires. *Orthod Fr*. 1998;69(1):61-67.
7. Hosgor H, Bas B, Celenk C. A comparison of the outcomes of four minimally invasive treatment methods for anterior disc displacement of the temporomandibular joint. *Int J Oral Maxillofac Surg*. 2017;46(11):1403-1410. doi:10.1016/j.ijom.2017.05.010
8. Indresano AT. Surgical arthroscopy as the preferred treatment for internal derangements of the temporomandibular joint. *J Oral Maxillofac Surg*. 2001;59(3):308-312. doi:10.1053/joms.2001.21001
9. Ohnuki T, Fukuda M, Nakata A, et al. Evaluation of the position, mobility, and morphology of the disc by MRI before and after four different treatments for temporomandibular joint disorders. *Dentomaxillofacial Radiol*. 2006;35(2):103-109. doi:10.1259/dmfr/25020275
10. Polso H, Näpänkangas R, Raustia A. Treatment Outcome In Patients with TMD – A Survey of 123 Patients Referred to Specialist Care. *Cranio*. 2010;28(3):156-165. doi:10.1179/crn.2010.022
11. Sahlström LE, Ekberg EC, List T, Petersson A, Eriksson L. Lavage treatment of painful jaw movements at disc displacement without reduction. A randomized controlled trial in a short-term perspective. *Int J Oral Maxillofac Surg*. 2013;42(3):356-363. doi:10.1016/j.ijom.2012.10.011
12. Sakamoto I, Yoda T, Tsukahara H, Imai H, Enomoto S. Comparison of the Effectiveness of Arthrocentesis in Acute and Chronic Closed Lock: Analysis of Clinical and Arthroscopic Findings. *Cranio*. 2000;18(4):264-271. doi:10.1080/08869634.2000.11746140
13. Schiffman E, Look J, Anderson Q, Jackson A. Arthrosis associated with four treatments for TMJ closed lock [Conference presentation abstract]. *2005 IADR/AADR/CADR General Session Baltimore Maryland, United States*.

14. Schiffman EL, Look JO, Hodges JS, et al. Randomized effectiveness study of four therapeutic strategies for TMJ closed lock. *J Dent Res.* 2007;86(1):58-63. doi:10.1177/154405910708600109

15. Stasko J, Statelova D, Janickova M, et al. Hyaluronic acid application vs arthroscopy in treatment of internal temporomandibular joint disorders. *Bratislava Med J.* 2020;121(5):352-357. doi:10.4149/BLL_2020_056

16. Tarro A. Clinical controversies in oral and maxillofacial surgery: surgical arthroscopy (part 1) or arthroscopic lysis and lavage (part 2) as the preferred treatment for internal derangement of the temporomandibular joint. *J Oral Maxillofac Surg.* 2001;59(8):962-963. doi:doi:10.1053/joms.2001.26043

17. Yoda T. Arthroscopic surgery and arthrocentesis of the temporomandibular joint - recent advances and long-term results. *J Med Dent Sci.* 1997;44:71-74.

18. Murakami KI, Hosaka H, Moriya Y, Segami N, Iizuka T. Short-term treatment outcome study for the management of temporomandibular joint closed lock. A comparison of arthrocentesis to nonsurgical therapy and arthroscopic lysis and lavage. *Oral Surgery, Oral Med Oral Pathol Oral Radiol.* 1995;80(3):253-257. doi:10.1016/S1079-2104(05)80379-8

19. Sanromán JF. Closed lock (MRI fixed disc): A comparison of arthrocentesis and arthoscopy. *Int J Oral Maxillofac Surg.* 2004;33(4):344-348. doi:10.1016/j.ijom.2003.10.005

20. Hobeich J, Salameh Z, Ismail E, Sadig W, Hokayem N, Almas K. Arthroscopy versus arthrocentesis: A retrospective study of disc displacement management without reduction. *Saudi Med J.* 2007;28(10):1541-1544.

21. Atteya A, Warda M, Fata M, Medra A, Monje F. Prospective randomized study between arthrocentesis and operative arthroscopy in the management of temporomandibular joint internal derangement. *Alexandria Dent J.* 2020;46(1):58-65. doi:10.21608/adjalexu.2020.25155.1051

22. Fridrich KL, Wise JM, Zeitler DL. Prospective comparison of arthroscopy and arthrocentesis for temporomandibular joint disorders. *J Oral Maxillofac Surg.* 1996;54(7):816-820. doi:10.1016/S0278-2391(96)90526-1

23. Goudot P, Jaquinet A, Hugonnet S, Haefliger W, Richter M. Improvement of pain and function after arthroscopy and arthrocentesis of the temporomandibular joint : a comparative study. *J Cranio-Maxillofacial Surg.* 2000;28:39-43. doi:10.1054/jcms.1998.0103

24. Tan DBP, Krishnaswamy G. A retrospective study of temporomandibular joint internal derangement treated with arthrocentesis and arthroscopy. *Proc Singapore Healthc.* 2012;21(1):73-78. doi:10.1177/201010581202100112

25. Xu Y, Lin H, Zhu P, et al. A comparative study between use of arthroscopic lavage and arthrocentesis of temporomandibular joint based on computational fluid dynamics analysis. *PLoS One.* 2013;8(11). doi:10.1371/journal.pone.0078953

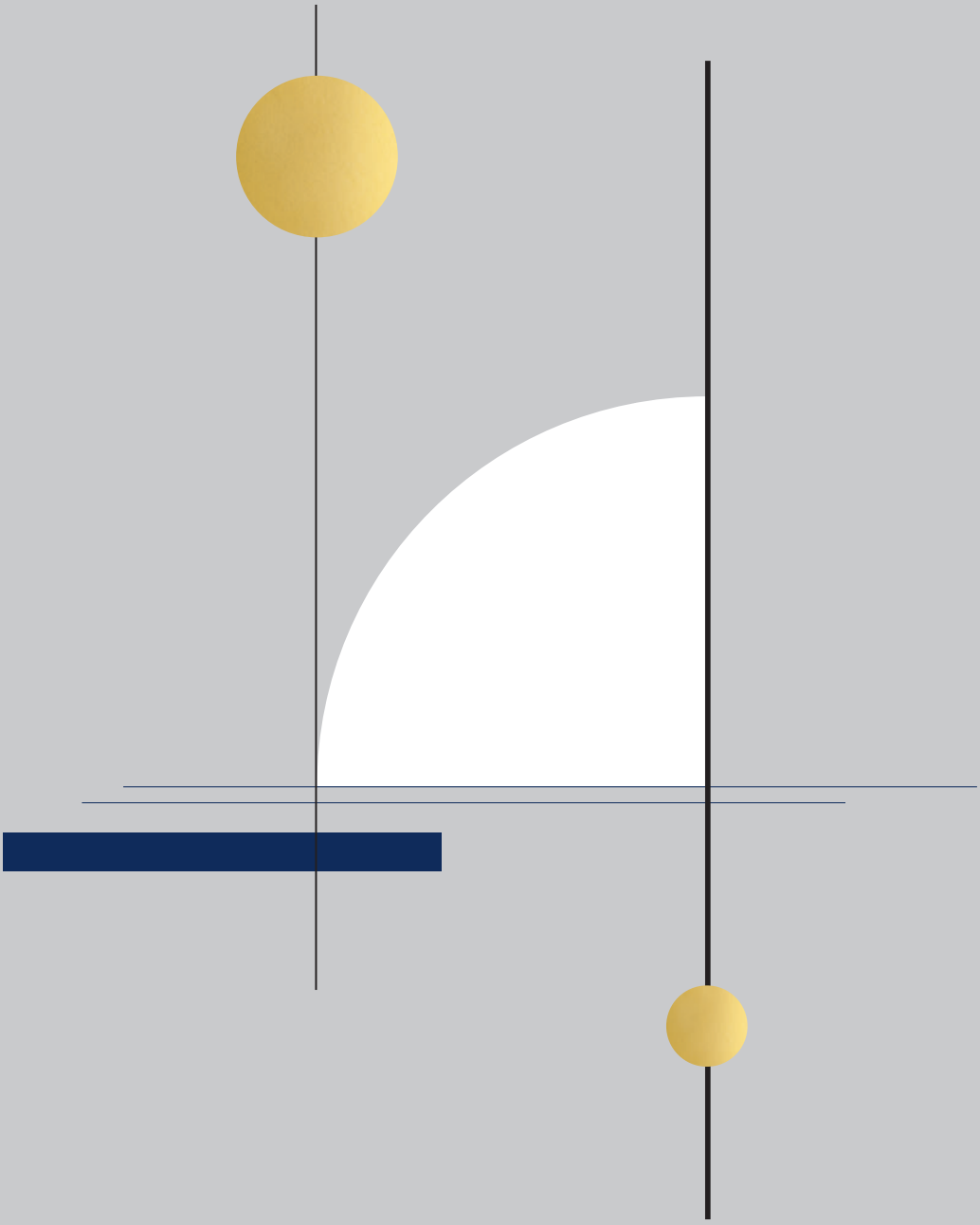
26. Rajpoot D, Anchlia S, Bhatt U, Dhuvad J, Patel H, Mansuri Z. Arthrocentesis versus level 1 arthroscopy in internal derangement of temporomandibular joint. *J Maxillofac Oral Surg.* 2023;22:94-101. doi:https://doi.org/10.1007/s12663-021-01627-9

27. Talaat W, Hamdoon Z, Ghoneim M. Minimally invasive surgeries for the treatment of temporomandibular disorders: Prognostic indicators and persistence of treatment outcomes over a 5-year follow-up. *Adv Biomed Heal Sci.* 2022;1(1):34-44.

28. Stegenga B, de Bont LGM, Dijkstra PU, Boering G. Short-term outcome of arthroscopic surgery of temporomandibular joint osteoarthrosis and internal derangement: A randomized controlled clinical trial. *Br J Oral Maxillofac Surg.* 1993;31(1):3-14. doi:10.1016/0266-4356(93)90089-F

29. McNamara DC, Rosenberg I, Jackson PA, Hogben J. Efficacy of arthroscopic surgery and midlaser treatments for chronic temporomandibular joint articular disc derangement following motor vehicle accident. *Aust Dent J.* 1996;41(6):377-387. doi:10.1111/j.1834-7819.1996.tb06023.x

30. Schiffman E, Velly A, Look J, et al. Effects of four treatment strategies for temporomandibular joint closed lock. *Int J Oral Maxillofac Surg.* 2014;43:217-226.



CHAPTER 6A

Comment on

"ARTHROSCOPY VERSUS ARTHROCENTESIS AND VERSUS CONSERVATIVE TREATMENTS FOR TEMPOROMANDIBULAR JOINT DISORDERS: A SYSTEMATIC REVIEW WITH META-ANALYSIS AND TRIAL SEQUENTIAL ANALYSIS"

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I read with great interest the recent article by Tang et al.[1] on the comparative efficacy of arthroscopy versus arthrocentesis and conservative treatments for temporomandibular joint (TMJ) disorders. This comprehensive systematic review and meta-analysis provides valuable insights into the relative benefits and limitations of these treatment modalities. However, I wish to highlight a critical aspect that was underexplored in the study: the long-term cost-effectiveness of these interventions.

TMJ disorders are known to impose significant economic burdens due to their chronic nature, which often necessitates prolonged treatment and multiple interventions. While Tang et al.[1] provided a robust analysis of clinical outcomes such as pain reduction and maximum mouth opening, the long-term economic implications of arthroscopy versus arthrocentesis and conservative treatments warrant further discussion.

In healthcare, cost-effectiveness is a pivotal factor influencing treatment decisions, especially for chronic conditions like TMJ disorders. The study by Tang et al.[1] mentions the lack of sufficient data to draw conclusions on cost-effectiveness. However, this aspect could be crucial in guiding both clinicians and patients towards more sustainable treatment options. For instance, while arthroscopy may offer superior short-term clinical outcomes, its higher upfront costs compared to arthrocentesis and conservative treatments might not justify its use unless it also demonstrates superior long-term cost benefits.

A previous study indicated that minimally invasive procedures like arthroscopy, despite higher initial costs, can potentially reduce long-term expenses by decreasing the need for repeated treatments and improving overall patient outcomes more effectively than conservative approaches[2]. However, these findings have been inconsistent, and more high-quality, long-term studies are needed to confirm these economic benefits. Specifically, the comprehensive assessment of costs, including those associated with rehabilitation and additional interventions, remains underexplored. Given that the cost of medical management is significantly lower compared to surgical interventions, incorporating cost–utility analyses in future research is essential.

Additionally, Tang et al.[1] rightly pointed out the heterogeneity in pre- and postoperative care regimens among the included studies. This variability significantly affects the overall cost and should be standardized in future research to enable a more accurate comparison of the economic impacts. For instance, incorporating

a uniform rehabilitation protocol could provide a clearer picture of the true costs associated with each treatment modality.

A possible approach to address this gap in the literature is to include a cost–utility analysis in future studies, which considers both the direct and indirect costs associated with each treatment option, along with quality-adjusted life years (QALYs). Such analyses would offer a more comprehensive understanding of the value provided by each treatment, beyond immediate clinical outcomes. This would be particularly beneficial in assessing the overall impact of treatments on patient quality of life, a factor that is often underrepresented in clinical studies but is crucial for chronic conditions.

Ethics approval and consent to participate

Not applicable.

Funding

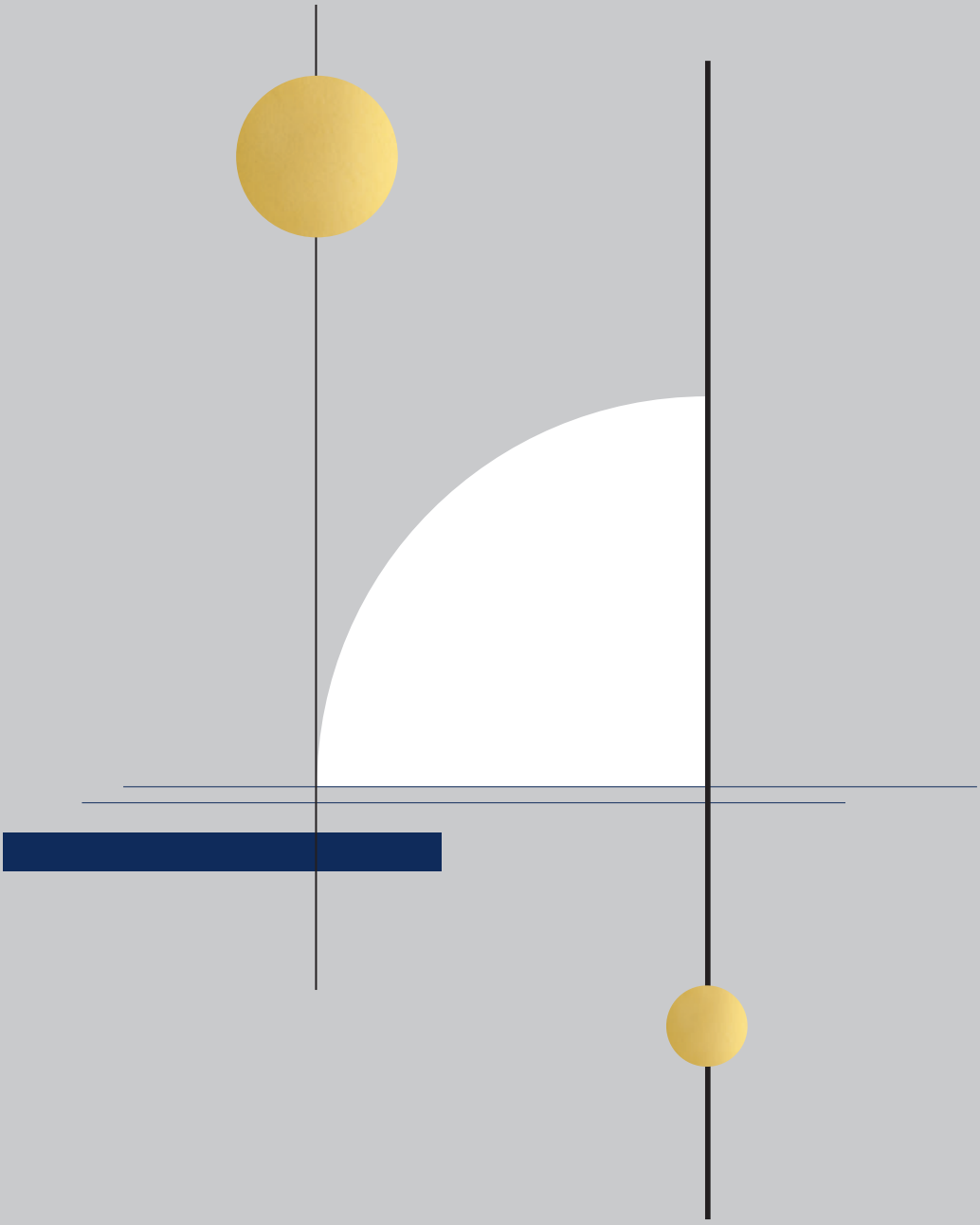
None.

Patient consent

Not required.

References

1. Tang Y, Bakelen N van, Gareb B, Spijkervet F. Arthroscopy versus arthrocentesis and versus conservative treatments for temporomandibular joint disorders: a systematic review with meta-analysis and trial sequential analysis. *Int J Oral Maxillofac Surg*. 2024;53:503-520.
2. Schiffman E, Velly A, Look J, et al. Effects of four treatment strategies for temporomandibular joint closed lock. *Int J Oral Maxillofac Surg*. 2014;43:217-226.



CHAPTER 6B

In reply to comment on

"ARTHROSCOPY VERSUS ARTHROCENTESIS AND VERSUS CONSERVATIVE TREATMENTS FOR TEMPOROMANDIBULAR JOINT DISORDERS: SYSTEMATIC REVIEW WITH META-ANALYSIS AND TRIAL SEQUENTIAL ANALYSIS"

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We would like to thank the reader for their interest in our systematic review on arthroscopy versus arthrocentesis and versus conservative treatments for temporomandibular joint (TMJ) disorders[1], as well as for drafting the valuable comments that are provided. The reader addresses the limited discussion of the long-term economic appraisal of treatments for TMJ disorders in our systematic review.

We fully agree that cost-effectiveness and cost–utility analyses are essential in a comprehensive evaluation of medical treatment modalities. Assessing the long-term costs of treatments against their potential health benefits or harms is necessary for making informed clinical decisions about optimal treatment choices. While we provided an overview of studies involving the costs and cost-effectiveness of treatments in the systematic review, we acknowledge that the economic aspects of the interventions and their clinical implications could have been discussed in greater detail. However, as also mentioned in our review, extensive economic appraisals of treatments in the field of TMJ disorders, like in other medical fields, are currently lacking.

Economic appraisals should encompass the direct medical costs associated with the treatments (e.g., medical equipment, operating room time, personnel) and indirect costs related to the disease (e.g., additional interventions or rehabilitation visits). In addition, current guidelines for economic evaluations in healthcare require evaluation of direct and indirect non-medical costs (e.g., productivity losses, travel expenses, and own contributions)[2]. Guidelines advocate for the use of standardized methods for registering these costs in clinical trials, such as the Productivity Cost Questionnaire (iPCQ) and the Medical Consumption Questionnaire (iMCQ) from the Institute for Medical Technology Assessment (iMTA)[3].

We support the statement of the reader that future clinical trials could enhance our understanding of the value of treatments by incorporating cost-effectiveness analyses based on clinical outcomes and cost–utility analyses based on quality-adjusted life years (QALYs). Of note, Vos et al.[4], from our institute, compared the cost-effectiveness of arthrocentesis with conservative treatments (i.e., physical therapy and splint therapy) in a randomized controlled trial . This study calculated the total cost-effectiveness per group and related this to TMJ pain and cost–utility in terms of QALYs. It was concluded that the total societal costs, including both direct and indirect medical and non-medical costs, were lower in the arthrocentesis group (mean costs of US $795) compared to the conservative treatment group (mean

costs of US $2266), while the health outcomes were also more favorable in the arthrocentesis group.

Indeed, the high heterogeneity between clinics in pre- and postoperative treatment regimens may influence health outcomes and overall cost evaluations. Conservative treatments employed before surgical interventions often vary between clinics, a factor frequently overlooked in study outcome evaluations. Furthermore, since there is ongoing debate about the ideal timing of subsequent surgical treatment, patients are currently subjected to varying lengths of conservative treatments prior to surgery. Therefore, we advocate for standardizing preoperative practices to gain a better understanding of treatment implications. For example, through a stepwise approach where treatments are employed for a standardized duration before initiating subsequent treatments. Simultaneously, we recognize the challenge of implementing uniform pre- and postoperative protocols due to an often needed patient-tailored treatment approach and differences in availability of financial resources between countries. Nevertheless, uniform practices are essential for producing more generalizable study results.

In conclusion, the currently available evidence may provide indications on the effectiveness of arthroscopy compared to arthrocentesis and to conservative treatments on health outcomes, but it only partially addresses the clinical and societal implications. Comprehensive economic appraisals of treatments for TMJ disorders require consideration before making definitive clinical decisions.

Ethics approval and consent to participate

Not applicable.

Funding

None.

Patient consent

Not required.

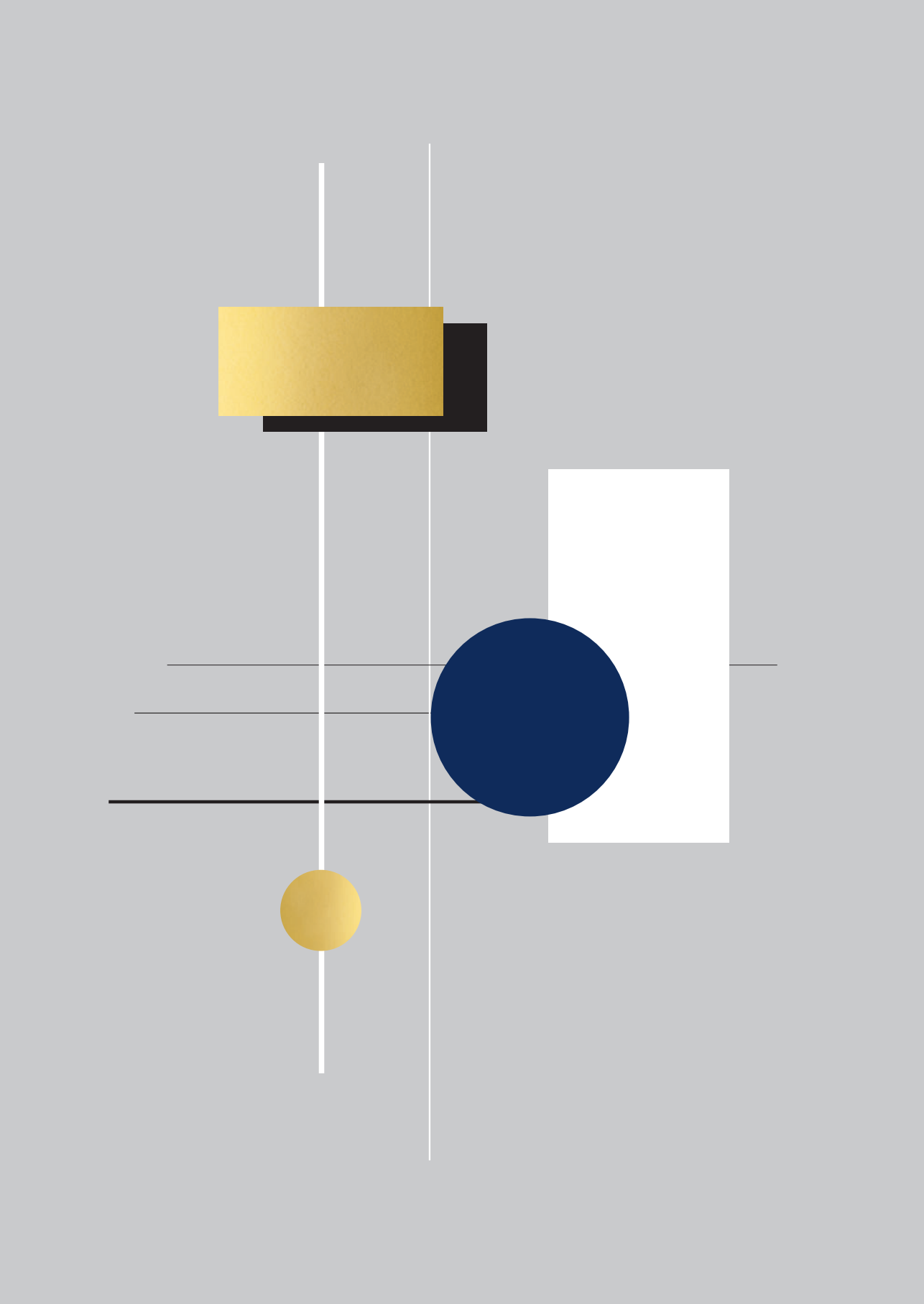
References

1. Tang Y, Bakelen N van, Gareb B, Spijkervet F. Arthroscopy versus arthrocentesis and versus conservative treatments for temporomandibular joint disorders: a systematic review with meta-analysis and trial sequential analysis. *Int J Oral Maxillofac Surg*. 2024;53:503-520.

2. Dutch Institute National Health Care (Zorginstituut Nederland). Guideline for economic evaluations in healthcare (2024 version). Zorginstituut Nederland. 2024. Accessed November 11, 2025. https://english.zorginstituutnederland.nl/documents/2024/01/16/guideline-for-economic-evaluations-in-healthcare

3. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Hakkaart-van Roijen L. The iMTA Productivity Cost Questionnaire: A Standardized Instrument for Measuring and Valuing Health-Related Productivity Losses.

4. Vos L, Stegenga B, Stant A, Quik E, Huddleston Slater J. Cost Effectiveness of Arthrocentesis Compared to Conservative Therapy for Arthralgia of the Temporomandibular Joint: A Randomized Controlled Trial. *J Oral Facial Pain Headache*. 2018;32(2):198-207. doi:10.11607/ofph.1457



CHAPTER 7

OFFICE-BASED ARTHROSCOPY VERSUS ARTHROCENTESIS AS TREATMENT FOR TEMPOROMANDIBULAR JOINT PAIN AND DYSFUNCTION

Preliminary results of a randomized controlled trial

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Abstract

Background/Objectives: Arthroscopy and arthrocentesis are routinely performed for temporomandibular joint (TMJ) disorders, but high-quality evidence regarding their efficacy relative to each other is scarce. The current study, as part of an ongoing randomized controlled trial, aimed to compare office-based arthroscopic lysis and lavage with arthrocentesis for TMJ pain and dysfunction. Methods: Adults (≥18 years old) referred to a tertiary care hospital with TMJ arthralgia were included. The exclusion criteria comprised systemic rheumatic disease, connective tissue disease, bony ankylosis, congenital or acquired dentofacial deformities, a history of significant jaw trauma, or systemic illnesses. The primary outcome was joint pain during mandibular movement/function (visual analog scale (VAS); 0–100 mm). The secondary outcomes included pain at rest (VAS), maximum mouth opening (mm), maximum mouth opening without increased pain (mm), protrusive and lateral movements (mm), joint noises (absent/present), and mandibular function (mandibular function impairment questionnaire score). The outcomes were registered at baseline and 3-, 6-, and 12-month follow-ups. Linear mixed models and mixed-effects logistic regressions were utilized to evaluate the effects of interventions on the repeated outcome measurements. Results: Twenty subjects were randomly allocated to office-based arthroscopic lysis and lavage (n = 10) or arthrocentesis (n = 10). Multivariable mixed-effects models showed significantly higher pain scores during mandibular movement/function in the arthrocentesis group compared with arthroscopy (22.42 mm (95% CI: 5.28 to 39.57); p = 0.011). The secondary outcomes were not significantly different between the interventions. Conclusions: The preliminary results show the superiority of office-based arthroscopy over arthrocentesis in reducing pain during mandibular movement/function over a follow-up period of 1 year while showing no differences between interventions regarding other study outcomes.

Introduction

Minimally invasive surgical therapies, such as arthroscopy and arthrocentesis, are frequently indicated for symptomatic temporomandibular joint (TMJ) disorders when conservative treatments fail to provide sufficient symptom relief[1]. Both procedures have demonstrated high effectiveness in symptom (i.e., pain and dysfunction) reduction, with reported success rates of approximately 80–90%[2–5].

Technological advancements have led to the differentiation of complexity and the possibility of reducing the invasiveness of arthroscopy. The successful development of office-based arthroscopy[6,7] under local anesthesia and arthrocentesis[8] has reduced the need for general anesthesia in initial surgical interventions following unsuccessful conservative treatments for TMJ pain and dysfunction.

Despite their routine use, the choice between arthroscopy and arthrocentesis remains debated and is often dictated by patient-specific factors and surgeon preferences. Arthroscopy offers the advantage of direct joint visualization for diagnostic purposes and the possibility for additional therapeutic maneuvers, while arthrocentesis is often preferred for its simplicity, lower invasiveness, and lower direct costs[3]. Notably, both procedures facilitate the adjuvant use of intra-articular injections, such as hyaluronic acid, which has been suggested to improve joint lubrication and, thus, clinical symptoms[9]. A recent systematic review found no significant difference between arthroscopy and arthrocentesis in reducing pain during mandibular movement, although the evidence was of low to very low quality. However, arthroscopic lysis and lavage was superior to arthrocentesis in maximum mouth opening (MMO) improvement at intermediate-term (6 months to 5 years) follow-up[10]. This review highlighted the lack of high-quality studies directly comparing these interventions. Only a handful of randomized controlled trials have assessed the efficacy of arthroscopic lysis and lavage versus arthrocentesis, with findings showing no significant differences between interventions in pain reduction[11,12]. However, these studies were performed over two decades ago, did not always report results sufficiently, and have a high risk of bias, highlighting the need for high-quality clinical trials to evaluate the efficacy of these treatments for TMJ pain and dysfunction.

The present study is part of an ongoing randomized controlled trial designed to assess the efficacy of office-based, single-portal arthroscopy versus arthrocentesis for the treatment of TMJ pain and dysfunction. Specifically, this study aimed to

evaluate post-operative TMJ pain, MMO, protrusive and lateral mandibular movements, joint noises, and patient-perceived mandibular functional impairment over a 1-year follow-up period.

Materials and methods

This study is reported according to the CONSORT 2010 statement and was conducted according to the principles of the Declaration of Helsinki (seventh version 2013, Fortaleza, Brazil) and the Dutch 'Medical Research Involving Human Subjects Act' (WMO).

Clinical Trial Design

A mono-center, parallel-group randomized controlled trial was performed at the University Medical Center Groningen (UMCG), the Netherlands, a tertiary care hospital. The trial was registered at the International Clinical Trials Registry Platform and the Overview of Medical Research in the Netherlands (NL-OMON20171) with the study acronym DIAMOND-trial. A pre-specified protocol was finalized before the trial initiation. Ethical approval was given by the Institutional Review Board of the UMCG (METc 2021/275), and all subjects signed informed consent forms prior to the start of study-related procedures.

Study Population

All study subjects were recruited at the outpatient clinic of the Department of Oral and Maxillofacial Surgery of the UMCG. Patients referred for the management of TMJ disorders were screened for inclusion in this study. The inclusion criteria were subjects of 18 years and older with unilateral symptoms of TMJ arthralgia (or bilateral symptoms in which the non-surgically treated joint had a pain score of <30 mm on a visual analog scale (VAS; scale: 0–100 mm)), proven with a diagnostic intra-articular injection with articaine (4%) and epinephrine (1:100,000)[13], and the presence of TMJ arthralgia after two weeks of non-steroidal anti-inflammatory drugs (NSAIDs) to exclude acute inflammatory pain. The exclusion criteria were subjects suffering from systemic rheumatic diseases, connective tissue disease, bony ankylosis of the TMJ, congenital or acquired dentofacial deformities, a history of jaw trauma that resulted in jaw or joint pain, bony changes or mandibular growth restrictions, a psychiatric disorder, or a medical comorbidity, such as coagulation disorders, diabetes mellitus, kidney failure, cardiac ischemia or failure, or a history of human immunodeficiency virus. Furthermore, subjects were excluded from participating when they had received prior TMJ surgery, were unwilling to participate, did not

speak English or Dutch, were pregnant, or used concurrent steroids, sedatives, muscle relaxants, or anti-inflammatory drugs other than the prescribed NSAIDs.

Sample Size Calculation

Prior to the study commencement, an estimation of sample size was performed based on a two-sided α of 0.05, power of 0.80, 3 follow-up measurements, an estimated ρ of 0.5, and an effect size f of 0.41 (based on a 10 mm pain VAS as a clinically relevant difference, as determined by the authors)[14]. The required sample size was estimated to be a total of 140 subjects after accounting for a 10% margin for dropouts. Since no proper effect sizes of office-based arthroscopy are available in the literature, an a priori-determined interim analysis was conducted after the inclusion of 10 subjects per arm, with a final follow-up of 1 year to obtain the most reliable effect sizes for a sample size re-calculation. Data received from unlocking the database for the purpose of sample size recalculation were used for the current study.

Study Procedures

All study subjects were randomly allocated (1:1 ratio) to either the intervention (arthroscopy) or control (arthrocentesis) group by the surgeon using a web-based randomization tool (ALEA clinical, version 18.7, FormsVision BV, Abcoude, The Netherlands) after signing the informed consent forms. Block randomization with random block sizes was performed for the distribution of subjects between the groups. Allocation concealment was ensured due to the central randomization process, thereby preventing the operators from deducing the allocation sequence. The treatment assignment was revealed to the operator immediately prior to the procedures via an email sent by the randomization software, preventing any influence on patient enrollment or baseline assessment. The researcher analyzing the data was blinded to the treatment allocation.

Subjects underwent radiographic assessment using cone-beam computed tomography (CBCT) for intra-operative orientation purposes and evaluation of the extent of pre-treatment bony changes observed. The evaluation of the CBCT images and degenerative joint disease (DJD) diagnoses was based on the classification of the Diagnostic Criteria for Temporomandibular Dysfunction (DC/TMD), as described by Ahmad et al.[15]. The anterior disc displacement (ADD) diagnostic categories were based on patient histories and clinical examinations, as described in the DC/TMD[16].

All procedures were performed under local anesthesia by two experienced TMJ surgeons (FKLS and NBvB). Arthroscopy was performed with a single portal. Prior to the procedure, the TMJ was locally anesthetized with articaine (4%) with epinephrine (1:100,000). Thereafter, an 18-gauge needle was inserted in the posterior recess of the superior joint space, 10–12 mm anterior to the mid-tragus, and 0.9% saline was used to insufflate this joint space. The first needle was replaced by a 1.9 mm diameter cannula with a sharp trocar to enter the joint. Next, the sharp trocar was replaced by a blunt obturator for further joint advancement. A 1.2 mm diameter arthroscope (OnPointTM Scope System; Zimmer Biomet, Warsaw, IN, USA) was then introduced into the cannula to allow the visualization of the articular space. A second 18-gauge needle was then introduced into the joint space as an outflow tract, 7–10 mm anteriorly and 7–10 mm caudally from the first insertion needle. After a diagnostic sweep, the outflow needle was used to cut intra-articular adhesions and/or to inject 0.5 mL of methylprednisolone (40 mg/mL subsynovially) into the inflamed tissue, if present and surgically possible. During the arthroscopy, an attempt was made to lavage the joint with a minimum of 100 mL of 0.9% saline. For the arthrocentesis, two 18-gauge needles were introduced into the upper joint space, in the same locations as during the arthroscopy, after locally anesthetizing the TMJ. Similar to the arthroscopic procedure, an attempt was made to flush a minimum of 100 mL of 0.9% saline through the joint once communication was established. No additional drugs or substances were applied. Following both procedures, a strict soft diet protocol was recommended for six weeks.

Outcome Measures

The primary study outcome was pain during mandibular movement and/or function using the VAS (range: 0–100 mm). The secondary study outcomes included pain at rest using the VAS (range: 0–100 mm), the maximum incisal mouth opening in millimeters using a sliding caliper (MMO; interincisal distance), the MMO without perceiving (increased) pain in millimeters using a sliding caliper, protrusive and lateral mandibular movements in millimeters using a dental probe, joint noises in the last month (present/absent), and the impairment of mandibular function using the validated mandibular function impairment questionnaire (MFIQ; 17 items scored on a Likert scale; score: 0–100)[17].

Outcome measurements were registered at baseline and at each post-operative follow-up control (3, 6, and 12 months) by the operating surgeon and analyzed by a blinded researcher (YHT). MFIQ was registered through digitally sent questionnaires at baseline and each follow-up. In the arthroscopy group, the number of subjects

who underwent adhesiolysis and/or subsynovial corticosteroid injections was recorded. Additionally, data were collected for cases where subjects did not receive adhesiolysis or corticosteroid injections, as well as instances where adhesions or synovitis were absent, respectively. Any additional treatment during follow-up was registered.

Statistical Analysis

The baseline characteristic registration included gender, age, diagnosis, the duration of symptoms that were so significant that help from a healthcare provider was sought, the total duration of symptoms, and the lavage volume during treatment.

The results were analyzed using the intention-to-treat principle. Continuous variables with a normal distribution were reported as means and standard deviations (SDs) and compared with the unpaired Student's t-test, whereas non-normally distributed variables were presented as medians with first and third quartiles (Q1–Q3) and compared using the Mann–Whitney U test. The normality of the data was evaluated through visual Q–Q plot inspection and the Shapiro–Wilk test. The categorical variables were expressed as frequencies and percentages and analyzed using Fisher's exact test. The abovementioned analyses were performed in IBM SPSS statistics for Windows, version 28 (IBM Corp., Armonk, NY, USA).

As primary statistical analyses, linear mixed models and mixed-effects logistic regression were applied to evaluate the effects of the interventions on the repeated outcome measurements. The multivariable models involved fixed effects for the treatment group and the follow-up in days. The study subjects were included as random effects. Additionally, the fixed interactions between the treatment group and time and/or the random effect of time were only included in the model if the multivariable model was significantly improved. Model improvement was tested using likelihood ratio tests. All models with continuous outcomes yielded an estimated regression coefficient (β) with a corresponding 95% confidence interval (95% CI). For outcome measures with dichotomous outcomes, odds ratios with a 95% CI were also calculated. All of the mixed-effects models were performed in R, version 4.0.5 (R Core team; R Foundation for Statistical Computing, Vienna, Austria), using the lme4 package[18]. A p-value of ≤0.05 (two-tailed) was considered statistically significant.

Results

The first 10 study subjects per study arm of the ongoing trial were enrolled between January 2022 and May 2023 and analyzed after a total follow-up completion time of 1 year. No study subjects were lost to follow-up (**Figure 1**). In the arthroscopy group, all subjects were females, with a mean age of 45.0 years (17.2). The median duration of symptoms that were so significant that help from a healthcare provider was sought was 4.0 months (2.4–10.5), while the median total duration of symptoms was 15.0 months (3.8–47.3). In the arthrocentesis group, 80% of subjects were female, with a mean age of 36.7 (15.3). The median duration of symptoms that were so significant that help from a healthcare provider was sought was 10.5 months (6.0–15.0), while the median total duration of symptoms was 15.0 months (9.8–48.0) (**Table 1**). The diagnosis of each study subject and the baseline outcome values are described in **Table 1**.

In each study arm, additional treatments were performed on three subjects during the follow-up period. In the arthroscopy group, two subjects received corticosteroid injections against the articular capsule, and one subject received arthroscopic surgery under general anesthesia 6 months after the initial treatment. In the arthrocentesis group, all three subjects who underwent an additional treatment received an office-based, single-portal arthroscopy under local anesthesia. During the initial arthroscopy, adhesiolysis was successfully performed in 4 subjects (40%). In 2 subjects (20%), surgical adhesiolysis was not feasible, while 4 subjects (40%) showed no visible intra-articular adhesions. With respect to subsynovial corticosteroid injections, this procedure was successfully carried out in 3 subjects (30%). However, in 6 subjects (60%), the injection could not be performed surgically, and in 1 subject (10%), no synovitis was observed.

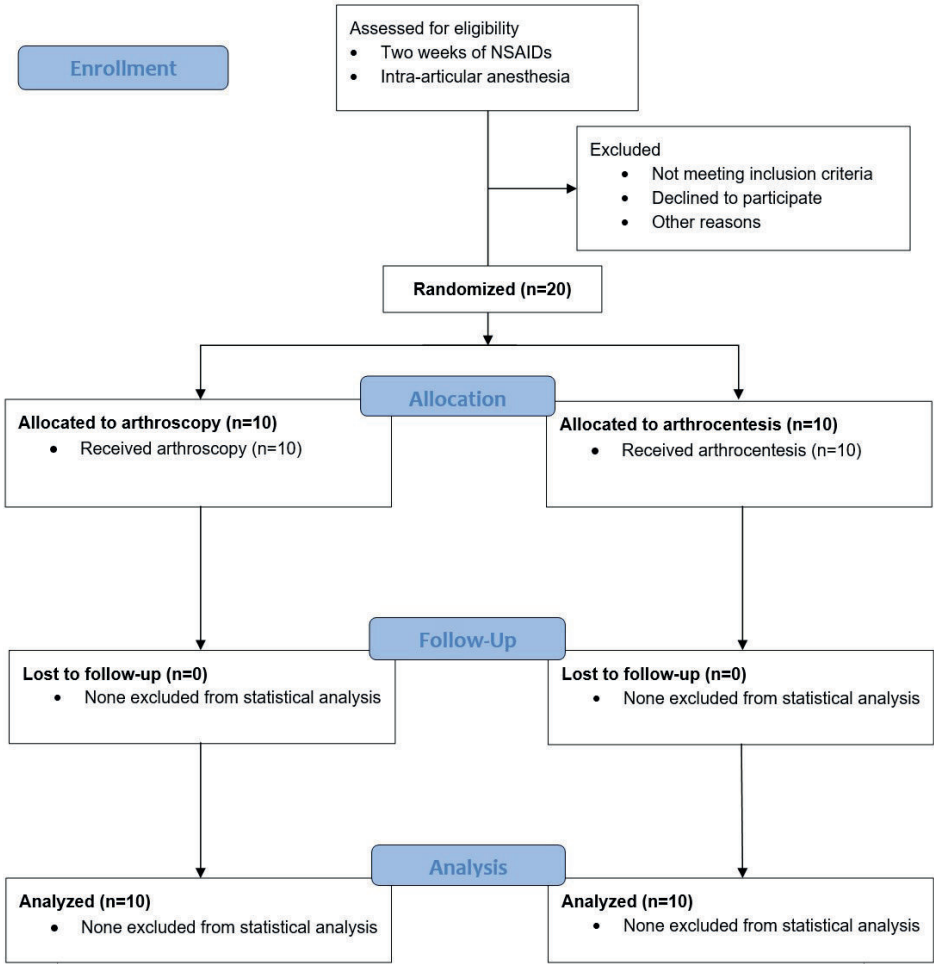

Figure 1. CONSORT flow diagram of subject enrolment, allocation, and follow-up. All subjects allocated to the treatment groups completed follow-up and were included in the analyses.

Table 1. Baseline characteristics.

Characteristics	*Arthroscopy*	*Arthrocentesis*
Sample size, n	10	10
Female, n (%)	10 (100)	8 (80)
Age (years), mean (SD)	45.0 (17.2)	36.7 (15.3)
Duration of symptoms that required healthcare provider assistance (months), median (Q1-Q3)	4.0 (2.4-10.5)	10.5 (6.0-15.0)
Total duration of symptoms (months), median (Q1-Q3)	15.0 (3.8-47.3)	15.0 (9.8-48.0)
ADD, n (%)		
No ADD	1 (10)	1 (10)
ADDwR	2 (20)	0 (0)
ADDwR with intermittent locking	2 (20)	1 (10)
ADDwoR with limited mouth opening	4 (40)	8 (80)
ADDwoR without limited mouth opening	1 (10)	0 (0)
DJD, n (%)		
No DJD	1 (10)	2 (20)
Indeterminate for DJD	1 (10)	0 (0)
Evidence for DJD	8 (80)	8 (80)
Lavage volume during treatment (ml), mean (SD)	380.0 (71.5)	332.5 (131.3)
Pain during mandibular movement (mm), mean (SD)	67.0 (10.6)	67.0 (16.4)
Pain at rest (mm), median (Q1-Q3)	0.0 (0.0-0.0)	0.0 (0.0-17.5)
MMO without (increase in) pain (mm), mean (SD)	29.6 (6.5)	30.7 (5.2)
MMO (mm), mean (SD)	33.3 (6.5)	36.2 (5.4)
Protrusive movement (mm), mean (SD)	6.2 (2.0)	5.6 (1.7)
Ipsilateral movement (mm), mean (SD)	9.2 (2.2)	7.4 (2.8)
Contralateral movement (mm), mean (SD)	7.2 (2.8)	7.4 (2.7)
MFIQ-score, mean (SD)	57.9 (11.8)	61.6 (10.9)
Joint noises present, n (%)	5 (50)	6 (60)

Abbr.: n number of patients; SD standard deviation; Q1-Q3 first and third quartiles; ADD anterior disc displacement; ADDwR anterior disc displacement with reduction; ADDwoR anterior disc displacement without reduction; DJD degenerative joint disease; MMO maximum mouth opening; MFIQ mandibular function impairment questionnaire.

Table 2. Results of study outcomes registered at each follow-up.

Study outcome	Follow-up (months)	Post-operative change scores^		*p*
		Arthroscopy	*Arthrocentesis*	
Pain during mandibular movement (mm)	3	-25.0 (-15.0 to -62.5)*	0.0 (12.5 to 0.0)*	**0.005**
	6	-35.5 (32.2)#	-6.0 (15.1)#	**0.021**
	12	-47.5 (23.0)#	-21.5 (25.2)#	**0.027**
Pain at rest (mm)	3	0.0 (0.0 to 0.0)*	0.0 (2.5 to -2.5)*	0.796
	6	0.0 (0.0 to 0.0)*	0.0 (10.0 to -10.0)*	0.529
	12	0.0 (0.0 to 0.0)*	0.0 (2.5 to -2.5)*	1.000
MMO without increase in pain (mm)	3	2.1 (3.8)#	4.2 (8.0)#	0.465
	6	5.2 (3.6)#	3.5 (10.7)#	0.640
	12	10.2 (7.0)#	5.6 (9.3)#	0.228
MMO (mm)	3	2.4 (4.0)#	1.4 (5.5)#	0.646
	6	5.0 (4.0)#	3.4 (8.8)#	0.607
	12	10.5 (6.7)#	4.3 (9.0)#	0.098
Protrusive movement (mm)	3	0.3 (-1.3 to 1.0)*	0.0 (-1.0 to 2.5)*	0.829
	6	0.5 (-0.8 to 1.4)*	1.0 (-0.5 to 3.5)*	0.549
	12	0.5 (0 to 2.3)*	0.0 (-2.0 to 2.5)*	0.905
Ipsilateral movement (mm)	3	0.5 (-1.5 to 2.3)*	2.0 (-1.5 to 2.5)*	0.905
	6	0.0 (-1.0 to 0.3)*	1.5 (1.0 to 3.0)*	**0.007**
	12	0.5 (-1.0 to 1.8)*	0.0 (-1.3 to 2.3)*	0.579
Contralateral movement (mm)	3	0.5 (-2.5 to 2.0)*	-0.5 (-2.5 to 1.5)*	0.661
	6	0.2 (2.7)#	0.6 (3.6)#	0.807
	12	1.7 (2.2)#	-0.6 (3.8)#	0.123
MFIQ-score	3	-13.7 (20.3)#	-8.8 (24.1)#	0.632
	6	-17.7 (27.3)#	-10.6 (17.7)#	0.501
	12	-37.2 (21.8)#	-11.9 (19.4)#	**0.013**
Study outcome	**Follow-up (months)**	**Post-operative scores**		***p***
		Arthroscopy	*Arthrocentesis*	
Joint noises present, n(%)	3	7 (70)	6 (60)	>0.999
	6	7 (70)	8 (80)	>0.999
	12	9 (90)	7 (70)	0.582

Abbr.: MMO maximum mouth opening; MFIQ mandibular function impairment questionnaire; n number of patients. ^ = Pre-operative score subtracted from the post-operative score, * = Median (first and third quartiles), # = Mean (standard deviation).

Table 3. Linear mixed model results of clinical study outcome.

Outcome	Predictors	Estimates	95% CI	*p*
Pain during mandibular movement (n= 20)				
	FU (weeks)	-0.60	-0.80 to -0.40	**<0.001**
	Treatment (ref= AS)	22.42	5.28 to 39.57	**0.011**
Pain at rest in mm (n= 20)				
	FU (weeks)	0.00	-0.11 to 0.12	0.961
	Treatment (ref= AS)	8.50	-2.68 to 19.68	0.134
MMO without pain in mm (n= 20)				
	FU (weeks)	0.13	0.08 to 0.18	**<0.001**
	Treatment (ref= AS)	0.03	-4.48 to 4.53	0.990
MMO in mm (n= 20)				
	FU (weeks)	0.13	0.09 to 0.18	**<0.001**
	Treatment (ref= AS)	0.63	-3.78 to 5.04	0.775
Protrusive movement in mm (n= 20)				
	FU (weeks)	0.02	0.01 to 0.03	**0.006**
	Treatment (ref= AS)	-0.24	-1.67 to 1.19	0.740
Ipsilateral movement in mm (n= 20)				
	FU (weeks)	0.01	-0.01 to 0.04	0.308
	Treatment (ref= AS)	-1.36	-3.08 to 0.36	0.119
Contralateral movement in mm (n= 20)				
	FU (weeks)	0.02	-0.01 to 0.04	0.145
	Treatment (ref= AS)	-0.14	-1.70 to 1.42	0.861
MFIQ-score (n= 20)				
	FU (weeks)	-0.39	-0.55 to -0.24	**<0.001**
	Treatment (ref= AS)	12.94	-0.58 to 26.46	0.060
Outcome	**Predictors**	**OR**	**CI**	***p***
Joint noises, present or absent (n= 20)				
	FU (weeks)	1.00	1.00 to 1.01	**0.048**
	Treatment (ref= AS)	0.82	0.09 to 7.40	0.856

Abbr.: CI Confidence interval; n number of patients; FU follow-up; ref reference; AS arthroscopy; MMO maximum mouth opening; MFIQ mandibular function impairment questionnaire; OR odds ratio.

The results of each outcome variable at each follow-up are presented in **Table 2**. The multivariable mixed models show significantly higher pain scores during movement and/or function in the arthrocentesis group compared with arthroscopy (22.42 mm (95% CI: 5.28 to 39.57)) (**Table 3**). The secondary outcomes were not significantly different between interventions (**Table 3**). Additionally, a significant improvement over time was observed for the outcomes of pain during movement and/or function, MMO without an increase in pain, MMO, protrusive movements, joint noises, and MFIQ scores, regardless of the treatment employed (**Table 3**).

One adverse event was registered in the arthroscopy group, which involved the perforation of the external acoustic meatus with the outflow needle. The procedure was stopped immediately after the flushing of saline into the external acoustic meatus was observed. The puncture hole resolved within a few days on its own without any sequelae. Two weeks later, a successful arthroscopy was performed on the same subject.

Discussion

This study, as part of an ongoing randomized controlled trial, aimed to investigate the efficacy of office-based arthroscopy compared with arthrocentesis for TMJ pain and dysfunction (i.e., painful ADD with/without reduction and DJD). The preliminary results of the trial indicate that arthroscopy was more efficacious in reducing pain during mandibular movement and/or function than arthrocentesis during the 12-month follow-up. No significant differences between the interventions were observed for the secondary outcomes (i.e., pain at rest, MMO without an increase in pain, MMO, protrusive and lateral movements, joint noises, and MFIQ scores).

It has been reported in a previous study that patients with temporomandibular dysfunction may show a large improvement in general health when an absolute pain reduction of 9–19 mm is achieved[19]. Therefore, the magnitude of the pain reduction observed between both treatments over the entire follow-up (22.4 mm on a 0–100 mm VAS) in the current study indicates both a significant and clinically relevant difference. Alternatively, a reduction in the chronic pain VAS score of 10–20% indicates a minimally clinically important difference, while a 30% reduction indicates a moderate difference clinically[20]. Considering the baseline pain scores in the current study of 67.0 mm (**Table 1**), the 33% difference between groups over the entire follow-up further emphasizes the clinically relevant difference.

A proposed mechanism for pain reduction in both arthrocentesis and arthroscopy is the washing out of pro-inflammatory cytokines and matrix-degrading enzymes responsible for the inflammatory response and subsequent pain[21–23]. However, since both arthroscopy and arthrocentesis allow the lavage of the upper joint space, this mechanism alone may not account for the superior effect in pain reduction with arthroscopy. Some studies suggest that factors, such as the lavage volume[21,24] and the duration of symptoms before the initial treatment[25], may influence the treatment outcomes. Alternatively, the superior efficacy of arthroscopy in pain reduction may be partly explained by the subsynovial corticosteroid injections performed during the procedure, which have recently been shown to be an effective maneuver for symptom reduction[26,27]. However, in this study, only three of the ten subjects undergoing arthroscopy received a corticosteroid injection, either because there was no synovitis present or it was surgically unfeasible to perform the injection. The final results will provide further clarification of the relationship in the current trial between the lavage volume, the duration of symptoms, and the subsynovial injection of corticosteroids and pain reduction.

The treatment choice did not appear to have a statistically significant effect on MMO improvement in the current study sample, despite the superiority of arthroscopy in pain reduction and its potential for the targeted lysis of intra-articular adhesions that might restrict mouth opening. These findings indicate that arthrocentesis may be similarly effective in addressing the mechanical intra-articular causes of restricted mouth opening, or that other factors may have played a role, such as secondary muscle contractures after a prolonged period of MMO restriction[28].

A cautious interpretation of the current findings in a clinical context is warranted due to the preliminary nature of this study. Moreover, beyond health outcomes alone, several additional factors are crucial for a comprehensive evaluation of medical interventions. First, economic assessments in relation to potential health benefits are necessary to support clinicians in making optimal treatment choices. The cost-effectiveness of both treatments (based on the primary study outcome and the total costs, and on the MFIQ score and the total costs) will be evaluated and presented after the final study's completion. Furthermore, the implementation of surgical treatments requires the consideration of the learning curve and the resources required for proper training. For example, performing TMJ arthroscopy requires extensive experience and specialized training to achieve expertise[29], which can limit its widespread adoption. Finally, the treatment choice should consider the additional diagnostic capabilities of arthroscopy that are absent in arthrocentesis.

Arthroscopy allows the direct visualization of the internal joint structures, enabling a more accurate understanding of pathological processes and guiding future treatment decisions if the initial surgery is unsuccessful.

A limitation of the current study was the lack of patient blinding, which may have influenced the perception and reporting of subjective patient-reported outcomes, such as pain. However, achieving effective blinding in interventional studies where procedures are performed without general anesthesia presents significant challenges. In the current study, attempts were made to blind the subjects as much as possible by using disposable sterile surgical sheets during the procedure and by using similar operating theatre set-ups. Nevertheless, subjects may have been able to identify their treatment allocation from procedure-specific maneuvers, rendering complete blinding unfeasible. Furthermore, since the current results are based on only a portion of the final sample size, the results are underpowered and may be subject to type-II errors (i.e., false-negative findings). Lastly, the single-center nature of this study, which is being conducted at a tertiary referral center, may limit the generalizability of the findings to the broader population of patients with TMJ disorders. Future studies incorporating a multicenter design would enhance the external validity and, thus, increase the generalizability.

One of the main strengths of the current study lies in its rigorous design, characterized by randomized subject enrolment and researcher blinding. Additionally, the a priori-determined sample size allows this study to be the first one comparing arthroscopy with arthrocentesis that achieves sufficient statistical power. The inclusion of a comprehensive set of patient outcomes allowed a comprehensive interpretation of the clinical effects of the treatments. The use of the MFIQ as a patient-reported outcome measure provided an accurate assessment of each patient's health status, free from clinician interpretation. Furthermore, mixed-models analysis allowed the longitudinal evaluation of outcomes after both interventions.

Conclusively, these preliminary results suggest a superiority of office-based arthroscopy over arthrocentesis in reducing pain during mandibular movement and/or function for the treatment of TMJ pain and dysfunction after 12 months of follow-up. No differences between the interventions were observed regarding the outcomes of pain at rest, MMO, protrusive and lateral movements, joint noises, and mandibular function. More definitively, better-powered results will be published after the completion of the trial.

Author contributions

Conceptualization, YHT, NBvB and FKLS; **methodology**, YHT, NBvB and BG; **software**, YHT and BG; **validation**, YHT and BG; **formal analysis**, YHT and BG; **investigation**, YHT, NBvB and FKLS; **resources**, YHT, NBvB and FKLS; **data curation**, YHT; **writing—original draft preparation**, YHT; **writing—review and editing**, YHT, NBvB, BG and FKLS; **visualization**, YHT and BG; **supervision**, NBvB, BG and FKLS; **project administration**, YHT and NBvB. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the University Medical Center Groningen, the Netherlands (METc 2021/275; date of approval: 30 August 2021).

Informed Consent Statement

Informed consent was obtained from all subjects involved in this study.

Conflicts of Interest

The authors declare no conflicts of interest.

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References

1. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain*. 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5
2. Israel HA. Intra-articular operative temporomandibular joint arthroscopy. *Front Oral Maxillofac Med*. 2021;3. doi:10.21037/fomm-20-34
3. Laskin DM. Arthroscopy Versus Arthrocentesis for Treating Internal Derangements of the Temporomandibular Joint. *Oral Maxillofac Surg Clin North Am*. 2018;30(3):325-328. doi:10.1016/j.coms.2018.04.008
4. Monje-Gil F, Nitzan D, González-Garcia R. Temporomandibular joint arthrocentesis. Review of the literature. *Med Oral Patol Oral Cir Bucal*. 2012;17(4). doi:10.4317/medoral.17670
5. Tang Y, Vos L, Tuin A, et al. Arthrocentesis versus non- surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. *Int J Oral Maxillofac Surg*. 2023;52:595-603.
6. Hossameldin RH, McCain JP. Outcomes of office-based temporomandibular joint arthroscopy: a 5-year retrospective study. *Int J Oral Maxillofac Surg*. 2018;47(1):90-97. doi:10.1016/j.ijom.2017.06.025
7. Weedon S, Ahmed N, Sidebottom AJ. Prospective assessment of outcomes following disposable arthroscopy of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2013;51(7):625-629. doi:10.1016/j.bjoms.2013.06.004
8. Nitzan D, Dolwick M, Martinez G. Temporomandibular joint arthrocentesis: A simplified treatment for severe, limited mouth opening. *J Oral Maxillofac Surg*. 1991;49(11):1163-1167. doi:10.1016/0278-2391(91)90409-F
9. Santagata M, De Luca R, Lo Giudice G, et al. Arthrocentesis and sodium hyaluronate infiltration in temporomandibular disorders treatment. Clinical and MRI evaluation. *J Funct Morphol Kinesiol*. 2020;5(1). doi:10.3390/jfmk5010018
10. Tang Y, Bakelen N van, Gareb B, Spijkervet F. Arthroscopy versus arthrocentesis and versus conservative treatments for temporomandibular joint disorders: a systematic review with meta-analysis and trial sequential analysis. *Int J Oral Maxillofac Surg*. 2024;53:503-520.
11. Goudot P, Jaquinet A, Hugonnet S, Haefliger W, Richter M. Improvement of pain and function after arthroscopy and arthrocentesis of the temporomandibular joint : a comparative study. *J Cranio-Maxillofacial Surg*. 2000;28:39-43. doi:10.1054/jcms.1998.0103
12. Fridrich KL, Wise JM, Zeitler DL. Prospective comparison of arthroscopy and arthrocentesis for temporomandibular joint disorders. *J Oral Maxillofac Surg*. 1996;54(7):816-820. doi:10.1016/S0278-2391(96)90526-1
13. Tjakkes GHE, TenVergert EM, De Bont LGM, Stegenga B. The effect of intra-articular injection of ultracain in the temporomandibular joint in patients with preauricular pain: A randomized prospective double-blind placebo-controlled crossover study. *Clin J Pain*. 2007;23(3):233-236. doi:10.1097/AJP.0b013e31802f0950

14. Vos L, Huddleston Slater J, Stegenga B. Arthrocentesis as initial treatment for temporomandibular joint arthropathy: A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2014;42(5):e134-e139. doi:10.1016/j.jcms.2013.07.010

15. Ahmad M, Hollender L, Anderson Q, et al. Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD): Development of Image Analysis Criteria and Examiner Reliability for Image Analysis. 2009;107(6):844-860. doi:10.1016/j.tripleo. 2009.02.023.

16. Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: Recommendations of the International RDC/TMD Consortium Network* and Orofacial Pain Special Interest Group. *J oral facial pain headache*. 2014;38(1):6-27.

17. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*. 1993;7(2):183-195.

18. Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4 | Bates | Journal of Statistical Software. *J Stat Softw*. 2015;67(1):1-48.

19. Calixtre L, Oliveira A, Alburquerque-Sendin F, Armijo-Olivo S. What is the minimal important difference of pain intensity, mandibular function, and headache impact in patients with temporomandibular disorders? Clinical significance analysis of a randomized controlled trial. *Musculoskelet Sci Pract*. 2020;46:2020.

20. Dworkin R, Turk D, Wyrwich K, et al. Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. *J pain*. 2008;9(2):105-121.

21. Kaneyama K, Segami N, Nishimura M, Sato J, Fujimura K, Yoshimura H. The ideal lavage volume for removing bradykinin, interleukin-6, and protein from the temporomandibular joint by arthrocentesis. *J Oral Maxillofac Surg*. 2004;62(6):657-661. doi:10.1016/j.joms.2003.08.031

22. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006

23. Celotti C, Martin-Granizo R, De La Sen O. Correlation of arthroscopic findings with clinical–radiological signs and symptoms of temporomandibular joint dysfunction: retrospective study of 829 joints. *Int J Oral Maxillofac Surg*. 2022;51:1069-1073.

24. Tsui HC, Lam CM, Leung YY, Li KY, Wong NSM, Li DTS. Lavage Volume of Arthrocentesis in the Management of Temporomandibular Disorders: A Systematic Review and Meta-Analysis. *Diagnostics*. 2022;12(11). doi:10.3390/diagnostics12112622

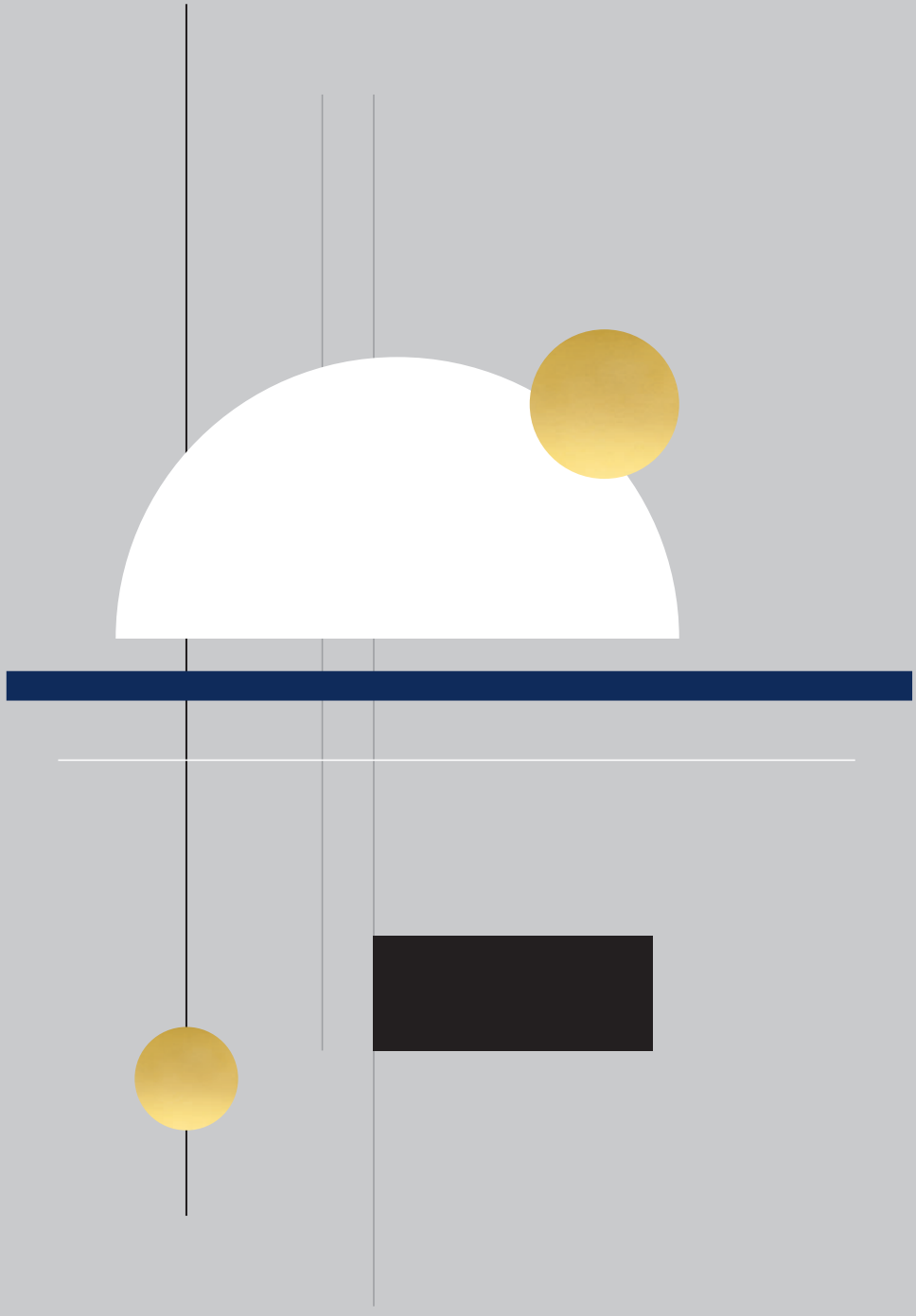
25. Emshoff R, Rudisch A. Determining predictor variables for treatment outcomes of arthrocentesis and hydraulic distention of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62(7):816-823. doi:10.1016/j.joms.2003.12.020

26. Martins I, Radaic P, Marchi L, Barreto G, Pastore G. Assessment of postoperative pain in patients undergoing temporomandibular joint arthroscopy with infiltration of dexamethasone disodium phosphate in different concentrations. A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2023;51(2):89-97.

27. Oren D, Dror A, Khalil T, et al. Comparisons between lysis and lavage, intra-articular steroid injections, and three-point subsynovial steroid injections using operative single-cannula arthroscopy d A retrospective analysis Daniel. *J Cranio-Maxillofacial Surg*. 2022;50(4):336-342.

28. Sidebottom A. How do I manage restricted mouth opening secondary to problems with the temporomandibular joint? *Br J Oral Maxillofac Surg*. 2012;51:469-472.

29. Bruning L, Rosner Y, Meisgeier A, Neff A. Arthroscopic Assessment of Temporomandibular Joint Pathologies—Is It Possible for Non-Specialists in Arthroscopy? Analysis of Variability and Reliability of Dental Students' Ratings after a Comprehensive One-Semester Introduction. *J Clin Med*. 2024;13(3995).



CHAPTER 8

RETREATMENT OUTCOMES AFTER UNSUCCESSFUL TEMPOROMANDIBULAR JOINT ARTHROCENTESIS

A two-decade cohort study

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Submitted

Abstract

When arthrocentesis for temporomandibular joint (TMJ) disorders provides insufficient symptom relief, retreatment involves non-surgical treatment, re-arthrocentesis, arthroscopy, open joint surgery or total joint replacement. The optimal retreatment strategy after unsuccessful initial arthrocentesis remains unclear. This retrospective cohort study assessed 5-year retreatment outcomes after unsuccessful initial arthrocentesis in adults with TMJ arthralgia. The primary outcome was patient-reported success at 5 years, defined as adequate perceived treatment without further intervention need. The secondary outcomes were retreatment prevalence and associated success rates. Of 438 subjects, 136 (31%) received retreatment and were included. Retreatment was successful in 114 (83%) subjects. Additional retreatments beyond the first one, regardless of treatment type, was not associated with success after 5 years (OR 1.00 (95% CI 0.95-1.06); p=0.879). Longer symptom duration before initial arthrocentesis was associated with lower retreatment success (OR 0.985 per month (95% CI 0.976-0.994); p= <0.001). Success rates did not differ between arthroscopic lysis and lavage, arthroscopic surgery or open joint surgery compared to re-arthrocentesis as retreatment. Conclusively, first retreatments may contribute to success, but additional retreatments offer limited benefit. As retreatment type does not significantly influence outcomes, decisions should be individualized. Moreover early arthrocentesis seems essential for improving outcome and preventing disease progression.

Introduction

Temporomandibular joint (TMJ) disorders represent a common group of disorders affecting approximately one third of the general population[1]. Symptoms like pain and dysfunction, although not always present, can significantly impair quality of life by affecting daily functions such as eating, speaking and laughing[2]. Among the various treatment modalities, arthrocentesis is widely accepted for patients unresponsive to conservative, non-surgical treatment management[3].

Despite its effectiveness[4,5], initial arthrocentesis does not always result in adequate symptom relief. In these situations, further interventions, such as re-arthrocentesis, arthroscopy or open joint surgery can be performed to manage symptoms. Currently, there is a significant variability among clinics regarding the timing and choice of these subsequent interventions. Decisions are often guided by clinician expertise and patient factors rather than standardized, evidence-based guidelines, highlighting the need for robust studies to optimize treatment strategies. A clearer understanding of retreatment outcomes may help guide more consistent, evidence-based decision-making and support individualized management strategies.

Although the topic is clinically relevant, the current literature lacks sufficient data regarding the outcomes and prevalence of necessary retreatments following unsuccessful initial arthrocentesis. Previous studies showed beneficial effect regarding pain improvement and maximum mouth opening improvement for repeated arthroscopy after unsuccessful arthroscopic surgery[6,7]. However, research investigating the entire spectrum of subsequent treatments following unsuccessful initial treatments for TMJ disorders remains scarce. To our knowledge, no previous study has comprehensively investigated the outcomes of retreatments for TMJ disorders after unsuccessful initial arthrocentesis.

The present study aims to evaluate whether the number and type of retreatments (i.e., re-arthrocentesis, arthroscopy, open-joint surgery, and total joint replacement) are associated with patient-reported success at 5-year follow-up among TMJ arthralgia patients who experienced insufficient symptom relief following initial arthrocentesis. In addition, the prevalence of retreatments and their associated success rates are examined.

Methods

Study design

All study participants of this retrospective cohort study were treated at the University Medical Center Groningen (UMCG), the Netherlands, a tertiary referral center and expertise center for TMJ surgery. Medical records of study subjects who had undergone TMJ arthrocentesis at least five years prior were reviewed retrospectively and consecutively, starting with the most recent cases and progressing chronologically backward.

Study population

All participants included in the current cohort were 18 years and older and received a surgical retreatment after an unsuccessful initial arthrocentesis at the Department of Oral and Maxillofacial Surgery of the UMCG. The initial arthrocentesis was performed for TMJ-arthralgia, which was proven with a diagnostic intra-articular injection with articaine (4%) and epinephrine (1:100,000)[8]. Individuals were excluded if they had systemic rheumatic or connective tissue disorders, bony ankylosis, congenital or acquired dentofacial deformities, limited mouth opening that was not arthralgia related or previous trauma leading to jaw or TMJ pain, bony changes or growth impairments. Additionally, subjects were excluded if they had surgical treatment of the joint prior to the initial arthrocentesis or the documentation regarding symptom duration or follow-up data were lacking.

Outcome measures

The primary outcome was the patient-reported success of the overall retreatment trajectory at 5-year follow-up. Success was defined as the patient's subjective feeling of sufficient therapeutic benefit and the absence of a need for further interventions. The secondary outcomes included the prevalence of each retreatment and the associated patient-reported success rates. Subsequent treatments were categorized as re-arthrocentesis, level I arthroscopic lysis and lavage (ALL), arthroscopic surgery (AS), open joint surgery (OJ; i.e., condylectomy, or (gap)arthroplasty) and total joint replacement (TJR).

Statistical analysis

The normality of continuous variables was assessed using visual inspection of Q-Q plots and the Shapiro-Wilk test. The non-normally distributed data were described as medians with first and third quartiles (Q1–Q3). Characteristics comparisons

between the successfully and unsuccessfully retreated group were performed using the Mann-Whitney U test and the Chi-squared or Fisher's Exact test.

The overall 5-year success rates and retreatment prevalence and corresponding success rates were presented as frequencies and percentages. Generalized estimating equations (GEE) models were employed to assess the effect of number of retreatments and type of retreatments on patient-reported success at 5-year follow-up while accounting for repeated measurements per subject over time. In addition, since primarily the duration of symptoms was associated with treatment success in this cohort[9], this predictor was also included in the model as prognostic factor. Additional retreatments were included as time-varying variables, accounting for the specific timing and sequence at which they were performed during follow-up. The concordance index (C-index) was calculated to assess the model's discriminatory performance.

Results of the GEE model were presented as odds ratios with corresponding 95% confidence interval (95% CI). Statistical analyses were conducted using R, version 4.5.0 (R Core team; R Foundation for Statistical Computing, Vienna, Austria), using the geepack package[10]. A two-tailed p-value of ≤0.05 was considered statistically significant.

Results

From the total cohort of 691 patient records dated between March 2000 and March 2020, 438 patients were initially treated with arthrocentesis. Of these, 136 (31.1%) underwent retreatment within 5 years and were included in the current study. Among the retreated subjects, 114 (83.8%) reported treatment success at 5-year follow-up. Baseline characteristics of the retreatment subgroup are depicted in **table 1**.

Results from the GEE model (C-index = 0.696) indicate that additional retreatments beyond the first, regardless of treatment type, did not significantly change patient-reported success at 5-year follow-up (OR 1.00 (95% CI 0.95-1.06); p= 0.879). Furthermore, ALL (OR 0.98 (95% CI 0.88-1.07); p= 0.603), AS (OR 1.03 (95% CI 0.92-1.16); p= 0.598) or OJ (OR 0.99 (95% CI 0.86-1.13); p= 0.846) compared to re-arthrocentesis as retreatment were not associated with improved success. Lastly, the duration of symptoms prior to the initial arthrocentesis was significantly

negatively associated with retreatment success at 5-year follow-up (OR 0.985 per month (95% CI 0.976-0.994); p= <0.001) **(Table 2)**.

Table 1. Characteristics of retreated patients.

	Total (*n= 136*)	**Successful (*n= 114*)**	**Unsuccessful (n= 22)**	***p***
Male, *n (%)*	11 (8.1)	10 (8.8)	1 (4.5)	1.000
Age in years, median (Q1-Q3)	36 (24-51)	34 (24-51)	43 (25-57)	0.239
Duration of symptoms in months, median (Q1-Q3)	23.5 (12.0-60.0)	22.0 (11.75-42.25)	76.0 (12.3-132.0)	**0.012**
Diagnosis				
ADDwR, *n (%)*	31 (22.8)	27 (23.7)	4 (18.2)	0.573
ADDwoR, *n (%)*	48 (35.3)	43 (37.7)	5 (22.7)	0.178
DJD, *n (%)*	60 (44.1)	48 (42.1)	12 (54.5)	0.282

Abbr.: Q1-Q3 first to third quartile; ADDwR anterior disc displacement with reduction; ADDwoR anterior disc displacement without reduction; DJD degenerative joint disease.

Table 2. Results of generalized estimating equations on patient-reported success.

Predictor	**OR (95% CI)**	***p***
Number of retreatments	1.00 (0.95–1.06)	0.879
Retreatment type (ref = AC)		
ALL	0.98 (0.88–1.07)	0.603
AS	1.03 (0.92–1.16)	0.598
OJ	0.99 (0.86–1.13)	0.846
Duration of symptoms	0.985 (0.976–0.994)	**<0.001**

Concordance index = 0.696. Abbr.: OR odds ratio; 95% CI 95% confidence interval; AC re-arthrocentesis; ALL arthroscopic lysis and lavage; AS arthroscopic surgery; OJ open joint surgery, N_{re} retreated subjects, N_{total} subjects in total cohort.

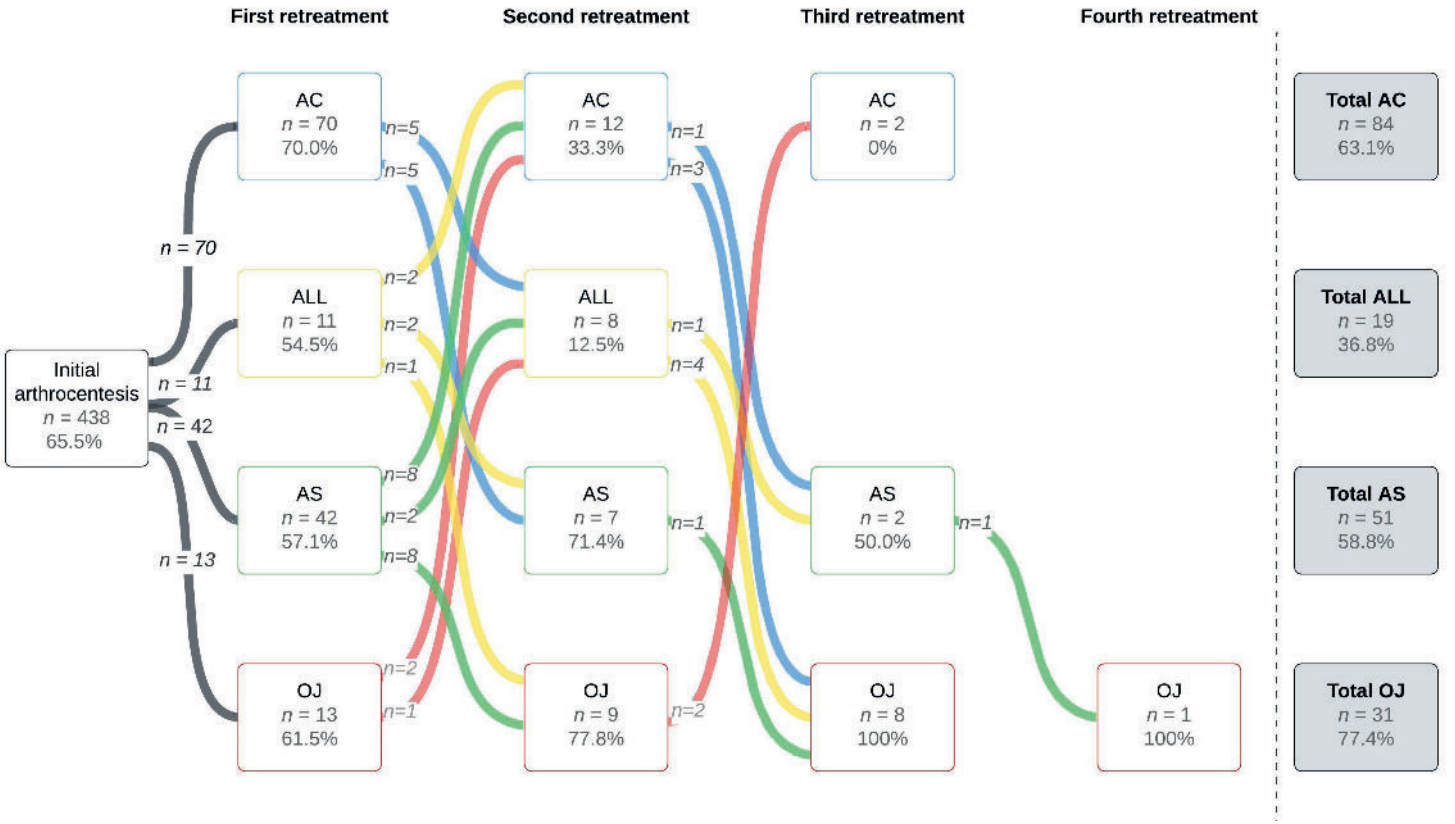

Figure 1. Sequential retreatment pathways and success rates in retreatment cohort. Each box represents a (re)treatment modality with corresponding sample size and success rates. Note: no total joint replacements within 5 years after initial arthrocentesis in study sample.
Abbr.: AC: re-arthrocentesis, ALL arthroscopic lysis and lavage; AS arthroscopic surgery; OJ open joint surgery, n number of retreated subjects.

The retreatment course differed between subjects, with a variety in number, type and sequences of procedures performed (**Figure 1)**. Re-arthrocentesis (*n*= 84) was the most commonly employed retreatment after unsuccessful initial arthrocentesis and was successful in 53 (63.1%) of the subjects. ALL was performed as retreatment in 19 subjects, from which 7 (36.8) experienced adequate symptom relief. AS was performed in 51 subjects, from which 30 (58.8%) resolved symptoms. OJ was performed in 31 subjects, from which 24 (77.4) resolved symptoms **(Figure 1).** Finally, no TJR was performed in all the subjects within the first 5 years after initial arthrocentesis. The sequential retreatment pathways and success rates of retreatment types are depicted in **figure 1**.

Discussion

This study assessed the outcomes of retreatments after unsuccessful initial arthrocentesis over a two-decade period. Within 5 years after initial arthrocentesis, 31.1% of the patients received a retreatment. From the retreated subjects, 83.3% achieved adequate symptom relief at 5-year follow-up. Symptoms were resolved with re-arthrocentesis in 63.1% of cases, ALL in 36.8%, AS in 58.0% and OJ in 77.4% of the cases. No patient progressed to TJR within 5 years following unsuccessful initial arthrocentesis.

Additional retreatments beyond the first, regardless of type, did not significantly affect the likelihood of treatment success at 5-year follow-up. Clinically, this suggests that the benefit of further retreatments after an unsuccessful first one may be limited, potentially because these patients are more likely to present with more severe and chronic conditions. Similar findings were reported previously, indicating that while arthroscopy may reduce the percentage of patients requiring open TMJ surgery, it may also lower the success rates of subsequent treatments when compared to patients who did not receive arthroscopy[11].

Furthermore, ALL, AS or OJ as retreatment modalities provided similar outcomes compared to re-arthrocentesis. The absence of a clear superior retreatment modality supports the current recommendation of a stepwise treatment approach, beginning with the least invasive option in most cases[3]. The lack of significant effect for retreatment type may reflect indication bias, where more invasive treatments are typically reserved for patients with more advanced disease, potentially masking their true efficacy. The findings that neither additional retreatments beyond the first nor the specific retreatment type significantly influenced treatment outcome highlight

the importance of an individualized approach for retreatment selection guided by patient preference, anatomical factors and clinician judgement.

Although data regarding retreatment efficacy after unsuccessful arthrocentesis remains scarce, the findings of the current study align with previous studies indicating successful retreatment outcomes following unsuccessful arthroscopy[6,7,12]. Several factors have been implicated to potentially influence the responsiveness of patients to initial arthrocentesis, such as the symptom duration[9]. Furthermore, the preoperative disease severity[13,14] and the extent of bony changes in the condyle[15] may also impact outcomes. Additionally, improper selection of patients, surgeon experience, post-operative complications and improper postoperative care have all been identified as potential contributors to treatment failure[14].

In the current GEE model, a longer symptom duration was significantly associated with lower treatment success at 5-year follow-up, consistent with previous findings[9]. These results support previous reports highlighting the importance of timely intervention[16–18]. In this context, retreatments cannot 'correct for' the negative effects of a delayed initial arthrocentesis. Combined with the observed limited benefit of additional retreatments, these findings suggest that the window of opportunity for recovery may be early in the disease process.

One limitation of the current study was its retrospective design, which relied on the accuracy and completeness of patient records. In addition, because retreatment orders were individualized for each patient, this may have introduced a degree of selection bias, where more subjects with more severe symptoms received more invasive treatments. Furthermore, while retreatment number and type were analyzed using GEE, the low number of subjects who did not achieve success at 5-year follow-up disallowed detailed analysis about particular treatment sequences and timing between procedures, or the addition of more predictor variables in the statistical model. Given the complexity and heterogeneity between treatment trajectories and clinical decisions made, current conclusions should be considered hypothesis-generative rather than conclusive. Furthermore, it needs to be acknowledged that the patient-reported outcome measure is subjective in nature and may be vulnerable to bias. However, the use of this outcome with robust analyses allows proper insights for the clinical practice, where clinicians often rely on patient feedback to guide their decision-making process. On the other hand, notable strengths of the study include the substantial patient population and the long-term follow-up period, allowing meaningful, population-level insights on the long-term.

Future studies should ideally be performed with a prospective, multi-center design to facilitate larger sample sizes. This approach would enhance generalizability of the results and allows more detailed analyses of retreatment types, specific treatment sequences and patient subgroups to whom this applies to. This would allow a deeper understanding of the treatment strategies and enables more personalized decision-making. Lastly, the use of standardized, objective and subjective outcomes measures, such as the interincisal maximum mouth opening, pain scores and the validated, quantifiable, patient-reported outcome Mandibular Function Impairment Questionnaire (MFIQ)[19], is necessary to allow cross-institutional comparisons and interpretations.

Conclusively, retreatments following initial arthrocentesis for TMJ disorders occur in roughly 31% of patients. From the retreated subjects, 83.8% reported treatment success at 5-year follow-up. While first retreatments may contribute to patient-reported success on the long-term, further retreatments appear to have limited benefit. The window of opportunity for recovery may, therefore, be early in the disease process. Given that retreatment type does not significantly impact success, decisions on retreatments should be individualized based on patient and surgeon factors, next to considerations about treatment invasiveness, resources and costs. Early intervention is essential for improving treatment outcome and preventing disease progression toward chronicity.

Ethical Approval

This study was carried out and documented while adhering to the principles of the International Conference on Harmonization Good Clinical Practice (ICH-GCP) and the Declaration of Helsinki (seventh version 2013, Fortaleza, Brazil). Ethical approval was given by the central ethics review board of the University Medical Center Groningen, the Netherlands (research registration number 20477).

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References

1. Valesan L, Da-Cas C, Réus J, et al. Prevalence of temporomandibular joint disorders: a systematic review and meta-analysis. *Clin Oral Investig.* 2021;25(2):441-453. doi:10.1007/s00784-020-03710-w
2. Almoznino G, Zini A, Zakuto A, et al. Oral health-related quality of life in patients with temporomandibular disorders. *J oral facial pain headache.* 2015;29(4):231-241. doi:10.11607/ofph.1413
3. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain.* 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5
4. Monje-Gil F, Nitzan D, González-Garcia R. Temporomandibular joint arthrocentesis. Review of the literature. *Med Oral Patol Oral Cir Bucal.* 2012;17(4). doi:10.4317/medoral.17670
5. Tang Y, Bakelen N van, Gareb B, Spijkervet F. Arthrocentesis versus conservative treatments for temporomandibular joint disorders: A systematic review with meta-analyses and trial sequential analyses. *J Craniomaxillofac Surg.* 2025;53:250-261.
6. Martin Granizo R, Correa Muñoz DC, Varela Reyes E. Rearthroscopy of the temporomandibular joint: A retrospective study of 600 arthroscopies. *J Cranio-Maxillofacial Surg.* 2018;46(9):1555-1560. doi:10.1016/j.jcms.2017.12.007
7. Mancha de la Plata M, Muñoz-Guerra M, Escorial Hernandez V, Martos Diaz P, Gil-Diez Usandizaga JL, Rodriguez-Campo FJ. Unsuccessful Temporomandibular Joint Arthroscopy: Is a Second Arthroscopy an Acceptable Alternative? *J Oral Maxillofac Surg.* 2008;66(10):2086-2092. doi:10.1016/j.joms.2008.06.043
8. Tjakkes GHE, TenVergert EM, De Bont LGM, Stegenga B. The effect of intra-articular injection of ultracain in the temporomandibular joint in patients with preauricular pain: A randomized prospective double-blind placebo-controlled crossover study. *Clin J Pain.* 2007;23(3):233-236. doi:10.1097/AJP.0b013e31802f0950
9. Tang Y, Bakelen N van, Gareb B, Spijkervet F. (In Press). Timing of arthrocentesis and its association with treatment success in painful temporomandibular joint disorders: a two-decade cohort study. *Int J Oral Maxillofac Surg.* Published online nov 2025.
10. Højsgaard S, Halekoh U, Yan J. The R package geepack for generalized estimating equations. *J Stat Softw.* 2006;15(2):1-11. doi:10.18637/jss.v015.i02
11. Tzanidakis K, Sidebottom AJ. Outcomes of open temporomandibular joint surgery following failure to improve after arthroscopy: Is there an algorithm for success? *Br J Oral Maxillofac Surg.* 2013;51(8):818-821. doi:10.1016/j.bjoms.2013.04.013
12. Ângelo DF, Sanz D, Cardoso HJ. Bilateral arthroscopy of the temporomandibular joint: clinical outcomes and the role of a second intervention—a prospective study. *Clin Oral Investig.* 2023;27(10):6167-6176. doi:10.1007/s00784-023-05233-6
13. Breik O, Devrukhkar V, Dimitroulis G. Temporomandibular joint (TMJ) arthroscopic lysis and lavage: Outcomes and rate of progression to open surgery. *J Cranio-Maxillofacial Surg.* 2016;44(12):1988-1995. doi:10.1016/j.jcms.2016.09.017

14. Vega LG, Gutta R, Louis P. Reoperative Temporomandibular Joint Surgery. *Oral Maxillofac Surg Clin North Am*. 2011;23(1):119-132. doi:10.1016/j.coms.2010.12.001

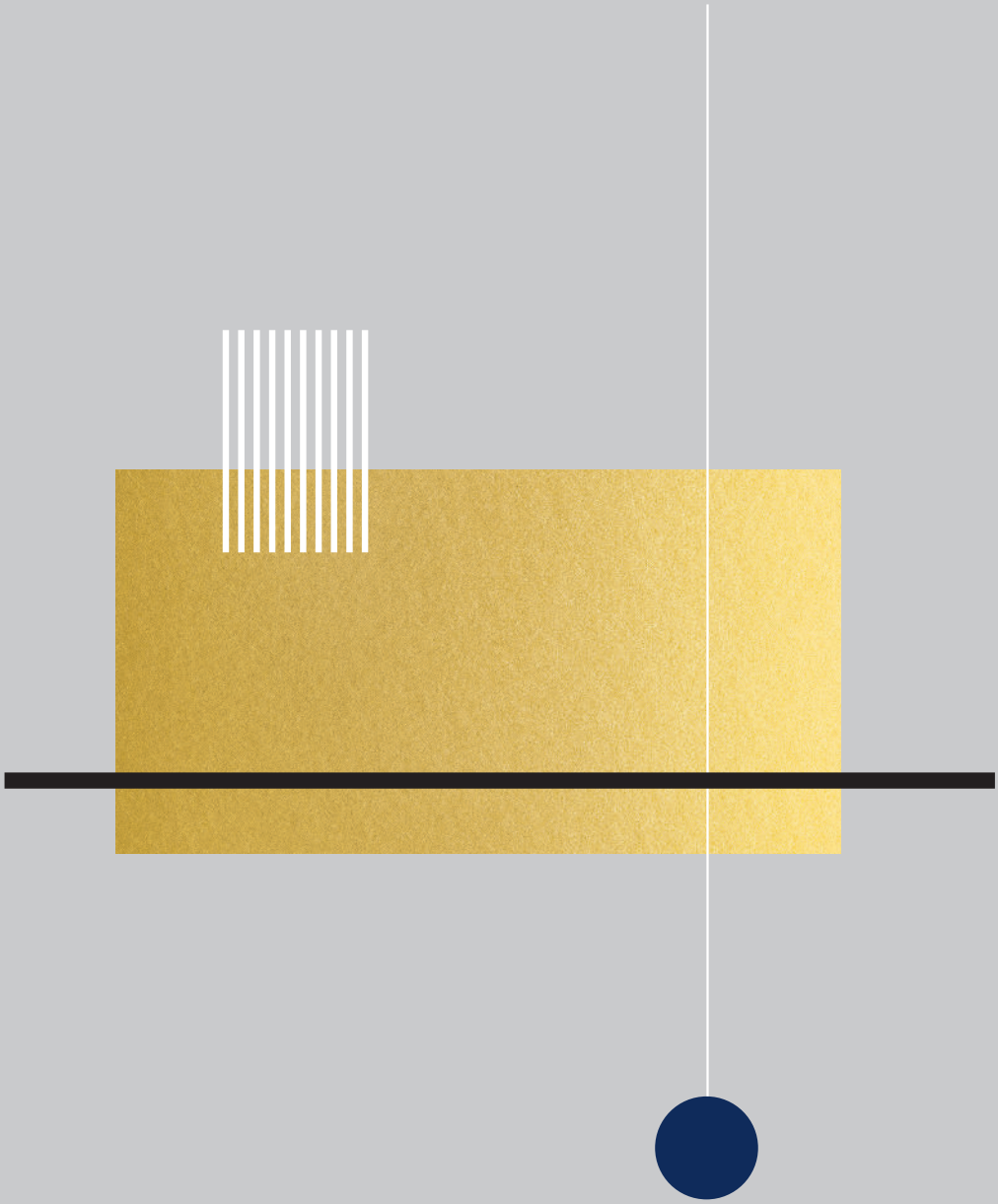
15. Honda K, Yasukawa Y, Fujiwara M, Abe T, Urade M. Causes of persistent joint pain after arthrocentesis of temporomandibular joint. *J Oral Maxillofac Surg*. 2011;69:2311-2315. doi:10.1016/j.joms.2011.02.025

16. Al-Moraissi E, Wolford L, Ellis E, Neff A. The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *J Cranio-Maxillofacial Surg*. 2020;48(1):9-23. doi:10.1016/j.jcms.2019.10.004

17. Tang Y, Vos L, Tuin A, et al. Arthrocentesis versus non- surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. *Int J Oral Maxillofac Surg*. 2023;52:595-603.

18. Tran C, Ghahreman K, Huppa C, Gallagher J. Management of temporomandibular disorders: a rapid review of systematic reviews and guidelines. *Int J Oral Maxillofac Surg*. 2022;51:1211-1225.

19. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*. 1993;7(2):183-195.



CHAPTER 9

GENERAL DISCUSSION

"Form follows function". This Bauhaus design principle postulates that the shape or design of an object should be determined by its function. This idea parallels current approaches to the management of degenerative temporomandibular joint (TMJ) disorders (which in this thesis refer specifically to symptomatic degenerative joint disease and disc displacements), where treatment should prioritize symptom relief and function restoration, rather than attempting anatomical correction or disc-manipulation[1–3]. Once normal joint function is restored, the surrounding structures often adapt to a new balance without requiring anatomical modification.

The first-line treatment option in TMJ disorders involves conservative, non-surgical treatments, aiming to reduce joint loading and inflammation[1,4,5]. Guidelines recommend the performance of minimally invasive surgery, such as arthroscopy and arthrocentesis, only when conservative, non-surgical treatments are insufficient in alleviating symptoms[1,6]. Open joint surgery, such as discectomy, (gap)arthroplasty and total joint replacement, often permanently alter anatomical structures and are indicated only in a very select group of cases, e.g., end-stage joint degeneration and ankylosis.

Although the current stepwise treatment framework for degenerative TMJ disorders provides guidance, its evidence base supporting the conservative-first approach remains limited. Several challenges exist within the current treatment paradigm. First, both the efficacy and optimal timing of minimally invasive treatments in degenerative TMJ disorders are not well defined[7], leading to uncertainty about when clinicians should escalate from conservative to surgical treatment. This lack of consensus contributes to variability in clinical practice and potential, unnecessary delays that may contribute to chronic TMJ pain and reduced treatment responsiveness[8]. Second, the indications and efficacy of arthrocentesis and arthroscopy remain insufficiently defined, as few, high-quality studies have compared these techniques directly. Third, limited evidence exists on how to manage patients with degenerative TMJ disorders who do not respond to initial minimally invasive surgery, including when to repeat a procedure and when to escalate.

Together, these gaps define the central aim of this thesis: to redefine the role of minimally invasive surgery in degenerative TMJ disorders by establishing their place within the broader treatment framework.

Efficacy of arthrocentesis and its timing

The first part of this thesis examined the efficacy and optimal timing of arthrocentesis for degenerative TMJ disorders. Before determining the optimal timing for arthrocentesis (defined here as its position within the treatment framework in relation to symptom duration and response to conservative therapy), it was necessary to establish whether arthrocentesis provides clinically meaningful benefit beyond continued conservative treatment. Questions regarding the optimal timing of arthrocentesis are only relevant if conservative treatments do not result in comparable outcomes. Establishing this comparative effectiveness is therefore a prerequisite for subsequently evaluating whether earlier intervention with arthrocentesis may improve treatment success.

Chapter 2 comprehensively compared the efficacy of arthrocentesis with conservative treatments in a systematic review with meta-analysis and trial sequential analysis. When considering only randomized controlled trials (RCTs), arthrocentesis demonstrated superior pain reduction at short- and intermediate-term follow-up. A statistically significant superiority in maximum mouth opening improvement was, however, clinically irrelevant. Other outcomes such as mandibular function, joint blocks and noises, lateral and protrusive movements, quality of life and cost-effectiveness were insufficiently or too heterogeneously reported to allow meaningful synthesis. These findings were strengthened by the results of the RCT in **chapter 3**, where arthrocentesis demonstrated superior efficacy over non-surgical treatments for pain reduction sustained over the long-term (≥ 5 years), while both treatments showed similar improvement in mandibular function. Together, these studies confirm arthrocentesis as a durable intervention that is superior to conservative care in pain management.

These findings are consistent with proposed biological mechanisms of joint lavage. Arthrocentesis is hypothesized to flush out intra-articular inflammatory mediators that perpetuate synovitis and pain, hence immediately contributing to the recuperation of the intra-articular homeostasis[9–11]. The observed superiority of arthrocentesis over conservative care supports this rationale and indicates that arthrocentesis is an effective treatment modality for TMJ disorders.

Chapter 4 evaluated the influence of the timing of arthrocentesis for painful TMJ disorders in a two-decade cohort study and demonstrated that each additional month of symptoms prior to treatment was associated with a 2.6% lower odds of

patient-reported success, suggesting that delayed arthrocentesis may compromise treatment outcomes. Furthermore, patients treated within 6 months of symptom onset had a 2.7 times higher odds of experiencing treatment success compared to patients who were treated after 6 months. Collectively, the results from **chapters 2-4** imply that timing of arthrocentesis is an important determinant of treatment success in degenerative TMJ disorders. Early consideration (i.e., within 6 months) of arthrocentesis may also prevent the transition from acute to chronic pain, since delayed adequate treatment risks the development of central sensitization[12,13], which may diminish responsiveness to subsequent interventions[14]. In this context, the window of opportunity for recovery may be early in the disease process.

Beyond biological considerations, arthrocentesis also offers practical advantages compared to conservative treatments. It is a single predictable procedure while conservative treatments are often extended over a prolonged period of time (for example, splint usage and medication consumption or multiple physiotherapy sessions spanning over several weeks or months), variable in nature and dependent on the often low patient compliance[15]. These factors of conservative treatments increase disease burden and complicates decision-making on treatment escalation. Moreover, prolonged conservative treatment may be less cost-effective due to higher societal costs incurred during the treatment period[16], a subject that warrants further economic evaluation in future research.

The findings of **chapters 2-4** align with previous systematic reviews[7,17] suggesting that earlier arthrocentesis may result in better outcomes in patients with degenerative TMJ disorders. In contrast to those reviews, **chapter 4** provides direct evidence that delaying surgery is associated with reduced success. Nevertheless, the optimal timing of intervention for degenerative TMJ disorders remains undefined. Notably, prospective, but non-randomized, studies in arthroscopy[18,19] have similarly reported better outcomes when treatment is performed early rather than late in the disease process, showing parallel support for the importance of timing. However, these results cannot be directly extrapolated to arthrocentesis. Definitive clarification would require a RCT comparing early versus delayed arthrocentesis. Ultimately, clinical decision making should balance the potential benefit of earlier intervention (do not delay) against the risk of overtreatment (do not harm). The optimal approach would be to let the decision of escalation to be guided by determining at-risk patients for unsuccessful conservative treatment, considering symptom severity and duration and psychosocial and quality of life factors.

Arthroscopy versus arthrocentesis

The second part of the thesis examined the comparative efficacy of arthroscopy versus arthrocentesis, a topic where robust evidence was lacking. Most TMJ arthroscopy studies are non-randomized studies without control groups, and considering the natural self-limiting course of degenerative TMJ disorders, true therapeutic effects of arthroscopy have been difficult to quantify in these studies[20–24].

The systematic review with meta-analysis and trial sequential analysis presented in **chapters 5** and **6** indicates that arthroscopy and arthrocentesis result in similar pain reduction and complication rates in patients with degenerative TMJ disorders. Arthroscopic lysis and lavage was statistically superior in increasing maximum mouth opening at intermediate-term follow-up. There was insufficient evidence available to draw any conclusions for the outcomes mandibular function, joint blocks and noises, mandibular range of motion, quality of life, and cost-effectiveness, nor for the comparison arthroscopy versus conservative care. The overall certainty of evidence was low to very low due to inconsistent reporting, small sample sizes and substantial methodological limitations, making the comparative efficacy of the treatments difficult to quantify.

Chapter 7 provides the first comprehensive, robust, comparative evidence between office-based arthroscopy and arthrocentesis in a randomized controlled trial (DIAMOND-trial). Preliminary results suggested that arthroscopy resulted in greater pain reduction, while improvements of other outcomes such as maximum mouth opening or mandibular function (although borderline significant) were similar. The discordance between these findings and those from **chapter 5** may be partially attributed to the use of subsynovial corticosteroid injections, a maneuver that has been previously shown to be effective at alleviating pain[25,26] and performed in **chapter 7**, but not in previous comparative studies between arthroscopy and arthrocentesis. While these preliminary results carefully suggest a superiority of arthroscopy, final results from the full cohort are required before definitive conclusions can be made.

The interpretation of studies on TMJ arthroscopy must account for substantial technological advancements[27] since its introduction by Onishi in 1975[28]. Modern systems utilize higher-definition optics, smaller instruments and can be performed in an increasing amount of circumstances under local anesthesia[22,29], making older

studies[24,30] increasingly less representative and comparisons across time susceptible to temporal bias.

Beyond clinical outcomes, practical and societal considerations should be considered when choosing between arthroscopy and arthrocentesis. Arthroscopy requires higher technical proficiency, specialized equipment and clinician training[31], which requires adequate infrastructure in specialized units, potentially limiting its widespread adoption. In contrast, arthrocentesis is less technically demanding, requires fewer resources and may thus be more accessible, making it particularly suitable for general oral and maxillofacial practice or practitioners without specialized arthroscopic surgical training and expertise. Furthermore, the economic appraisal of treatments is also essential to consider. As discussed in **Chapter 6**, such evaluations can be performed through cost-effectiveness analyses based on clinical outcomes and cost–utility analyses based on quality-adjusted life years (QALYs). A comprehensive analysis should include direct (e.g., equipment, operating time, personnel) and indirect medical costs (e.g., additional interventions or rehabilitation) as well as direct and indirect non-medical costs (e.g., productivity losses, travel expenses, and patient contributions)[32,33]. Although arthroscopy incurs higher initial costs, it may ultimately prove to be cost-effective by reducing recurrence, absenteeism or the need for subsequent retreatment. However, robust evidence regarding economic evaluations is still lacking.

Finally, it is important to consider that arthroscopy offers the advantage of direct visualization of intra-articular structures and targeted therapeutic maneuvers, allowing additional diagnostic insights when initial treatment is unsuccessful. Identifying patient subgroups who are most likely to benefit from these arthroscopic advantages may result in developing a treatment framework where both techniques are complementary to each other rather than competitors, with each procedure having distinct indications depending on patient characteristics, resource availability and surgical expertise.

Retreatment options when arthrocentesis fails

The final challenge addressed in this thesis concerns the management of patients with degenerative TMJ disorders who do not experience adequate symptom relief after initial arthrocentesis. **Chapter 8** shows that approximately 31% of patients initially treated with arthrocentesis undergo retreatment, which consists of re-arthrocentesis, arthroscopy and/ or open joint surgery. Importantly, 83.3% of those

who received at least one retreatment achieved patient-reported success at 5-year follow-up, resulting in an overall 5-year success rate of approximately 95% of the full treatment trajectory. No patients underwent a total joint replacement within the first five years, most likely indicating the slow progression of TMJ degeneration and that the treatment is generally reserved for severely disabling end-stage disease.

However, **chapter 8** demonstrated that while the first retreatment provided added benefit, subsequent retreatments did not significantly increase the odds for long-term success, indicating decreasing therapeutic effects with each retreatment as disease chronicity increases. This diminishing therapeutic effect concurs with the negative association between symptom duration and treatment success, reinforcing the notion that the negative effects of a delayed initial treatment cannot be fully compensated by later procedures. Together, these findings suggest that the "window of opportunity" for optimal benefit from arthrocentesis lies early in the disease process (e.g., within 6 months, as discussed in chapter 4).

The results are consistent with studies reporting that repeat arthroscopy may yield favorable outcomes after unsuccessful initial arthroscopy[34,35]. This suggests that the current treatment framework should not be viewed as a rigid stepwise hierarchy but as a continuum in which repeating the same surgery may be appropriate in some cases. An initially unfavorable outcome should therefore not automatically be interpreted as a definitive treatment failure requiring treatment escalation. Similarly, symptom recurrence after an initially successful intervention may justify repeating the same procedure.

Despite this, a clear evidence-based framework for retreatments is still lacking and it remains unclear which retreatment modality is most appropriate in specific situations. **Chapter 8** showed that retreatment type does significantly influence success beyond the first retreatment, highlighting that decisions should be individualized and guided by anatomical considerations, clinician judgement and overall clinical context instead of procedural hierarchy alone. The development of a structured algorithm could help reduce variability and aid clinicians in making appropriate decisions in retreatment sequencing.

Finally patient factors need to be carefully evaluated. Repeated, similar procedures may contribute to treatment fatigue, undermining patient confidence and adherence[36], and increase healthcare costs. In this context, prolonged treatment trajectories without proper patient guidance may also promote "medical shopping",

particularly with patients with unmet expectations. Shared-decision making is therefore essential. Patients should be informed about the reduced likelihood of benefit with each additional retreatment and the associated risks, allowing individual cost-benefit assessments to guide whether further interventions are in line with their expectations.

Quality of evidence and clinical interpretation

Quality of evidence

The findings of this thesis should be interpreted in the context of the methodological quality of the available evidence. Regarding arthrocentesis versus conservative treatments for degenerative TMJ disorders, the primary analyses presented in **chapter 2** demonstrated high quality of evidence for short-term pain improvement and moderate quality of evidence for intermediate-term pain improvement and maximum mouth opening improvement according to GRADE criteria[37,38]. Trial sequential analyses[39] confirmed that the required information sizes were met, indicating that outcomes were not subject to false-neutral conclusions. Together with the results from the RCT in **chapter 3**, there is a reasonable certainty in the therapeutic value of arthrocentesis and its superiority over conservative treatments in pain reduction for degenerative TMJ disorders.

Contrarily, the comparative evidence for arthroscopy versus arthrocentesis for degenerative TMJ disorders presented in **chapters 5** and **6** was low to very low, largely due to the lack of RCTs, small sample sizes, unexplained heterogeneities between study results and the overall high risk of bias. Required information sizes were not met in most analyses after trial sequential analyses. Hence, major evidence gaps existed at the time of review. **Chapter 7** addresses this gap through a rigorously designed RCT, but the results remain preliminary and underpowered. Therefore, evidence regarding the efficacy of arthroscopy versus arthrocentesis remains of reduced quality and definitive conclusions cannot yet be drawn.

Finally, the retrospective cohort studies in **chapters 4** and **8** should be viewed as hypothesis-generating. Their retrospective design potentially introduces selection and attrition bias, particularly because treatment and retreatment choices could have been clinician dependent and possibly influenced by disease severity and anatomical considerations. Hence, observed results, while insightful, require confirmation in future prospective studies.

Clinically relevant differences

Statistical significance does not always reflect a clinical benefit for patients. In TMJ disorder research, the minimal clinically important difference (MCID) is estimated as 9-19mm absolute pain improvement on a 0-100 visual analog scale[40], or a 10-20% relative improvement, with a 30% reduction indicating a moderate clinical difference[41]. For maximum mouth opening improvement, the MCID is estimated to be 6-9mm improvement[42].

Considering these thresholds, the short- and intermediate-term between-group differences in pain reduction observed in **chapter 2** (14.5mm and 14.2mm in favor of arthrocentesis), represent both statistically significant and clinically relevant improvements. In contrast the between-group differences in maximum mouth opening improvement (2.2mm and 2.4mm in favor of arthrocentesis) were statistically significant but clinically irrelevant. In **chapter 3**, the long-term between-group difference in pain reduction (10.2mm) falls within the absolute and above the relative MCID range, indicating a clinically meaningful, though modest, benefit of arthrocentesis over continued conservative care. However, because the estimated treatment effect reflects the average across the entire 5-year follow-up, it may underrepresent any early symptomatic benefit of arthrocentesis. Earlier short-term results[43], the initial trajectory of pain scores in **chapter 3**, and the short- and intermediate-term findings in **chapter 2,** all suggest that arthrocentesis produces faster symptom reduction than conservative treatment in patients with degenerative TMJ disorders. This early advantage is clinically relevant, particularly when considering the tendency of some degenerative TMJ disorders to improve spontaneously over time, causing between-group differences to converge at long-term follow-up. Hence, the true early clinical benefit of arthrocentesis may be underestimated in the statistical model, but this could not be assessed due to the absence of a "treatment-by-time" interaction in the model. In **chapter 5**, the greater increase in maximum mouth opening after arthroscopic lysis and lavage relative to arthrocentesis (4.9mm) does not reach the MCID, indicating a clinically irrelevant difference. Nevertheless, the upper bound of the 95% confidence interval (7.1mm) of this outcome overlaps the MCID, suggesting that a clinically relevant effect cannot be ruled out for certain. In **Chapter 7**, the 22.4mm greater reduction in pain after arthroscopy compared to arthrocentesis exceeds the MCID, suggesting a potentially clinically relevant difference in favor of arthroscopy.

Heterogeneity and generalizability

Heterogeneity in disease presentation, treatment approaches and research remains a major challenge in degenerative TMJ disorders, limiting comparability, interpretability and generalizability of outcomes. Although the clinical diversity in meta-analysis (CDIM)-tool indicated low overall clinical heterogeneity in the meta-analyses of **chapters 2** and *5*, a substantial variation was observed within the *intervention* domain, particularly regarding procedural modalities and techniques. Between clinics, the technical execution of arthroscopy and arthrocentesis may differ considerably, including the adjuvant co-medication administered (e.g., hyaluronic acid, corticosteroids, platelet-rich plasma)[44–46], the number of needles or portals used[47–50], the type of anesthesia (local or general) applied[51,52], the lavage volume[53] and irrigation fluid[54] used, the arthroscopic surgical level performed (level 1, 2 or 3)[55,56] and the pre- or postoperative regimens employed. These differences reflect real-world variability in surgical practice and limit comparability across studies. Overcoming this problem requires methodological standardization and multicenter collaboration to ultimately increase the robustness of evidence.

Heterogeneity is also inherent to the TMJ disorders themselves. TMJ conditions encompass a spectrum of intra-articular pathologies, occur concurrently with myogenous disorders, and may vary in symptom presentation, structural degeneration and psychological burden[57–59]. This makes it challenging to isolate disease severity and treatment effects. Moreover, outcomes beyond pain and mouth opening are inconsistently reported, limiting interpretability of overall disease severity and hindering meaningful evidence synthesis.

Furthermore, the pooling of different diagnoses or procedural techniques in **chapters 2** and *5*, which were necessary to allow evidence synthesis, could have reduced external applicability. Lastly, generalizability may have been limited because the RCTs (**chapters 3** and *7*) and cohort studies (**chapters 4** and *8*) were conducted at a tertiary referral hospital, where patients typically present with more severe, more chronic or previously treated symptoms. As such, while the evidence provided in the current thesis provide valuable insights, caution must be exercised when applying them to primary or secondary care settings.

Clinical recommendations

1. Timely and responsive stepwise management

Conservative treatment should remain the first-line option for degenerative TMJ disorders, but prolonged treatment without improvement risks unnecessary symptom persistence and progression towards chronicity. Clinicians should re-evaluate patients at defined intervals and consider treatment escalation rather early when clinical improvement stagnates (e.g., within 6 months). Current evidence supports arthrocentesis as more efficacious and predictable for pain reduction than continued conservative care, with similar effects on mouth opening. Existing data suggest that symptom duration is a predictor of treatment success and hence that earlier intervention may be advantageous. Although the window of opportunity is likely to be early in the disease, the exact optimal timing needs yet to be determined in a prospective comparative trial. Early identification of non-responders and timely referral or escalation are therefore essential. Nevertheless, arthrocentesis remains a surgical procedure and requires an individualized risk–benefit assessment.

2. Arthroscopy or arthrocentesis

Both arthrocentesis and arthroscopy are effective minimally invasive options for degenerative TMJ disorders, but high-quality comparative evidence is still limited. Preliminary results suggest a potential advantage of office-based arthroscopy for pain reduction, while improvements in mouth opening and other outcomes appear comparable. Arthroscopy provides additional diagnostic and therapeutic capabilities but requires specialized training and infrastructure. Importantly, arthroscopy ranges from simple office-based treatment to more advanced arthroscopic surgery and its availability varies between centers worldwide. In settings without such expertise, arthrocentesis remains a simple, accessible and effective alternative.

3. Retreatment after minimally invasive surgery

Evidence on retreatment strategies following unsuccessful minimally invasive surgery for degenerative TMJ disorders is scarce. Current, mostly hypothesis-generating, evidence indicates that a first retreatment can still yield meaningful benefit, but additional retreatments beyond that do not actively contribute to treatment success. Retreatments should therefore not be repeated indefinitely, and clinicians should reassess the diagnosis, evaluate psychosocial comorbidity and involve multidisciplinary care when symptoms persist after repeated unsuccessful interventions.

4. Multidisciplinary care and broader treatment goals

Since TMJ disorders are multifactorial and heterogeneous, effective treatment requires addressing not only intra-articular pathology but also comorbidities, muscle involvement and psychosocial factors. Although not directly researched in this thesis, a multidisciplinary approach can improve diagnostic accuracy and treatment efficacy[60]. Treatment should take place in a broader, holistic context and success should be defined beyond pain and mouth opening alone, incorporating functional recovery, quality of life and patient satisfaction[61]. Similarly, perceived "unsuccessful treatment" should prompt reassessment of treatment goals and psychosocial factors, not automatic treatment escalation[62]. Clear patient education and shared decision-making are essential to align expectations.

Future perspectives

Scientific interest in TMJ disorders has expanded substantially in the recent two decades, with PubMed entries on "temporomandibular joint" increasing more than three-fold since the start of this century. Despite this growth, important knowledge gaps remain regarding disease mechanisms, diagnostics and optimal management trajectories. The following sections outline several directions for future research aimed at improving patient care.

Identifying at-risk patients for disease chronicity and progression

Although most TMJ disorders improve spontaneously, a substantial subset develops chronic symptoms and progressive joint degeneration. Future research should focus on identifying at-risk patients for disease progression through factors such as clinical characteristics[63,64], psychosocial factors[64,65], imaging[66,67], molecular biomarkers[68] or genetics[58]. Quantitative measures such as the number-needed-to-treat and number-needed-to-harm analyses may reduce overtreatment or harmful delay treatment. Despite an increasing insight into individual risk factors, their relative contributions and interactions remain insufficiently understood. High-quality prospective studies are therefore needed to clarify which patients are most vulnerable to treatment resistance and disease progression, allowing more timely and targeted treatment.

Developing predictive models for treatment selection

Current comparative studies evaluate TMJ surgical treatments at a general, TMJ population level, implying that all patients share the same indication. This does not reflect clinical reality where patients differ in disease characteristics, comorbidities and response to prior treatments. Future studies should therefore focus on developing

evidence-based predictive models that integrate clinical and patient-specific factors to guide treatment selection. Such models are for example needed to guide the selection between arthroscopy and arthrocentesis.

Diagnostic tools may play an important role in both the identification of at-risk patients and the development of predictive models for treatment selection and success. Although conventional imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) are frequently used for diagnosis, their role in guiding treatment choice or predicting treatment response is understudied. Previous studies show an association between MRI-detected joint effusion and symptom severity[66,69,70], but validated imaging biomarkers of disease progression and treatment responsiveness are still lacking. Emerging technologies, like artificial intelligence-assisted image analysis, may help detect indicators of disease severity. Including these advanced imaging tools into predictive frameworks could improve early identification of patients at risk for chronicity, optimize selection for minimally invasive procedures and enable better monitoring of treatment response.

Expanding treatment outcomes

Current clinical research primarily evaluates whether symptoms eventually resolve, but this outcome does not fully reflect patient-relevant outcomes in clinical practice. Because many TMJ disorders improve spontaneously over time, the rate of improvement might be just as clinically meaningful as final level of recovery. In this context, arthrocentesis or arthroscopy "buy time" by accelerating symptom relief. Future studies should therefore also assess the speed of symptom improvement and functional recovery. Furthermore, future studies should include broader, patient-centered outcomes using validated tools such as the MFIQ[71] or the OHIP[72] to gain a more complete understanding of the therapeutic effects of the treatments. Lastly, economic evaluations like cost-effectiveness and cost-utility analyses are needed to determine the societal impact of treatments.

Determining optimal treatment timing

An important unresolved question is when conservative treatment should be considered insufficient and when minimally invasive interventions should be offered. Although findings from this thesis suggest that delayed arthrocentesis may reduce the likelihood of patient-reported success, the specific timing at which arthrocentesis provides most benefit remains unclear. Future prospective, ideally prospective, controlled trials evaluating early versus delayed arthrocentesis could clarify when

transitioning from conservative care to arthrocentesis offers maximal benefit and whether a true therapeutic "window of opportunity" exists.

Treatment within broader biopsychosocial and interdisciplinary framework

Although this thesis focuses on intra-articular interventions, future research requires moving beyond a purely structural or joint-centered perspective. TMJ disorders involve an interplay between structural, functional and biopsychosocial factors[60,73]. The correlation between structural abnormalities and symptom severity is limited[60,74], and psychosocial factors such as stress, anxiety, depression, catastrophizing strongly influence pain and disability perception and treatment response[73].

Despite this, psychosocial factors remain underrecognized[75] or recognized in isolation, reflecting the tendency to focus on isolated domains (i.e., biomechanical, molecular or psychosocial) in clinical practice and research, rather than integrating them into a unified comprehensive model[60]. A shift towards interdisciplinary models, combining expertise of TMJ surgeons, dentists, physiotherapists, psychologists, pain specialists and neuroscientists is essential[60]. Placing TMJ disorder research within the broader field of pain science may facilitate a more comprehensive understanding of disease mechanisms and improve clinical management.

Biological mechanisms and treatment approaches

Finally, although outside the primary scope of this thesis, a deeper understanding of molecular and cellular mechanisms underlying TMJ inflammation and degeneration should be a target for future research. Pre-clinical research integrating molecular biology and genetics may allow better understanding of disease etiology, progression, treatment responsiveness and support the development of novel biologically targeted interventions. Emerging treatments, such as the use of intra-articular adipose-derived stromal vascular fraction[76] or stem-cell based therapies[77], may offer promising ways to modulate intra-articular homeostasis and warrant further investigation.

Key findings and conclusion

The current literature indicates that arthrocentesis for degenerative TMJ disorders provides statistically and clinically superior pain reduction compared to conservative treatments at short- and intermediate-term follow-up, while differences in maximum mouth opening are not clinically relevant. Other outcomes and cost-effectiveness could not be evaluated due to inconsistent or lack of reporting **(Chapter 2)**.

Arthrocentesis is more effective than conservative treatments in reducing pain during mandibular movement over ≥5 years, but both treatments result in similar improvements in mandibular function for patients with degenerative TMJ disorders **(Chapter 3)**.

Symptom duration is negatively associated with patient-reported success of initial arthrocentesis for degenerative TMJ disorders at 5-year follow-up. Each additional month before arthrocentesis is associated with a 2.6% reduction in odds of treatment success and patients treated within 6 months have 2.7 times higher odds of success than those treated later. Performing arthrocentesis at an earlier stage may increase the odds of achieving success **(Chapter 4)**.

The current literature indicates that arthroscopy leads to similar pain reduction and complication rates as arthrocentesis for degenerative TMJ disorders, and although arthroscopic lysis and lavage results in a greater mouth-opening improvement, this difference is clinically irrelevant. Conclusions are limited due to low to very low quality of evidence, indicating a current knowledge gap. Other outcomes and cost-effectiveness, and the comparison of arthroscopy versus conservative treatments, could not be evaluated due to inconsistent or lack of reporting **(Chapter 5)**.

Preliminary results from the first rigorous RCT suggests that office-based arthroscopy results in greater reduction in pain during mandibular movement at 12 months compared with arthrocentesis for degenerative TMJ disorders, while other outcomes are comparable between treatments. Final results of our currently running DIAMOND-trial are required before drawing definitive conclusions. **(Chapter 7)**.

Approximately 31% of patients require retreatment after an initial arthrocentesis for degenerative TMJ disorders. Among those, 83.3% achieve patient-reported treatment success at 5-year follow-up, indicating an overall 5-year success rate of approximately 95% across the entire treatment trajectory. The first retreatment offers meaningful benefit, but additional retreatments do not further improve success. Retreatment type does not significantly influence success. Early intervention remains essential for optimizing treatment outcome **(Chapter 8)**.

References

1. Bouloux GF, Chou J, DiFabio V, et al. The Contemporary Management of Temporomandibular Joint Intra-Articular Pain and Dysfunction. *J Oral Maxillofac Surg*. 2024;82(6):623-631. doi:10.1016/j.joms.2024.01.003
2. Dolwick MF. Intra-articular disc displacement part I: Its questionable role in temporomandibular joint pathology. *J Oral Maxillofac Surg*. 1995;53(9):1069-1072. doi:10.1016/0278-2391(95)90126-4
3. Mercuri L, Greene C, Manfredini D. The temporomandibular joint disc: A complex fable about an elusive butterfly. *Cranio*. Published online 2025:1-8. doi:https://doi.org/10.1080/08869634.2025.2477963
4. Bouloux G, Greene C, Mercuri L. Intraarticular TMJ pain and dysfunction – 2024 – invited guest editorial. *Cranio*. 2024;42(5):481-482.
5. Wieckiewicz M, Boening K, Wiland P, Shiau YY, Paradowska-Stolarz A. Reported concepts for the treatment modalities and pain management of temporomandibular disorders. *J Headache Pain*. 2015;16(1):1-12. doi:10.1186/s10194-015-0586-5
6. Murphy MK, MacBarb RF, Wong ME, Athanasiou KA. Temporomandibular Disorders: A Review of Etiology, Clinical Management, and Tissue Engineering Strategies. *Int J Oral Maxillofac Implants*. 2013;28(6):e393-e414. doi:10.11607/jomi.te20
7. Li D, Wong N, Li S, McGrath C, Leung Y. Timing of arthrocentesis in the management of temporomandibular disorders: an integrative review and meta-analysis. *Int J Oral Maxillofac Surg*. 2021;50:1078-1088.
8. Emshoff R, Rudisch A. Determining predictor variables for treatment outcomes of arthrocentesis and hydraulic distention of the temporomandibular joint. *J Oral Maxillofac Surg*. 2004;62(7):816-823. doi:10.1016/j.joms.2003.12.020
9. Kaneyama K, Segami N, Nishimura M, Sato J, Fujimura K, Yoshimura H. The ideal lavage volume for removing bradykinin, interleukin-6, and protein from the temporomandibular joint by arthrocentesis. *J Oral Maxillofac Surg*. 2004;62(6):657-661. doi:10.1016/j.joms.2003.08.031
10. Gulen H, Ataoglu H, Haliloglu S, Isik K. Proinflammatory cytokines in temporomandibular joint synovial fluid before and after arthrocentesis. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2009;107(5). doi:10.1016/j.tripleo.2009.02.006
11. Celotti C, Martin-Granizo R, De La Sen O. Correlation of arthroscopic findings with clinical–radiological signs and symptoms of temporomandibular joint dysfunction: retrospective study of 829 joints. *Int J Oral Maxillofac Surg*. 2022;51:1069-1073.
12. Cayrol T, Van Den Broeke EN, Gerard E, et al. Chronic temporomandibular disorders are associated with higher propensity to develop central sensitization: A case-control study. *Pain*. 2023;164(5):E251-E258. doi:10.1097/j.pain.0000000000002803
13. La Touche R, Paris-Alemany A, Hidalgo-Pérez A, López-de-Uralde-Villanueva I, Angulo-Diaz-Parreño S, Muñoz-García D. Evidence for Central Sensitization in Patients with Temporomandibular Disorders: A Systematic Review and Meta-analysis of Observational Studies. *Pain Pract*. 2018;18(3):388-409. doi:10.1111/papr.12604

14. Monaco A, Cattaneo R, Marci MC, Pietropaoli D, Ortu E. Central Sensitization-Based Classification for Temporomandibular Disorders: A Pathogenetic Hypothesis. *Pain Res Manag*. 2017;5:1-13. doi:doi: 10.1155/2017/5957076

15. Pihut M, Maga W, Gala A. Assessing the Reliability of Compliance with the General Treatment Recommendations by Patients Treated for Temporomandibular Disorders. *J Clin Med*. 2025;14(18). doi:10.3390/jcm14186674

16. Vos L, Stant A, Quik E, Slater J, Stegenga B. Cost effectiveness of arthrocentesis as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial. *Int J Oral Maxillofac Surg*. 2013;42(10):1369. doi:10.1016/j.ijom.2013.07.710

17. Al-Moraissi E, Wolford L, Ellis E, Neff A. The hierarchy of different treatments for arthrogenous temporomandibular disorders: A network meta-analysis of randomized clinical trials. *J Cranio-Maxillofacial Surg*. 2020;48(1):9-23. doi:10.1016/j.jcms.2019.10.004

18. Machoň V, Šedý J, Klíma K, Hirjak D, Foltán R. Arthroscopic lysis and lavage in patients with temporomandibular anterior disc displacement without reduction. *Int J Oral Maxillofac Surg*. 2012;41(1):109-113. doi:10.1016/j.ijom.2011.07.907

19. Israel H, Behrman D, Friedman J, Silberstein J. Rationale for Early Versus Late Intervention With Arthroscopy for Treatment of Inflammatory/Degenerative Temporomandibular Joint Disorders. *J Oral Maxillofac Surg*. 2010;68:2661-2667.

20. Ângelo DF, Sanz D, Cardoso HJ. Bilateral arthroscopy of the temporomandibular joint: clinical outcomes and the role of a second intervention—a prospective study. *Clin Oral Investig*. 2023;27(10):6167-6176. doi:10.1007/s00784-023-05233-6

21. McCain JP, Sanders B, Koslin MG, Quinn JD, Peters PB, Indresano AT. Temporomandibular joint arthroscopy: A 6-year multicenter retrospective study of 4,831 joints. *J Oral Maxillofac Surg*. 1992;50(9):926-930. doi:10.1016/0278-2391(92)90047-4

22. Hossameldin RH, McCain JP. Outcomes of office-based temporomandibular joint arthroscopy: a 5-year retrospective study. *Int J Oral Maxillofac Surg*. 2018;47(1):90-97. doi:10.1016/j.ijom.2017.06.025

23. Breik O, Devrukhkar V, Dimitroulis G. Temporomandibular joint (TMJ) arthroscopic lysis and lavage: Outcomes and rate of progression to open surgery. *J Cranio-Maxillofacial Surg*. 2016;44(12):1988-1995. doi:10.1016/j.jcms.2016.09.017

24. Murakami KI, Tsuboi Y, Bessho K, Yokoe Y, Nishida M, Iizuka T. Outcome of arthroscopic surgery to the temporomandibular joint correlates with stage of internal derangement: Five-year follow-up study. *Br J Oral Maxillofac Surg*. 1998;36(1):30-34. doi:10.1016/S0266-4356(98)90744-6

25. Oren D, Dror A, Khalil T, et al. Comparisons between lysis and lavage, intra-articular steroid injections, and three-point subsynovial steroid injections using operative single-cannula arthroscopy d A retrospective analysis Daniel. *J Cranio-Maxillofacial Surg*. 2022;50(4):336-342.

26. Martins I, Radaic P, Marchi L, Barreto G, Pastore G. Assessment of postoperative pain in patients undergoing temporomandibular joint arthroscopy with infiltration of dexamethasone disodium phosphate in different concentrations. A randomized controlled trial. *J Cranio-Maxillofacial Surg*. 2023;51(2):89-97.

27. Murakami K. Rationale of arthroscopic surgery of the temporomandibular joint. *J oral Biol craniofacial Res*. 2013;3:126-134.

28. Onishi M. Arthroscopy of the temporomandibular joint. *Jap Stomatol*. 1975;42:207-213.

29. Weedon S, Ahmed N, Sidebottom AJ. Prospective assessment of outcomes following disposable arthroscopy of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2013;51(7):625-629. doi:10.1016/j.bjoms.2013.06.004

30. Sanders B. Arthroscopic surgery of the temporomandibular joint: Treatment of internal derangement with persistent closed lock. *Oral Surgery, Oral Med Oral Pathol*. 1986;62(4):361-372. doi:10.1016/0030-4220(86)90282-3

31. Bruning L, Rosner Y, Meisgeier A, Neff A. Arthroscopic Assessment of Temporomandibular Joint Pathologies—Is It Possible for Non-Specialists in Arthroscopy? Analysis of Variability and Reliability of Dental Students' Ratings after a Comprehensive One-Semester Introduction. *J Clin Med*. 2024;13(3995).

32. Dutch Institute National Health Care (Zorginstituut Nederland). Guideline for economic evaluations in healthcare (2024 version). Zorginstituut Nederland. 2024. Accessed November 11, 2025. https://english.zorginstituutnederland.nl/documents/2024/01/16/guideline-for-economic-evaluations-in-healthcare

33. Hakkaart-van Roijen L, van der Linden N, Bouwmans C, Kanters T, Swan Tan S. Kostenhandleiding: Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg. *Dutch Natl Heal Care Inst*. Published online 2016:1-73.

34. Martin Granizo R, Correa Muñoz DC, Varela Reyes E. Rearthroscopy of the temporomandibular joint: A retrospective study of 600 arthroscopies. *J Cranio-Maxillofacial Surg*. 2018;46(9):1555-1560. doi:10.1016/j.jcms.2017.12.007

35. Mancha de la Plata M, Muñoz-Guerra M, Escorial Hernandez V, Martos Diaz P, Gil-Diez Usandizaga JL, Rodriguez-Campo FJ. Unsuccessful Temporomandibular Joint Arthroscopy: Is a Second Arthroscopy an Acceptable Alternative? *J Oral Maxillofac Surg*. 2008;66(10):2086-2092. doi:10.1016/j.joms.2008.06.043

36. Heckman BW, Mathew AR, Carpenter MJ. Treatment burden and treatment fatigue as barriers to health. *Curr Opin Psychol*. 2015;5:31-36. doi:10.1016/j.copsyc.2015.03.004

37. Atkins D, Best D, Briss P, Eccles M, Falck-Ytter Y, Flottorp S. Grading quality of evidence and strength of recommendations. The GRADE Working Group. *Br Med J (Clin Res Ed)*. 2004;(June):328(7454):1490.

38. Duhailib Z, Granholm A, Alhazzani W, Oczkowski S, Belley-Cote E, Moller M. GRADE pearls and pitfalls—Part 1: Systematic reviews and meta-analyses. *Acta Anaesthesiol Scand*. Published online 2024:1-9.

39. Wetterslev J, Jakobsen J, Gluud C. Trial sequential analysis in systematic reviews with meta-analysis. *BMC Med Res Methodol*. 2017;17(39):1-18.

40. Calixtre L, Oliveira A, Alburquerque-Sendin F, Armijo-Olivo S. What is the minimal important difference of pain intensity, mandibular function, and headache impact in patients with temporomandibular disorders? Clinical significance analysis of a randomized controlled trial. *Musculoskelet Sci Pract.* 2020;46:2020.

41. Dworkin R, Turk D, Wyrwich K, et al. Interpreting the Clinical Importance of Treatment Outcomes in Chronic Pain Clinical Trials: IMMPACT Recommendations. *J pain.* 2008;9(2):105-121.

42. Kropmans T, Dijkstra P, Stegenga B, Stewart R, Bont L de. Smallest detectable difference of maximal mouth opening in patients with painfully restricted temporomandibular joint function. *Eur J Oral Sci.* 2000;108:9-13.

43. Vos L, Huddleston Slater J, Stegenga B. Arthrocentesis as initial treatment for temporomandibular joint arthropathy: A randomized controlled trial. *J Cranio-Maxillofacial Surg.* 2014;42(5):e134-e139. doi:10.1016/j.jcms.2013.07.010

44. Bouloux G, Chou J, Krishnan D, et al. Is Hyaluronic Acid or Corticosteroid Superior to Lactated Ringer Solution in the Short Term for Improving Function and Quality of Life After Arthrocentesis? Part 2. *J Oral Maxillofac Surg.* 2017;75(1):63-72. doi:10.1016/j.joms.2016.08.008

45. Bouloux G, Chou J, Krishnan D, et al. Is Hyaluronic Acid or Corticosteroid Superior to Lactated Ringer Solution in the Short-Term Reduction of Temporomandibular Joint Pain After Arthrocentesis? Part 1. *J Oral Maxillofac Surg.* 2017;75(1):52-62.

46. Derwich M, Mitus-kenig M, Pawlowska E. Mechanisms of action and efficacy of hyaluronic acid, corticosteroids and platelet-rich plasma in the treatment of temporomandibular joint osteoarthritis—a systematic review. *Int J Mol Sci.* 2021;22(14). doi:10.3390/ijms22147405

47. Bhargava D. Is Single Puncture Superior to Double Puncture Arthrocentesis in Patients With Wilkes III Internal Derangement? *J Oral Maxillofac Surg.* 2023;81(10):1204-1214. doi:10.1016/j.joms.2023.07.140

48. Guarda-Nardini L, Ferronato G, Manfredini D. Two-needle vs. single-needle technique for TMJ arthrocentesis plus hyaluronic acid injections: A comparative trial over a six-month follow up. *Int J Oral Maxillofac Surg.* 2012;41(4):506-513. doi:10.1016/j.ijom.2011.11.007

49. Nagori SA, Jose A, Roychoudhury A. Comparison of intraoperative outcomes with single and double puncture techniques of arthrocentesis of the temporomandibular joint. *Br J Oral Maxillofac Surg.* 2020;58(8):928-932. doi:10.1016/j.bjoms.2020.04.011

50. Keskin Tunç S, Mizrak YR, Başkan Önal A, Sümer S, Atay G, Ciğerim L. Comparison of single-needle double-cannula and double-needle arthrocentesis techniques in the disc displacement without reduction: A pilot study. *Cranio - J Craniomandib Sleep Pract.* 2025;epub ahead. doi:10.1080/08869634.2025.2579330

51. Mehra P, Arya V. Temporomandibular joint arthrocentesis: Outcomes under intravenous sedation versus general anesthesia. *J Oral Maxillofac Surg.* 2015;73(5):834-842. doi:10.1016/j.joms.2014.11.018

52. Tuz HH, Baslarli O, Adiloglu S, Gokturk T, Meral SE. Comparison of local and general anaesthesia for arthrocentesis of the temporomandibular joint. *Br J Oral Maxillofac Surg*. 2016;54(8):946-949. doi:10.1016/j.bjoms.2016.06.026

53. Tsui HC, Lam CM, Leung YY, Li KY, Wong NSM, Li DTS. Lavage Volume of Arthrocentesis in the Management of Temporomandibular Disorders: A Systematic Review and Meta-Analysis. *Diagnostics*. 2022;12(11). doi:10.3390/diagnostics12112622

54. Siewert-Gutowska M, Pokrowiecki R, Kaminski A, Zawadzki P, Stopa Z. State of the Art in Temporomandibular Joint Arthrocentesis—A Systematic Review. *J Clin Med*. 2023;12.

55. Hakim M, McCain J, Ahn D, Troulis M. Minimally Invasive Endoscopic Oral and Maxillofacial Surgery. *Oral Maxillofac Surg Clin North Am*. 2019;31(4):561-567.

56. González-García R. Categorizing temporomandibular joint arthroscopic procedures for a better clinical practice and teaching. *J Stomatol Oral Maxillofac Surg*. 2024;125(5). doi:10.1016/j.jormas.2024.101808

57. Stegenga B. Osteoarthritis of the Temporomandibular Joint Organ and Its Relationship to Disc Displacement. *J Orofac Pain*. 2001;15(3):193-205.

58. Slade GD, Ohrbach R, Greenspan JD, et al. Painful temporomandibular disorder: decade of discovery from OPPERA studies. *J Dent Res*. 2016;95(10):1084-1092.

59. Silva MAG, Pantoja LLQ, Dutra-Horstmann KL, et al. Prevalence of degenerative disease in temporomandibular disorder patients with disc displacement: A systematic review and meta-analysis. *J Cranio-Maxillofacial Surg*. 2020;48(10):942-955. doi:10.1016/j.jcms.2020.08.004

60. Chen P, Embree MC, Chung MK, et al. Bridging Temporomandibular Joint Structure, Function, and Pain: An Integrated Multiscale Perspective. *J Dent Res*. 2025;Epub ahead. doi:10.1177/00220345251376295

61. Rodrigues ALP, Cardoso HJ, Ângelo DF. Patient experience and satisfaction with different temporomandibular joint treatments: A retrospective study. *J Cranio-Maxillofacial Surg*. 2023;51(1):44-51. doi:10.1016/j.jcms.2023.01.006

62. Rollman GB, Gillespie JM. The role of psychosocial factors in temporomandibular disorders. *Curr Rev Pain*. 2000;4(1):71-81. doi:10.1007/s11916-000-0012-8

63. Emshoff R. Clinical factors affecting the outcome of arthrocentesis and hydraulic distension of the temporomandibular joint. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2005;100(4):409-414. doi:10.1016/j.tripleo.2004.12.024

64. Ulmner M, Kruger-Weiner C, Lund B. Patient-Specific Factors Predicting Outcome of Temporomandibular Joint Arthroscopy: A 6-Year Retrospective Study. *J Oral Maxillofac Surg*. 2017;75(8):1643.e1-1643.e7. doi:10.1016/j.joms.2017.04.005

65. Manfredini D, Favero L, Del Giudice A, Masiero S, Stellini E, Guarda-Nardini L. Axis II psychosocial findings predict effectiveness of TMJ hyaluronic acid injections. *Int J Oral Maxillofac Surg*. 2013;42(3):364-368. doi:10.1016/j.ijom.2012.10.033

66. Emshoff R, Rudisch A. Temporomandibular Joint Internal Derangement and Osteoarthrosis: Are Effusion and Bone Marrow Edema Prognostic Indicators for Arthrocentesis and Hydraulic Distention? *J Oral Maxillofac Surg*. 2007;65(1):66-73. doi:10.1016/j.joms.2005.11.113

67. Vervaeke K, Verhelst PJ, Orhan K, et al. Correlation of MRI and arthroscopic findings with clinical outcome in temporomandibular joint disorders: a retrospective cohort study. *Head Face Med*. 2022;18(1). doi:10.1186/s13005-021-00305-y

68. Hamada Y, Kondoh T, Holmlund AB, et al. Inflammatory cytokines correlated with clinical outcome of temporomandibular joint irrigation in patients with chronic closed lock. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2006;102(5):596-601. doi:10.1016/j.tripleo.2005.11.010

69. Rudisch A, Innerhofer K, Bertram S, Emshoff R. Magnetic resonance imaging findings of osteoarthrosis and effusion in patients with unilateral temporomandibular joint pain. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Oral Maxillofac Radiol*. 2002;92(5):566-571. doi:10.1054/ijom.2002.0314

70. Park HN, Kim KA, Koh KJ. Relationship between pain and effusion on magnetic resonance imaging in temporomandibular disorder patients. *Imaging Sci Dent*. 2014;44(4):293-299. doi:10.5624/isd.2014.44.4.293

71. Stegenga B, de Bont LG, de Leeuw R, Boering G. Assessment of mandibular function impairment associated with temporomandibular joint osteoarthrosis and internal derangement. *J Orofac Pain*. 1993;7(2):183-195.

72. Slade GD. Derivation and validation of a short-form oral health impact profile. *Community Dent Oral Epidemiol*. 1997;25(4):284-290. doi:10.1111/j.1600-0528.1997.tb00941.x

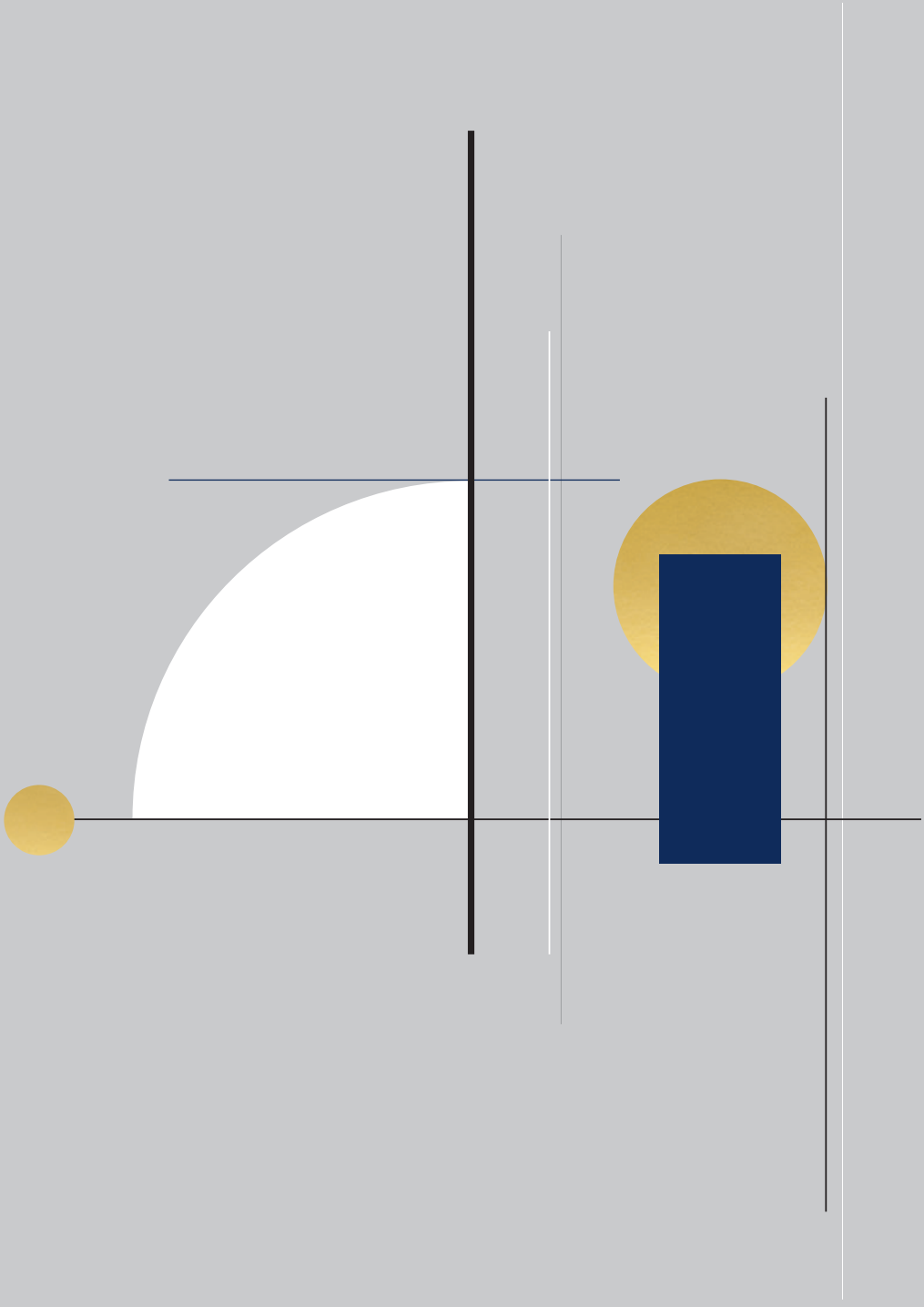
73. Wan J, Lin J, Zha T, et al. Temporomandibular disorders and mental health: shared etiologies and treatment approaches. *J Headache Pain*. 2025;26(1). doi:10.1186/s10194-025-01985-6

74. Chung MK, Wang S, Alshanqiti I, Hu J, Ro JY. The degeneration-pain relationship in the temporomandibular joint: Current understandings and rodent models. *Front Pain Res*. 2023;4. doi:10.3389/fpain.2023.1038808

75. Manfredini D, Bender S. The professional burden of protecting TMD patients. *Cranio*. 2024;42(6):639-640.

76. Schipper JAM, Tuin AJ, van Dongen JA, van Bakelen NB, Harmsen MC, Spijkervet FKL. Intra-Articular Injection of Adipose-Derived Stromal Vascular Fraction in Osteoarthritic Temporomandibular Joints: Study Design of a Randomized Controlled Clinical Trial. *Bioengineering*. 2024;11(2). doi:10.3390/bioengineering11020171

77. Matheus HR, Özdemir D, Guastaldi FPS. Stem cell-based therapies for temporomandibular joint osteoarthritis and regeneration of cartilage/osteochondral defects: a systematic review of preclinical experiments. *Osteoarthr Cartil*. 2022;30(9):1174-1185. doi:10.1016/j.joca.2022.05.006



CHAPTER 10

ENGLISH SUMMARY

Degenerative temporomandibular joint (TMJ) disorders are commonly managed through a stepwise treatment framework, in which conservative, non-invasive, reversible treatments are the first-line option. These include patient education, physiotherapy, splints and medications, aimed at reducing joint load, easing symptoms and maintaining or improving function. When these measures do not provide sufficient symptom relief, minimally invasive surgical procedures such as arthrocentesis and arthroscopy may be considered. Arthrocentesis involves flushing the upper joint space of the TMJ to remove inflammatory mediators and aid joint adaptation to a new homeostatic balance. Arthroscopy allows direct visualization of intra-articular structures of the upper joint space and enables targeted interventions such as releasing adhesions, injecting medication into the joint tissue or performing anatomical modifications, while simultaneously flushing the joint. Open joint surgery is reserved for a select group of refractory cases involving severe TMJ degeneration after all other options have been exhausted.

Despite the widespread use of this stepwise approach, important knowledge gaps in TMJ disorder management research contribute to variability in clinical practice. First, there is no consensus on when conservative treatment should be considered unsuccessful, which makes the timing of escalation to minimally invasive surgery unclear. Furthermore, when minimally invasive treatment is indicated, there is limited guidance on choosing between arthrocentesis and arthroscopy. Lastly, it is unclear how to best manage patients who do not respond adequately to initial arthrocentesis. This thesis addresses these gaps to redefine the role of minimally invasive surgical procedures and to support more consistent and effective management of degenerative TMJ disorders.

Efficacy of arthrocentesis and its timing

Before determining the optimal timing of arthrocentesis (defined as its position in the current treatment framework regarding symptom duration and conservative treatment response) for degenerative TMJ disorders, its efficacy was evaluated compared to conservative treatments. In chapter 2, a systematic review with meta-analysis and trial sequential analysis was conducted to evaluate the comparative efficacy of arthrocentesis versus conservative treatments for degenerative TMJ disorders. The last systematic search was performed in August 2024. The primary meta-analyses across randomized controlled trials indicated that for pain reduction (visual analog score; 0-100 mm), arthrocentesis resulted in a statistically significant and clinically relevant superiority over conservative treatments at short- (<6 months,

MD 14.5 mm [95% CI 9.7; 19.4], k= 9 RCTs, n= 545 subjects, I2= 48%, high quality of evidence) and intermediate-term follow-up (6 months to 5 years, MD 14.2 mm [95% CI 7.3; 21.1], k=9 RCTs, n= 547 subjects, I2= 81%, moderate quality of evidence). Furthermore, a statistical superiority of arthrocentesis for maximum mouth opening improvement was observed at short- and intermediate-term follow-up, but this was not clinically relevant. Trial sequential analyses supported the robustness of the primary analyses. Results at long-term follow-up (≥5 years) and for other study outcomes (i.e., pain at rest, mandibular function, joint blocks and noises, protrusive and lateral movements, quality of life and costs/ cost-effectiveness) were either lacking or too heterogeneous for meta-analysis. Overall, this study suggests with moderate to high confidence that arthrocentesis is superior to conservative care at short- (<6 months) and intermediate-term (6 months to 5 years) follow-up for pain management, but not for mouth opening improvement.

In chapter 3, a randomized controlled trial with long-term follow-up (≥5 years) was conducted comparing arthrocentesis with conservative treatments for degenerative TMJ disorders. A total of 84 subjects were randomly allocated to either treatment group. Linear mixed models indicated that arthrocentesis resulted in greater pain reduction (visual analog score; 0-100 mm) over the entire follow-up period compared to conservative treatments (pain during movement: −10.23 mm [95% CI −17.86; −2.60]; pain at rest: − 8.39 mm [95% CI −13.70; −3.08]). The mandibular function improvement was similar between both groups. Fewer subjects required additional treatment during follow-up in the arthrocentesis group (6% vs. 26%). Conclusively, this study suggests that arthrocentesis is more efficient in pain reduction than conservative treatments over the long-term, while maintaining similar mandibular function.

Because the optimal timing of arthrocentesis remained undefined, a two-decade retrospective cohort study was performed of 438 subjects with painful degenerative TMJ disorders in chapter 4. This study evaluated the impact of symptom duration on patient-reported success of initial arthrocentesis over a 5-year period. Generalized estimating equations models indicated that longer symptom duration was associated with reduced odds of success (OR 0.974 per month [95% CI 0.966; 0.983]), whereas treatment within 6 months of symptom onset more than doubled the odds of a favorable outcome (OR 2.71 [95% CI 1.40; 5.26]). These findings highlight the importance of timely referral and early arthrocentesis initiation in patients with degenerative TMJ disorders.

Arthroscopy versus arthrocentesis

Once minimally invasive surgery is indicated, clinicians can choose between arthrocentesis and arthroscopy, yet the evidence regarding their relative efficacy had not been clearly established. To address this, a systematic review with meta-analysis and trial sequential analysis comparing arthroscopy with arthrocentesis as well as with conservative treatments was performed in chapter 5. The systematic search was last performed in February 2023. Arthroscopy was stratified based on complexity into arthroscopic lysis and lavage (ALL) and arthroscopic surgery (AS) for all analyses. Meta-analysis indicated that arthroscopy and arthrocentesis resulted in comparable pain reduction and complication rates. ALL resulted in a slightly greater increase in maximum mouth opening at intermediate-term follow-up (6 months to 5 years), but this difference was not clinically relevant. At other follow-up intervals, and in comparisons involving AS, no significant differences in maximum mouth opening improvement were observed or insufficient data were available. Evidence for long-term outcomes (≥5 years), for comparisons between arthroscopy and conservative treatments, and for other study outcomes (i.e., pain at rest, mandibular function, joint blocks and noises, protrusive and lateral movements, quality of life and costs/cost-effectiveness) was too scarce or heterogeneous for meta-analysis. Overall, no differences were observed in efficacy between arthroscopy and arthrocentesis, but conclusions were limited by low methodological quality of the primary studies and substantial heterogeneity across studies.

The letter-to-the-editor with reply in chapter 6 expands on the discussion in chapter 5, emphasizing the need for comprehensive economic evaluations, including cost-effectiveness and cost-utility analyses, to place the clinical outcomes on TMJ surgery within the broader context of societal and healthcare considerations. Clinically, this implies that when arthrocentesis and arthroscopy demonstrate comparable efficacy in symptom reduction, arthrocentesis may be preferred because it is associated with lower costs, fewer resource requirements, and less technical demand on the surgeon.

To address the lack of high-quality comparative evidence, preliminary findings from an ongoing randomized controlled trial are presented in chapter 7. This study compares office-based arthroscopic lysis and lavage with arthrocentesis for degenerative TMJ disorders over a follow-up period of 1 year. For the preliminary results, a total of 20 subjects were randomly allocated to either treatment group. Multivariable linear mixed models showed a significantly worse reduction in pain during mandibular function (visual analog score; 0-100 mm) with arthrocentesis

compared to arthroscopy (22.42 mm [95% CI: 5.28; 39.57]). The secondary outcomes (i.e., pain at rest, maximum mouth opening, maximum mouth opening without increased pain, protrusive and lateral movements, joint noises, and mandibular function) were not significantly different between interventions. These preliminary results suggest a potential superiority of arthroscopy over arthrocentesis in pain reduction after one-year follow-up, but definitive conclusions require completion of the full trial.

Retreatment after arthrocentesis

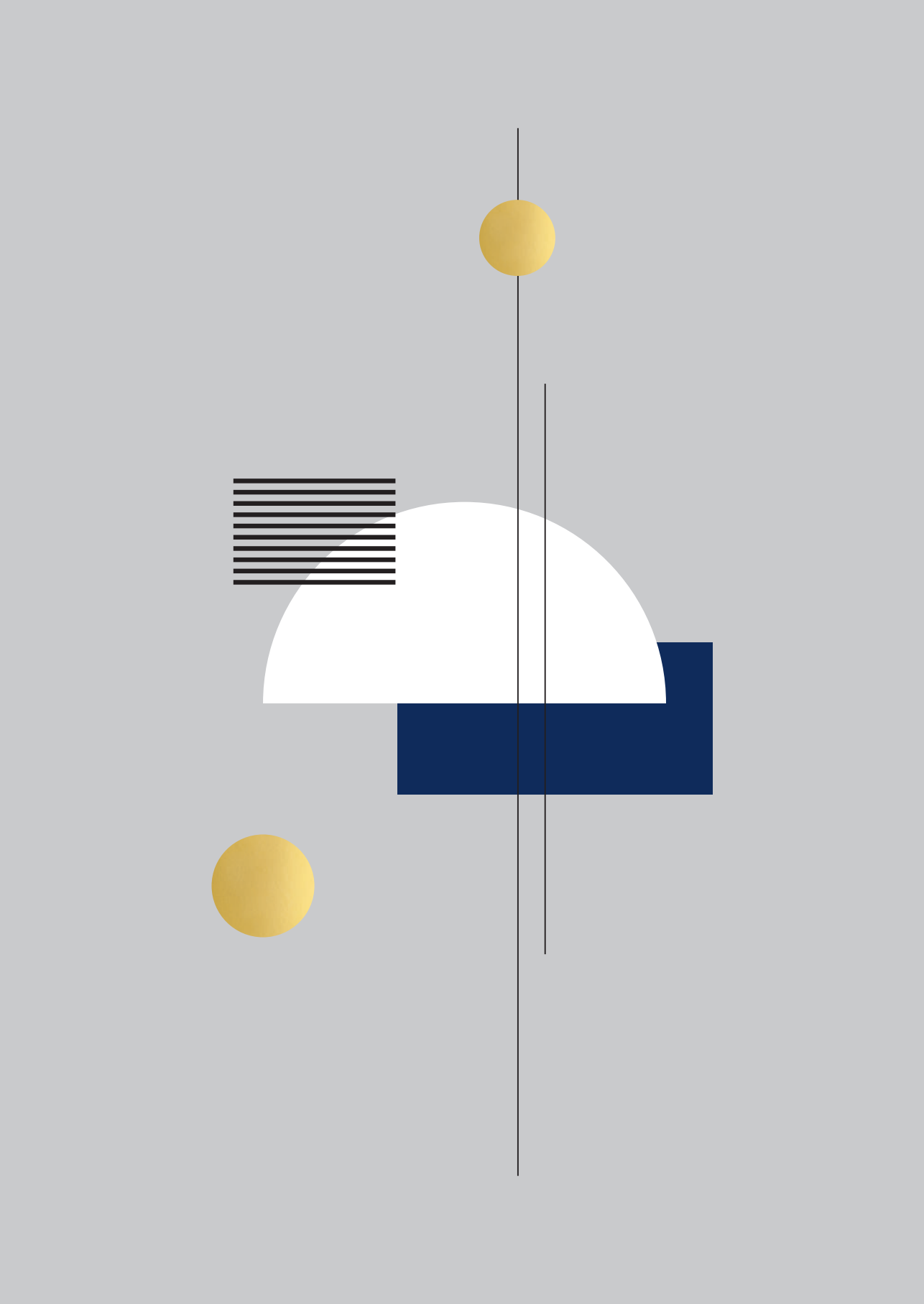
Since the evidence on retreatment strategies following unsuccessful minimally invasive surgery was scarce, a two-decade retrospective cohort study was conducted in chapter 8. In this study, the 5-year retreatment outcomes after unsuccessful initial arthrocentesis were evaluated. Approximately 31% of subjects required retreatment, which consisted of repeat arthrocentesis, arthroscopy or open joint surgery. Of those subjects, 83% were retreated successfully, indicating an overall 5-year success rate of approximately 95% across the entire treatment trajectory. However, additional retreatments beyond the first one, regardless of treatment type, did not improve long-term success at 5 years, suggesting decreasing efficacy with each additional retreatment. Furthermore, retreatment modality did not influence outcomes, supporting individualized retreatment strategies. Lastly, symptom duration before initial arthrocentesis was associated with lower odds of retreatment success in the retreated study population (OR 0.985 per month [95% CI 0.976; 0.994]), emphasizing the importance of timely intervention.

Integration and implications

In chapter 9, the findings of this thesis are summarized and interpreted in the context of the methodological quality of the available evidence, their clinical relevance and the heterogeneity in research and clinical practice. In this general discussion, the quality of evidence of each individual study of this thesis is discussed, distinguishing between more certain and less certain or hypothesis-generative evidence. It furthermore emphasizes that treatment effects should be interpreted in terms of clinically relevant differences alongside statistically significant results and acknowledges that heterogeneity in disease presentation, surgical techniques and treatment settings may limit generalizability of study results in TMJ research.

Following these considerations, four clinical recommendations are proposed. These include following a stepwise treatment strategy for degenerative TMJ disorders, starting with the least invasive interventions and escalating treatment in a timely manner. Furthermore, the choice between arthroscopy and arthrocentesis should be individualized and based on clinical context, available resources and surgeon expertise. While a first retreatment after unsuccessful arthrocentesis may still provide benefit, further retreatments are less likely to provide benefit and should lead to the critical reassessment of diagnosis and treatment strategies.

Finally, future research should aim at addressing remaining knowledge gaps in TMJ research, like identifying at-risk patients for disease chronicity, developing predictive models for treatment selection, expanding the range of treatment outcomes assessed, determining the optimal treatment timing of minimally invasive surgery in prospective studies, placing treatment within a broader biopsychosocial framework and further investigating the biological mechanisms underlying TMJ degeneration.



CHAPTER 11

NEDERLANDSE SAMENVATTING

Degeneratieve aandoeningen van het kaakgewricht (temporomandibulair gewricht) worden doorgaans behandeld op een stapsgewijze manier, waarbij conservatieve, reversibele, niet-invasieve therapieën als eerste worden ingezet. Deze behandelingen omvatten onder andere een duidelijke voorlichting omtrent de aandoening en het te verwachten beloop, (orofaciale) fysiotherapie, een stabilisatieopbeetplaat en medicatie (zoals pijnstillers, spierverslappers of antidepressiva). Het doel van deze behandelingen is het reduceren van klachten en het verbeteren of behouden van de functie van het kaakgewricht. Wanneer deze maatregelen onvoldoende effect hebben, kan minimaal invasieve chirurgie, zoals artrocentese of artroscopie, worden overwogen. Bij artrocentese wordt de bovenste gewrichtskamer van het kaakgewricht gespoeld om ontstekingsstoffen te verwijderen en zo het adaptieve herstelproces van het gewricht te ondersteunen. Bij artroscopie wordt, naast het spoelen van het gewricht, ook directe visualisatie van de interne gewrichtsstructuren mogelijk gemaakt. Hierdoor kunnen aanvullende therapeutische handelingen worden uitgevoerd, zoals het losmaken van intra-articulaire verklevingen of het inspuiten van medicatie in ontstoken gewrichtsweefsel. Opengewrichtschirurgie wordt uitsluitend toegepast bij een selecte groep patiënten die ernstige, eindstadium degeneratie van het gewricht hebben en onvoldoende reageren op andere, minder invasieve therapieën.

Hoewel dit stapsgewijze behandelalgoritme vaak wordt toegepast, bestaan er belangrijke kennishiaten die bijdragen aan een grote variatie tussen behandelaars met betrekking tot de praktijkvoering. Ten eerste ontbreekt er consensus over wanneer conservatieve, reversibele behandelingen voor degeneratieve kaakgewrichtsaandoeningen als onvoldoende effectief worden beschouwd, waardoor het optimale moment voor het inzetten van de daaropvolgende minimaal invasieve behandeling onduidelijk blijft. Ten tweede zijn er onvoldoende studies die artroscopie met artrocentese vergelijken, waardoor de keuze tussen beide behandelmodaliteiten onvoldoende berust op wetenschappelijk bewijs. Ten derde is er weinig bekend over de optimale behandelstrategie wanneer een eerste minimaal invasieve ingreep onvoldoende effectief is. De studies in dit proefschrift onderzoeken de bovenstaande kennishiaten, om hiermee wetenschappelijk onderbouwde handvatten te bieden voor meer consistente en effectieve inzet van minimaal invasieve chirurgie bij degeneratieve aandoeningen van het kaakgewricht.

Effectiviteit van artrocentese en het belang van timing

Alvorens de optimale timing van artrocentese (gedefinieerd als op welk moment deze wordt ingezet in het kader van het huidige behandelalgoritme) voor degeneratieve kaakgewrichtsaandoeningen vast te stellen, werd eerst de effectiviteit van artrocentese in vergelijking met conservatieve behandelingen vastgesteld op basis van de bestaande literatuur. In Hoofdstuk 2 wordt een systematisch literatuuronderzoek met meta-analyse en trial sequential analyse beschreven waarin de effectiviteit van artrocentese werd vergeleken met conservatieve behandelingen. De laatste zoekactie in de literatuur werd uitgevoerd in augustus 2024. Meta-analyses van uitsluitend gerandomiseerde onderzoeken met controlegroep (RCT's) toonden aan dat artrocentese statistisch én klinisch superieur was aan conservatieve behandelingen met betrekking tot pijnvermindering (visual analog score; 0-100 mm) op zowel de korte (<6 maanden, MD 14.5 mm [95% CI 9.7; 19.4], k= 9 RCT's, n= 545 proefpersonen, I2= 48%, hoge bewijskwaliteit) als op de middellange termijn (6 maanden tot 5 jaren, MD 14.2 mm [95% CI 7.3; 21.1], k=9 RCT's, n= 547 proefpersonen, I2= 81%, matige bewijskwaliteit). Hoewel artrocentese voor verbetering in maximale mondopening statistisch gezien superieur bleek te zijn, was dit verschil klinisch niet relevant. Resultaten op de lange termijn (≥5 jaren) en voor andere uitkomsten (pijn in rust, mandibulaire functie, gewrichtsgeluiden en -blokkades, protrusieve en laterale bewegingen, kwaliteit van leven en de kosteneffectiviteit) bleken onvoldoende gerapporteerd te zijn of te heterogeen om een meta-analyse uit te kunnen voeren. Concluderend kan met matige tot hoge zekerheid gesteld worden dat, op basis van de huidige literatuur, artrocentese effectiever is dan conservatieve behandelingen op de korte- (< 6 maanden) en middellange termijn (6 maanden tot 5 jaar) voor pijnvermindering bij degeneratieve kaakgewrichtsaandoeningen.

In Hoofdstuk 3 wordt een RCT met een lange-termijn follow-up (≥ 5 jaar) gepresenteerd waarin artrocentese werd vergeleken met conservatieve behandelingen bij 84 willekeurig toegewezen proefpersonen. Linear mixed models toonden aan dat artrocentese gemiddeld over de gehele follow-up periode resulteerde in een grotere pijnreductie (visual analog score; 0-100 mm) dan conservatieve behandelingen (pijn bij bewegen: −10.23 mm [95% CI −17.86; −2.60]; pijn in rust: − 8.39 mm [95% CI −13.70; −3.08]). De verbetering in mandibulaire functie was vergelijkbaar tussen beide groepen. Daarnaast was aanvullende behandeling minder vaak nodig in de artrocentese-groep (6% versus 26%). Deze resultaten suggereren dat artrocentese voor degeneratieve kaakgewrichtsaandoeningen ook op de lange termijn superieur

is aan conservatieve zorg met betrekking tot de pijnvermindering, terwijl verbetering in functionele uitkomsten vergelijkbaar is.

Omdat de optimale timing voor het inzetten van artrocentese nog onduidelijk was, werd in hoofdstuk 4, middels een retrospectieve cohortstudie met 438 patiënten, de associatie tussen symptoomduur en patiënt-gerapporteerd succes onderzocht over een periode van 5 jaar. Generalized estimating equations modellen toonden aan dat een langere symptoomduur vóór de behandeling geassocieerd was met een lagere odds op succes (OR 0.974 per maand [95% CI 0.966; 0.983]). Behandeling binnen 6 maanden na aanvang van klachten resulteerde in een meer dan verdubbeling van de odds op behandelsucces (OR 2.71 [95% CI 1.40; 5.26]). Deze resultaten benadrukken het belang van vroege verwijzing naar behandelaars die beschikken over specialistische kennis over kaakgewrichtsaandoeningen en het tijdig inzetten van artrocentese bij degeneratieve kaakgewrichtsaandoeningen.

Artroscopie versus artrocentese

Wanneer minimaal invasieve chirurgie geïndiceerd is bij degeneratieve kaakgewrichtsaandoeningen, kunnen zowel artrocentese als artroscopie ingezet worden. Om een indruk te krijgen over welke behandeling effectiever is, is in Hoofdstuk 5 een systematisch literatuuronderzoek met meta-analyse en trial sequential analyse uitgevoerd, waarin artroscopie (onderverdeeld in artroscopische lysis en lavage [ALL] en artroscopische chirurgie [AS]) werd vergeleken met zowel artrocentese als conservatieve behandelingen. De laatste zoekactie in de literatuur werd uitgevoerd in februari 2023. De meta-analyses toonden aan dat artroscopie en artrocentese even effectief waren in het reduceren van pijn en vergelijkbare complicatierisico's hadden. ALL was gering effectiever dan artrocentese in het verbeteren van de mondopening op de middellange termijn (6 maanden tot 5 jaar), maar deze superioriteit was klinisch niet relevant. Voor de verbetering van de mondopening werden op andere follow-up momenten en bij vergelijkingen met betrekking tot AS geen significante verschillen gevonden of was er onvoldoende data beschikbaar. Resultaten op de lange termijn (≥5 jaren) en omtrent andere studie uitkomsten (pijn in rust, mandibulaire functie, gewrichtsgeluiden en -blokkades, protrusieve en laterale bewegingen, kwaliteit van leven en de kosteneffectiviteit) werden onvoldoende gerapporteerd of te heterogeen voor meta-analyse. Samengevat werden geen relevante verschillen in effectiviteit gevonden tussen artrocentese en artroscopie. De interpretatie van deze conclusie werd echter beperkt

door de heterogeniteit en de lage methodologische kwaliteit van de beschikbare studies.

In Hoofdstuk 6 wordt in de vorm van een letter-to-the-editor, en de reactie daarop, de noodzaak voor aanvullende economisch evaluaties, zoals kosteneffectiviteits- en kostenutiliteitsanalyses, bij vergelijkende onderzoeken naar chirurgische ingrepen bediscussieerd. Zodoende kunnen behandelingen worden beoordeeld in een bredere maatschappelijke en zorgcontext. Vertaald naar de kliniek zou, bij gelijke effectiviteit tussen artroscopie en artrocentese, de voorkeur kunnen worden gegeven aan artrocentese, aangezien deze behandeling gepaard gaat met lagere kosten, minder gebruik van middelen en minder vaardigheden van de operateur vereist.

Omdat er een gebrek was aan wetenschappelijk bewijs omtrent de effectiviteit tussen artroscopie en artrocentese als gevolg van de heterogeniteit van studies en lage methodologische kwaliteit, worden in hoofdstuk 7 de voorlopige resultaten van een lopende RCT gepresenteerd. In deze nog lopende studie wordt artroscopische lysis en lavage onder lokale anesthesie vergeleken met artrocentese. In de voorlopige resultaten werden 20 proefpersonen gerandomiseerd naar een van beide behandelgroepen. Na een evaluatieperiode van één jaar was artroscopie effectiever in het reduceren van pijn bij bewegen (visual analog score; 0-100 mm) dan artrocentese (22.42 mm [95% CI: 5.28; 39.57]). Verbetering in de secundaire uitkomsten (pijn in rust, maximale mondopening, mandibulaire functie, gewrichtsgeluiden en -blokkades, protrusieve en laterale bewegingen) verschilden niet tussen beide groepen. Deze bevindingen suggereren een mogelijke superioriteit van artroscopie ten aanzien van pijnreductie, maar definitieve conclusies kunnen pas worden getrokken na voltooiing van de volledige studie.

Herbehandeling na artrocentese

In Hoofdstuk 8 werd, in een retrospectieve cohortstudie, de uitkomst van herbehandeling na onvoldoende resultaat van een initiële artrocentese voor degeneratieve kaakgewrichtsaandoeningen onderzocht over een periode van 5 jaar. Ongeveer 31% van de patiënten die initieel met artrocentese werden behandeld onderging een herbehandeling, variërend van her-artrocentese tot artroscopie of opengewrichtschirurgie. Van deze herbehandelde groep, werd bij 83% alsnog patiënt-gerapporteerd succes behaald, wat resulteert in een patiënt-gerapporteerd behandelsucces van ongeveer 95% van het complete behandeltraject. Een tweede of daaropvolgende herbehandeling droeg echter niet meer bij aan patiënt-

gerapporteerd succes. Evenmin had het type herbehandeling invloed op het resultaat. Een langere symptoomduur voorafgaand aan de eerste artrocentese was wél geassocieerd met lagere odds op een succesvolle herbehandeling (OR 0.985 per maand [95% CI 0.976; 0.994]), wat het belang van tijdige behandelswitch van niet-invasieve, conservatieve therapie naar een minimaal invasieve interventie opnieuw benadrukt.

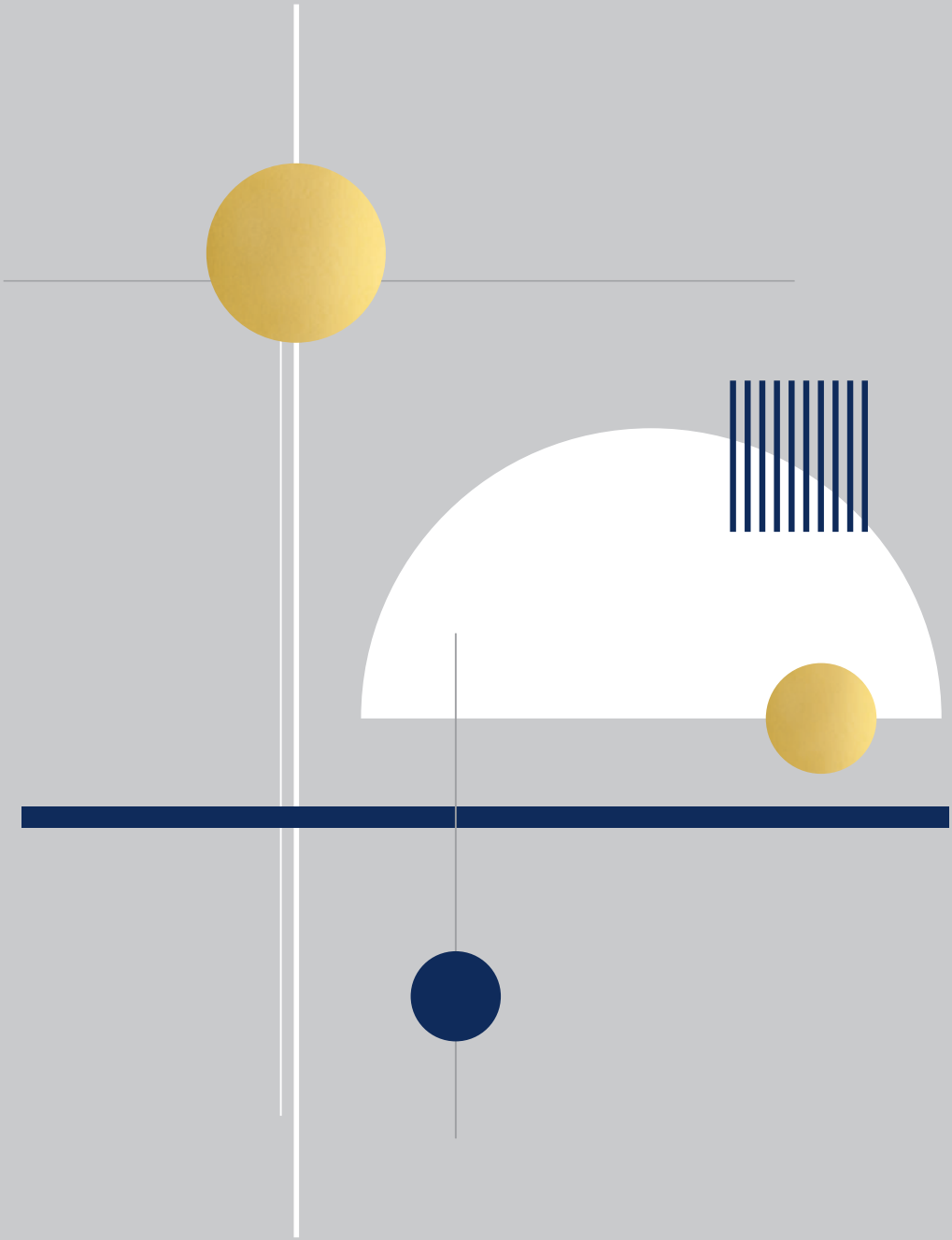
Interpretatie van resultaten en implicaties

In hoofdstuk 9 worden de bevindingen van dit proefschrift geïnterpreteerd in de bredere context van de kwaliteit van het beschikbare bewijs, klinische relevantie en de heterogeniteit in ziektepresentatie en behandeling. Met betrekking tot de kwaliteit van het beschikbare bewijs kan op basis van de studies in dit proefschrift met redelijke zekerheid worden gesteld dat artrocentese effectiever is dan conservatieve zorg in het reduceren van pijn bij degeneratieve kaakgewrichtsaandoeningen. Deze superioriteit is niet alleen statistisch significant, maar ook klinisch relevant. Voor de vergelijking tussen artroscopie en artrocentese is het beschikbare bewijs beperkt en van lage kwaliteit, mede door het gebrek aan goed uitgevoerde RCT's. In het systematisch literatuuronderzoek in dit proefschrift werd geen klinisch relevant verschil in effectiviteit tussen beide behandelingen gevonden. De voorlopige resultaten van de daarna uitgevoerde RCT laten echter wél een klinisch relevante superioriteit van artroscopie zien voor pijnreductie. Bij de interpretatie van de bevindingen in dit proefschrift dient rekening te worden gehouden met de heterogeniteit in zowel ziektepresentatie als behandeling bij degeneratieve kaakgewrichtsaandoeningen. Variatie in chirurgische technieken en aanvullende behandelingen tussen studies en behandelcentra kan de vergelijkbaarheid van studies beperken. Daarnaast vormen kaakgewrichtsaandoeningen een heterogene groep aandoeningen en zijn studies in dit proefschrift uitgevoerd in een tertiair zorgcentrum, waardoor interpretatie en generaliseerbaarheid van de resultaten beperkt kunnen zijn.

Vanuit de bevindingen van dit proefschrift kunnen de volgende klinische aanbevelingen gedaan worden voor de behandeling van degeneratieve kaakgewrichtsaandoeningen. Ten eerste wordt geadviseerd om binnen de huidige stapsgewijze behandelstrategie, waarbij wordt gestart met conservatieve behandeling, bij onvoldoende effect tijdig (binnen 6 maanden) te escaleren naar een minimaal invasieve behandeling. Daarnaast dient de keuze tussen artroscopie en artrocentese geïndividualiseerd te worden, vanwege het gebrek aan hoog kwaliteit bewijs omtrent de effectiviteit van beide behandelingen. Daarom dient de keuze

gebaseerd te zijn op de klinische context, beschikbare middelen en de mate waarin de behandelaar beschikt over voldoende specifieke kennis en vaardigheden op het gebied van kaakgewrichtspathologie. Verder kan een eerste herbehandeling na een ineffectieve initiële artrocentese bijdragen aan een succesvolle behandeluitkomst, maar zal de effectiviteit van elke opeenvolgende behandeling steeds verder dalen. Ineffectiviteit van een behandeling is aanleiding voor een kritische herbeoordeling van de diagnostiek en de behandelstrategie.

Toekomstig onderzoek dient zich te richten op het identificeren van patiënten met een verhoogd risico op het ontwikkelen van chronische klachten. Ook het ontwikkelen van predictiemodellen voor behandelkeuze en het gebruik van meer patiënt-gerapporteerde uitkomstmaten in prospectieve studies zullen verder bijdragen aan de effectiviteit van behandelingen van degeneratieve kaakgewrichtsaandoeningen.



APPENDICES

ABOUT THE AUTHOR

LIST OF PUBLICATIONS

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About the author

Yang Hang Tang was born on 14 December 1994 in Leeuwarden, the Netherlands. Shortly after his birth, he moved to Nanjing, China. In 1999, he returned to the Netherlands, where he grew up in Groningen and graduated with a bilingual diploma from the Maartenscollege in Haren in 2013.

In the same year, he began studying Medicine at the University of Groningen, during which he participated in several committees. After obtaining his bachelor's degree in Medicine, he completed a master's degree in Healthcare Management at the Erasmus University Rotterdam in 2018, while simultaneously pursuing his master's degree in Medicine in Groningen. His graduation thesis in Rotterdam focused on the consequences of accountable care units and decentralization in hospitals for hospital manageability and the physician-manager relationship. Before obtaining his master's degree in Medicine in 2020, Yang Hang completed his final clinical rotation and research thesis at the Department of Oral and Maxillofacial Surgery at the University Medical Center Groningen (UMCG).

In 2021, he continued at the same department as a PhD candidate under the supervision of Prof. dr. F.K.L. Spijkervet, dr. N.B. van Bakelen and dr. B. Gareb, where he investigated the role of minimally invasive surgery for degenerative temporomandibular joint disorders. In the same year, Yang Hang also started studying Dentistry at the University of Groningen. During his PhD, he was involved in setting up a clinical trial (*DIAMOND trial*) and presented his work at several national and international conferences, including the *International Conference on Oral and Maxillofacial Surgery* in Vancouver and the *Annual Conference of the European Society of Temporomandibular Joint Surgeons* in Bratislava.

Yang Hang plans to defend his PhD dissertation on 6 May 2026. Since January 2026, he has started his residency in Oral and Maxillofacial Surgery at the UMCG. He will receive his master's degree in Dentistry upon completing his first year of residency.

In his free time, Yang Hang enjoys road cycling, running and cooking. He currently lives in Groningen with his wife Paula, whom he married in August 2025.

List of publications

1. **Tang YH**, van Bakelen NB, Gareb B, Spijkervet FKL. Timing of arthrocentesis and its association with treatment success in painful temporomandibular joint disorders: a two-decade cohort study. Int J Oral Maxillofac Surg. 2026 Jan 28:S0901-5027(26)00019-6. Epub ahead of print.

2. **Tang YH**, van Bakelen NB, Gareb B, Spijkervet FKL. Office-Based Arthroscopy Versus Arthrocentesis as Treatment for Temporomandibular Joint Pain and Dysfunction: Preliminary Results of a Randomized Controlled Trial. J Clin Med. 2025 Apr 24;14(9):2929.

3. **Tang YH**, van Bakelen NB, Gareb B, Spijkervet FKL. Arthrocentesis versus conservative treatments for temporomandibular joint disorders: A systematic review with meta-analyses and trial sequential analyses. J Craniomaxillofac Surg. 2025 Mar;53(3):250-261.

4. **Tang YH**, van Bakelen NB, Gareb B, Spijkervet FKL. In Reply to Comment on "Arthroscopy versus arthrocentesis and versus conservative treatments for temporomandibular joint disorders: a systematic review with meta-analysis and trial sequential analysis". Int J Oral Maxillofac Surg. 2025 Jan;54(1):99.

5. **Tang YH**, van Bakelen NB, Gareb B, Spijkervet FKL. Arthroscopy versus arthrocentesis and versus conservative treatments for temporomandibular joint disorders: a systematic review with meta-analysis and trial sequential analysis. Int J Oral Maxillofac Surg. 2024 Jun;53(6):503-520.

6. **Tang YH**, van Bakelen NB, Spijkervet FKL. Minimaal invasieve behandelingen en opengewrichtschirurgie voor aandoeningen van het kaakgewricht [Minimally invasive treatments and open joint surgery for disorders of the temporomandibular joint]. Ned Tijdschr Tandheelkd. 2024 May;131(5):223-230.

7. **Tang YH**, Vos LM, Tuin AJ, Huddleston Slater JJR, Gareb B, van Bakelen NB, Spijkervet FKL. Arthrocentesis versus non-surgical intervention as initial treatment for temporomandibular joint arthralgia: a randomized controlled trial with long-term follow-up. Int J Oral Maxillofac Surg. 2023 May;52(5):595-603.

8. Vonk J, de Wit JG, Voskuil FJ, **Tang YH**, Hooghiemstra WTR, Linssen MD, van den Broek E, Doff JJ, de Visscher SAHJ, Schepman KP, van der Vegt B, van Dam GM, Witjes MJH. Epidermal Growth Factor Receptor-Targeted Fluorescence Molecular Imaging for Postoperative Lymph Node Assessment in Patients with Oral Cancer. J Nucl Med. 2022 May;63(5):672-678.

Dankwoord

Het is een bijzonder voorrecht om na de afgelopen jaren van onderzoek doen aan het einde van een promotietraject te mogen staan. Ik kijk met veel plezier terug op deze periode, waarin ik gaandeweg veel heb mogen leren van de mensen met wie ik heb samengewerkt. Het doen van onderzoek is zelden een solistische onderneming, en teamwork is dan ook het fundament geweest voor het tot stand komen van dit proefschrift. Bovendien had dit onderzoek niet kunnen plaatsvinden zonder de **patiënten** die bereid waren deel te nemen aan de studies. Daarvoor ben ik hen zeer dankbaar. Graag wil ik in het bijzonder de volgende mensen nog benoemen en bedanken:

Geachte **prof. dr. F.K.L. Spijkervet**, hooggeleerde promotor, beste Fred, hartelijk bedankt voor jouw altijd prettige en duidelijke begeleiding tijdens mijn promotietraject. Jouw expertise op het gebied van de kaakgewrichtschirurgie heeft in belangrijke mate bijgedragen aan dit onderzoek. Je was zeer betrokken bij de projecten, maar gaf mij tegelijkertijd de ruimte om het onderzoek op mijn eigen manier vorm te geven. Een van de hoogtepunten tijdens mijn promotie was het gezamenlijke bezoek aan het ESTMJS-congres in Bratislava, waar ik met veel plezier op terugkijk. Daarnaast wil ik je bedanken voor de mogelijkheid om het duale traject van tandheelkunde en promotieonderzoek te doen, en voor jouw voormalige rol als afdelingshoofd, waarin je een belangrijke bijdrage hebt geleverd aan de prettige en stimulerende werkcultuur binnen de afdeling. Hartelijk dank voor jouw vertrouwen en steun!

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