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The Comparison of Various Diagnostic Magnetic Resonance Imaging Sequences for the Early Morphological and Degenerative Changes in the Articular Disc of Temporomandibular Disorders: A Systematic Review

Temporomandibular Bozuklukların Eklem Diskindeki Erken Morfolojik ve Dejeneratif Değişiklikler İçin Çeşitli Tanısal Manyetik Rezonans Görüntüleme Dizilerinin Karşılaştırılması: Sistemik Bir İnceleme

ABSTRACT

Objective: Magnetic Resonance Imaging (MRI) is the gold standard for the imaging the Temporomandibular Joint (TMJ) disc. Ultra-structural changes in the disc occur even before the morphological changes, which can be assessed by various MRI sequences. This systematic review aimed to compare and evaluate the diagnostic accuracy of various MRI sequences for detecting TMJ dysfunction.

Methods: In this search strategy, we employed PubMed, PubMed Central, Scopus, Web of Science, Google Scholar, Science Direct, and the Cochrane Library. Articles from the last decade were included in the search. The search yielded 48 papers. However, only 10 papers met the criteria for inclusion in the systematic review. The potential for bias in the included studies was evaluated.

Results: Various MRI sequences have been discussed in this review. Among them T2 mapping sequence uses T2 transverse relaxation time ranging from 39.284 ± 5.634 ms to 30.982 ± 3.205 ms in the control and the patient groups. dGEMRIC is the T1 mapping sequence assess glycosaminoglycans in the connective tissues. The mean T1 values in the post-contrast patient group and control group were 326.3ms and 441.9ms, respectively.

Conclusion: Among the various imaging sequences evaluated in this systematic review, T2 mapping and dGEMRIC emerge as powerful tools for the quantitative evaluation and early identification of cartilage degeneration within the articular disc of the TMJ. Implementing these MRI sequences as a routine diagnostic protocol in symptomatic young adults may allow clinicians to detect degenerative abnormalities at a reversible stage, guiding appropriate and timely interventions to help terminate disease progression.

Keywords: Articular disc, temporomandibular joint, derangement, magnetic resonance imaging, sequences.

ÖZ

Amaç: Manyetik Rezonans Görüntüleme (MRG), Temporomandibular Eklem (TMJ) diskini görüntülemek için altın standarttır. Diskteki ultra yapısal değişiklikler, morfolojik değişikliklerden önce bile meydana gelir ve çeşitli MRG sekansları ile değerlendirilebilir. Bu sistemik inceleme, TMJ disfonksiyonunu tespit etmek için çeşitli MRG sekanslarının tanısal doğruluğunu karşılaştırmayı ve değerlendirmeyi amaçlamıştır.

Yöntemler: Bu arama stratejisinde PubMed, PubMed Central, Scopus, Web of Science, Google Scholar, Science Direct ve Cochrane Kütüphanesi kullanılmıştır. Son on yıla ait makaleler aramaya dahil edilmiştir. Arama sonucunda 48 makale bulunmuştur. Ancak, sistemik incelemeye dahil edilme kriterlerini karşılayan sadece 10 makale mevcuttur. Dahil edilen çalışmalarda olası yanlılık değerlendirilmiştir.

Bulgular: Bu incelemede çeşitli MRG sekansları ele alınmıştır. Bunlar arasında T2 haritalama sekansı, kontrol ve hasta gruplarında 39.284 ± 5.634 ms ile 30.982 ± 3.205 ms arasında değişen T2 enine gevşeme süresini kullanır. dGEMRIC, bağ dokularındaki glikozaminoglikanları değerlendiren T1 haritalama sekansıdır. Kontrast sonrası hasta grubunda ve kontrol grubunda ortalama T1 değerleri sırasıyla 326.3 ms ve 441.9 ms idi.

Sonuç: Bu sistematik incelemede değerlendirilen çeşitli görüntüleme sekansları arasında, T2 haritalama ve dGEMRIC, temporomandibular eklem (TMJ) eklem diskindeki kıkırdak dejenerasyonunun kantitatif değerlendirilmesi ve erken teşhisi için güçlü araçlar olarak ortaya çıkmaktadır. Bu MRI sekanslarının semptomatik genç yetişkinlerde rutin bir tanı protokolü olarak uygulanması, klinisyenlerin dejeneratif anormallikleri geri dönüşümlü bir aşamada tespit etmelerine ve hastalığın ilerlemesini sonlandırmaya yardımcı olmak için uygun ve zamanında müdahalelere rehberlik etmelerine olanak sağlayabilir.

Anahtar kelimeler: Eklem diski, temporomandibular eklem, bozukluk, manyetik rezonans görüntüleme, sekanslar.

INTRODUCTION

Temporomandibular disorder (TMD) can occur when conditions affect the masticatory muscles, the TMJ, or tissues around these areas. They are a significant cause of orofacial pain and dysfunction, affecting up to 25% of the population, predominantly in young adults. The health of the articular disc, particularly its structural and biochemical integrity, is a key factor in the progression of these disorders.¹ Symptoms and signs of TMD include limited and/or abnormal range of motion, clicking, popping, or crepitus in function with or without locking of the jaw, TMJ pain, jaw opening pain, orofacial pain, otalgia, tinnitus and headache.² Intra-articular abnormalities and trauma are the leading causes of temporomandibular joint (TMJ) pain.³ "Internal derangement (ID) of the TMJ refers to an improper relationship of the disc with respect to the condyle, articular eminence, or articular fossa".⁴ Anterior displacement of the disc is more prevalent than any other types (posterior, lateral, or medial).⁵

Early diagnosis is important for managing the TMD's.⁶ Magnetic resonance imaging (MRI) is the gold standard for imaging TMJ components, including the articular disc, ligaments, and muscles, because of its high spatial resolution.⁷⁻⁹ It provides range of sequences that can aid in assessing both morphology and composition.

Although MRI is a versatile diagnostic imaging modality, morphological imaging restricts ultrastructural imaging of the articular cartilage, which can be evaluated by biochemical analysis using modified MRI sequences.^{10,11}

Among them few were studied for evaluating TMJ articular cartilage, such as Fast Imaging Employing Steady-State Acquisition (FIESTA), Delayed Gadolinium Enhancement of Magnetic Resonance Imaging of Cartilage (dGEMRIC), T2 mapping, Fluid Attenuated Inversion Recovery (FLAIR), Multiple Echo Data Image Combination (MEDIC), Half-Fourier Acquisition Single-Shot Turbo Spin Echo (HASTE), Double Echo Steady State (DESS).

Currently, there is a lack of consensus and standardization in their application, and the diagnostic utility of these sequences in the context of TMJ disorders is still underexplored and somewhat conflicting in the literature. Some studies suggest that T2 mapping correlates with water content and collagen disarray, while dGEMRIC may reflect glycosaminoglycan depletion yet their respective roles in the early detection and progression of TMJ abnormalities remain a matter of debate. Furthermore, many previous reviews have not comprehensively evaluated their comparative performance or the robustness of their diagnostic metrics.

To address these gaps, we conducted a systematic review to synthesize and critically appraise the current evidence in evaluating articular disc degeneration in the TMJ. Our aim is to clarify their respective roles, identify weaknesses and inconsistencies in the literature, and provide guidance for future research and eventual clinical application.

METHODS

This systematic study addressed the following question: Can different MRI modifications improve diagnostic reliability for early intervention in patients with TMJ internal derangement?

The PRISMA 2020 standards were used to conduct the systematic review.

The research question was formulated by using the PICO format.

P- Patients with and without internal disc derangement of the TMJ, I- Various MR imaging sequences, C- Traditional MR imaging of the temporomandibular joint, O- Identifying internal abnormalities in TMJ in its earliest stages.

Search strategy

This systematic review was entered into the International Prospective Register of Systematic reviews (PROSPERO) database with the identifier CRD4202344477. The search approach adhered to the standards set out by Cochrane for systematic reviews. Boolean operators and Medical Subject Headings (MeSH) keywords "diagnostic" OR "diagnostical" ("reliabilities" OR "reliability" AND ("temporomandibular joint" OR ("temporomandibular" AND "joint" AND ("magnetic resonance imaging" OR ("magnetic" AND "resonance" AND "imaging" ("articular" AND "disc" OR "articular disc AND ("derange OR "derangement" AND "sequence" OR "sequencing" OR "sequences" were utilized to search articles on databases such as PubMed, PubMed Central, Scopus, Web of Science, Google Scholar, Science Direct, and the Cochrane Library.

Inclusion criteria

The years from 2013 to 2023 were used to find applicable research. Prospective, retrospective studies, clinical trials, cohort studies, case-control studies, and cross-sectional studies originally published in English were included. "Modified sequencing of MRI for early diagnosis and intervention in patients with diagnostic criteria for TMD DC/TMD criteria, ³ Axis 1 for internal disc derangement (with reduction, with reduction and intermittent locking, without reduction and limited opening, without reduction and limited opening)" were considered.

Exclusion criteria

Grey literature studies, reviews, editorials, letters, published errata, historical pieces. Patients with history of trauma or developmental problems of TMJ, and individuals currently receiving therapy for TMDs were excluded.

Evaluation of the Studies' Quality: The studies were assessed for quality using the QUADAS 2 technique. Review Manager 5.4.1 received the data and generated numerous color-coded diagrams showing bias and relevance risks (Figure 1).

RESULTS

Study selection

Initial online searches yielded forty-eight studies of MRI sequences of TMJ were identified from the databases. Among them, 12 duplicate records, 4 ineligible records, 6 unretrievable records, 2 abstract - only

articles, 2 other than in vivo articles, and 12 due to other reasons were excluded. This systematic review closely examined ten articles (Figure 2).

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

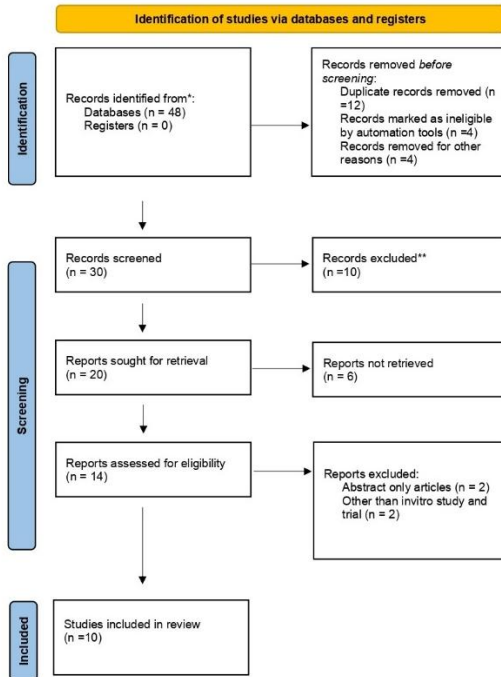


Figure 1. PRISMA (Items Favoured in Systematic Reviews and Meta-Analyses for Reporting) flow chart

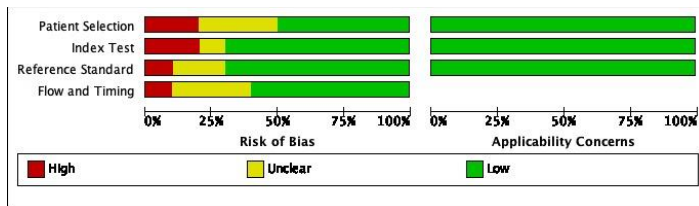


Figure 2. Concerns regarding applicability and risk of bias graph

General characteristics of the included studies

There were 10 articles evaluating the diagnostic accuracy of various MRI sequences in the early diagnosis of TMDs. All the study participants were assessed only once at one particular point in time in all the included studies. The study design was cross – sectional and case- control studies. There were 95 healthy volunteers, 845 TMD patients, who underwent various MRI sequences (Table 1). Two studies performed biochemical MRI sequences; one performed the FLAIR sequence to evaluate joint effusion, while few studies performed dynamic sequences. All these sequences were performed as an adjunct to the conventional sequences. Almost all studies had positive results stating that the sequences had better visualization of the TMJ, but one study stated that due to lower image quality, dynamic sequences are not sufficient for evaluating TMJ independently.

Table 1. The characteristics of the included studies.

Author	Study design	Sample distribution	MRI sequences	Results	Inference
Zhao Z et al ¹³	Case-control	Control group n=57, Group DDWR 45, Group DDwOr- 63	FST2WI, sagittal T1WI, coronal T2WI, MERGE, and T2 mapping	The mean T2 value of control group was 39.284 ±5.634 ms for ADDwR- 33.634 ±4.235 ms, ADDw/oR- 30.982 ±3.205 ms	T2 mapping gives an accurate quantitative evaluation of temporomandibular disc than conventional MRI in individuals with derangement
Eder J et al ¹⁶	Case-control	Control group n= 6 Study group n= 11 (22 TMJs)	inversion-recovery (IR), morphological PDWI FSE, and 3D DESS	The dGEMRIC postcontrast T1 value dropped in both groups, 326.3ms in the patient group and 441.9ms in the control group.	The dGEMRIC is a useful T1 quantitative biochemical protocol, which implies the early diagnosis of degenerative changes in TMD.
Otonari-Yamamoto et al ¹⁴	Cross-sectional	n= 45 (48 joints)	PDWI, T2WI FLAIR	The median SIR of joint effusion was 0.97 in normal 1.00 in the DWR category, 1.19 in the DWOR category, and 1.47 in the OA category	FLAIR is a highly sensitive technique to evaluate joint effusion content changes compared to conventional MRI.
Uchiyama Y et al ¹⁵	Cross-sectional	23 patients (n= 46 joints)	Oblique sagittal images acquired using PD-weighted, T1WI, T2WI, and MERGE sequences	AD of the disc was seen in 22 joints (47.8%). MERGE was significantly better than PD-weighted FSE $P < 0.0125$ (0.05/4)] at the middle and medial parts of the TMJ.	PD-weighted FSE is helpful for recognising a disc with Anterior Displacement, whereas MERGE is helpful for detecting a disc and cortex of the condylar head in their usual positions.
Aksoy S et al ⁶	Cross-sectional	n= 60 patients	Frequency-selected FS T2W (FS T2W), FSE T2W (3D), and 3D FIESTA-C	Interobserver agreement on disc configuration closed and open mouth disc position was good for 3D FIESTA-C sequences	High-resolution, dynamic MR images of the TMJ may be obtained using 3D FIESTA-C sequences can be integrated into standard MRI procedures.
Sun Q et al ⁸	Case-control	n=20 in the control group TMJs n = 92 (cyc;2300 = cycles of open-closed mouth = 3) and group 2 = 58 (cyc;2300 = cycles of open-closed mouth >= 3)	Static MRI- PDWI AND T2WI Dynamic FIESTA sequence	In a sample of 160 TMJs, 23.13 percent of the TMJs had joint effusions, and 79 TMJs had ADDw/oR. statistically significant difference in "jumping sign" in the ADDwR group and the DDw/Or group.	The FIESTA-MRI provides better contrast between the TMJ disc and the joint effusion and helps in real-time evaluation
Ravanelli M et al ¹⁷	Cross-sectional	N= 50 subjects (99 TMJs)	(TSE)T2, Parasagittal Spin-Echo (SE)T1, and Fat-Saturated PD Sequences, together with a T2 HASTE sequence for real time rTMRI.	In a statistically significant comparison between static and rTMRI, the mean score for image quality analysis of 99 TMJs was 3.41 for static MRI and 3.82 for rMRI.	The rt MRI with HASTE helps observe opening and closing movements and better evaluates ID.
Cassetta M et al ²⁷	Cross-sectional	194 patients (388 TMJs)	dynamic PDWI/TSE T2 weighted sequences, HASTE.	In the evaluation of disc position, 25 (6.4%) normal disc positions, 274 (70.6%) DDwR and 89 (23.0%) DDw/oR were found on dynamic imaging.	The HASTE sequence has smaller motion artefacts and a good spatial resolution achieved in a shorter acquisition time and evaluates the disc re-capture time in ADDR.
Barchetti F et al ¹⁸	Cross-sectional	n=194 patients, 388 TMJs	Static MRI- PD weighted/TSE T2-weighted sequences, Dynamic MRI-HASTE sequence	The static and dynamic sequences are not concordant in evaluating disc position.	Because of the lower quality of the images, dynamic sequences cannot be the only tool to evaluate TMD.
Yen P et al ²⁰	Cross-sectional	n= 12 subjects (24 volunteers)	Static MRI- T1WI, T2WI, FSE PDWI, Dynamic MRI-EPI, HASTE, and true FISP pulse sequences	Disc position and dynamics were best depicted in a sagittal plane of imaging that varied between subjects and often between joints in the same subject.	Visualization of the TMJ was best in true FISP sequence due to high spatial resolution.

Risk of bias and applicability concern

Overall, the included studies showed low risk of bias and very few of them showed uncertain and high risk (Figure 3). The risk of bias was ambiguous in the selected studies, and the risk of generalizability concerns was low. A pair of experts checked the evaluation quality. The reliability coefficients for comparisons of the data extraction and assessment were consistently high, with values of 0.920, and 0.930,

which indicate a strong level of agreement among the reviewers. Since two independent reviewers does not have disagreement, a third-party adjudicator was not used.

	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Aksoy S et al. ⁶	?	+	?	+	+	+	+
Barchetti F et al. ¹⁸	?	-	+	+	+	+	+
Cassetta M et al. ²⁷	+	+	?	+	+	+	+
Eder J et al. ¹⁶	-	?	-	?	+	+	+
Otonari et al. ¹⁴	-	-	+	+	+	+	+
Ravanelli et al. ¹⁷	+	+	+	?	+	+	+
Sun Q et al. ⁸	+	+	+	+	+	+	+
Uchiyama et al. ¹⁵	+	+	+	-	+	+	+
Yen P et al. ²⁰	?	+	+	+	+	+	+
Zhao Z et al. ¹³	+	+	+	?	+	+	+

 High
  Unclear
  Low

Figure 3. Summary of the included studies

The diagnostic accuracy tool was evaluated in four broad domains: patient sampling, index test, reference standard, flow, and timing. Every category included anything from two to four questions, all of which could be answered "yes", "no" or "unclear". High risk is present in index test for Barchetti et al.,¹⁸ and Otonari-Yamamoto et al.,¹⁴ patient selection for Eder et al.,¹⁶ and Otonari-Yamamoto et al.,¹⁴ reference standard for Eder et al.,¹⁶ and flow and timing for Uchiyama et al.,¹⁵ Adequate data were unclear in following domains- Aksoy et al.,⁶ Barchetti et al.,¹⁸ Yen et al.,²⁰ in the patient selection, Eder et al.,¹⁶ in the index test, Aksoy et al.,⁶ and Cassetta et al.,²⁷ in the reference standard, Eder et al.,¹⁶ Ravanelli et al.,¹⁷ and Zhao et al.,¹³ in the flow and timings. Following appropriate study protocol improves the quality of studies in the future.

DISCUSSION

The most cutting-edge imaging technique for identifying TMJ disorders is MRI. It is regarded as non-invasive and has the capacity to produce excellent tomographic imaging in any plane with spatial resolution for both bone and soft tissue. Patients are also not exposed to any biological dangers or ionising radiation. MRI sensitivity, specificity, and diagnostic accuracy are considered as gold standard in articular disc imaging.¹²

In the included studies, there were biochemical sequences- T2 mapping, dGEMRIC, dynamic sequences- HASTE, FIESTA, FISP (Fast Imaging with Steady-State Precession), FLAIR, MEDIC/ MERGE (Multiple-Echo Recombined Gradient Echo). However, the TMJ is much smaller

than other joints, detecting early inflammatory changes in the joints might be challenging using conventional approaches before they lead to morphological alterations which were discussed in detail.

To diagnose disc degeneration before morphological alteration occurs and to monitor longitudinal changes in the TMJ structure over time, Zhao et al.¹³ performed T2 mapping sequences in the articular disc displacement of the TMJ in young adults. MRI T2 mapping is a technique that elucidates metabolic factors and structural alterations by quantifying T2 transverse relaxation time. The beneficial aspects are fast imaging, excellent resolution, and isotropic 3D cartilage evaluation, and utilizes commercially available pulse sequences and integrated processing software without contrast media administration. The T2 MRI time constant detects slow molecular movements of water protons and tissue network anisotropy. The restricted transportation of cartilage fluid in an extremely heterogeneous network results in T2 values ranging from 15 to 60 milliseconds. Lack of collagen and proteoglycan in degenerative cartilage enhances water movement, leading to increased signal intensity on T2-weighted imaging. In his study T2 relaxation time in the control and the patient groups was 39.284 ± 5.634 ms and 30.982 ± 3.205 ms. The control group had the highest T2 value, while the group with articular disc displacement without reduction had the lowest T2 value. Thus, he stated that it provides accurate quantitative evaluation by assessing the water content in the collagen of the disc and concluded that T2 mapping is appropriate for early diagnosis in asymptomatic individuals and also be used to monitor the longitudinal changes in MR structure and function of individuals before and after treatment.

TMJ derangement internally manifests with joint effusion. A high signal intensity in the upper and lower joint spaces on T2-weighted images indicates fluid collection in the TMJ. If there is a correlation between bone marrow changes and TMJ pain, it is likely that pain will arise even if the change is too minimal to be visible on proton density- or T2-weighted imaging. It is influenced by the quantity of protein cytokine receptors in synovial fluid. The FLAIR sequence allows for the non-invasive study of variations in protein concentrations in the joint fluid by measuring increases in FLAIR signal intensity. Otonari-Yamamoto et al.,¹⁴ analysed the signal intensity of joint effusion on FLAIR images in TMJ disorders. The median Signal intensity ratio (SIR) of joint effusion gradually increased from the normal disc category through the Disc displacement With Reduction, Disc displacement Without Reduction, and Osteoarthritis categories and concluded that FLAIR is a more sensitive approach than traditional MRI for assessing changes in effusion content in patients with TMD.¹⁵

dGEMRIC provides quantitative imaging for the indirect assessment of glycosaminoglycan content, making it a clinically useful method for assessing the early stages of cartilage deterioration in various joints, such as the knee, ankle joint, and hip in individuals with risk factors for osteoarthritis. T1 mapping quantitatively revealed that contrast agent absorption was negatively linked with GAG concentration. More GAG is needed to replace degenerating cartilage. Hence, T1 relaxation times decrease with increasing contrast agent absorption. Eder et al.¹⁶ examined the morphology of each patient's TMJ using conventional MR imaging. The contrast agent was administered as a twofold dosage of 0.2 mmol/kg of Gd diethylenetriamine Penta acetic acid ion per kilogram body weight. Using inversion-recovery (IR), morphological proton-density (PD) weighted FSE, and 3D Dual- Echo Steady State (DESS) sequences TMJ internal derangement was investigated using the dGEMRIC approach." The mean T1 values in the post-contrast patient group and control group were 326.3ms and 441.9ms, respectively.

The TMJ's articular disc may be so thin in the center that it is undetectable on sagittal sections. In order to overcome this, a novel gradient-echo sequence was created, using the MERGE approach to produce good picture contrast and a high signal-to-noise ratio (SNR). It captures and adds numerous gradient echoes at different echo times automatically. Due to its excellent picture contrast, MERGE has frequently been employed to represent the spinal nerves. Uchiyama et al.¹⁵ compared MERGE, PD-weighted Fast Spin Echo sequence (FSE), T1-weighted FSE, and T2-weighted FSE sequences the diagnostic imaging of the temporomandibular joint (TMJ). He concluded that PD-weighted FSE would be useful in detecting a disk with Anterior Displacement, while MERGE would be useful in detecting a normally positioned disk and cortex of the condylar head.

In recent years, dynamic MRI has been used in combination with other dynamic measures of joint function. Dynamic pictures taken as the patient opens and closes his lips utilizing optimized sequences for image acquisition are becoming more common in research.¹⁷⁻¹⁹ Using cinematic software, they could recreate the opening and closing the mouth. optimized echo planar imaging, FISP, and HASTE sequences by Yen et al., Ravanelli et al., FIESTA sequence by Sun Q. et al., Aksoy. S et al., were studied. They give more accurate imaging than pseudo-dynamic sequences in real time. Therefore, it is more challenging to diagnose TMD when a patient complains of pain without a systemic disease or the appearance of skeletal anomalies. MRI is essential for assessing the TMJ's intra-articular components.²⁰⁻²⁷

Limitations

This systematic review has few limitations, such as a small sample size- As there were various MRI sequences only ten studies satisfied the inclusion criteria in the previous ten years, larger studies in MRI of TMD's are required in the future which can increase the quality of the studies. Other potential techniques (e.g. ultra-high-resolution MRI) were not included. They were only cross-sectional studies which means that long-term changes cannot be monitored. Lack of standardization and heterogeneity, bias and confounding factors. The included studies demonstrated heterogeneity in terms of patient selection, variability in sample size, MRI sequences performed. As these were observational heterogeneity and thus no formal statistical assessment of heterogeneity (e.g. Chi-square test) was conducted. The study and the control population in the included studies were not even.

Future perspectives

In the future, MRI biomarkers can be associated with different diseases and serve as indicators of disease progression and treatment response, leading to more personalized and targeted therapies. The AI algorithm can be used to analyse large datasets of TMJ MRI scans, assisting radiologists and clinicians in detecting early TMJ abnormalities. Ongoing research and clinical trials will validate these advancements in real-world medical practice.

CONCLUSION

Among various sequences discussed in this systematic review, T2 mapping and dGEMRIC sequences help in the quantitative evaluation and early identification of cartilage degeneration changes in the articular disc of the TMJ. Routine implementation of these MRI sequences in symptomatic young adults may enable earlier therapeutic interventions and prevent irreversible TMJ degeneration. Collaborative and standardization of imaging protocols can improve the quality and consistency of future research in this area. However more high-quality studies with larger sample sizes are required to validate the results and

assess the clinical applicability of these MRI sequences for early TMJ dysfunction.

Ethics Committee Approval: Since it is a review study, there is no ethics committee approval.

Informed Consent: No patient data was used for the study.

Ethics Committee Approval: As this is a review study, ethics committee approval is not required.

Informed Consent: No patient data was used in this study.

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