

What Role Does Synovitis Play in Craniomandibular Dysfunction (CMD)? A 3T-MRI Study

Welche Rolle spielt die Synovialitis bei der kranio-mandibulären Dysfunktion (CMD)? Eine 3T-MRT-Studie

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ABSTRACT

Purpose The purpose of the present study was to investigate the degree and clinical relevance of synovitis in craniomandibular dysfunction.

Materials and Methods In total, 140 temporomandibular joints were examined using a 3 T MRI scanner. Quantitative analysis of synovial enhancement was performed and interrelated with arthrosis deformans, degenerative disc disease, joint effusion, bone marrow edema and restriction of motion.

Results We found a statistically high and significant correlation between the degenerative changes as mentioned above and the intensity of synovial enhancement.

Conclusion The study shows that typical MRI findings in CMD patients are often combined with signs of synovitis. Presumably joint inflammation has an effect on the clinical signs and symptoms and also the prognosis of CMD. These results should be taken into consideration when selecting treatment.

Key Points:

- 3T-MRI using a dedicated coil is the method of first choice in the examination of CMD syndrome.
- MR imaging allows quantification of increased synovial enhancement.
- There is a highly significant correlation between degenerative changes of the disc or cartilage and synovitis.
- Results of the study are relevant for the clinical assessment and therapy of CMD syndrome.

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ZUSAMMENFASSUNG

Ziel Ziel der vorliegenden Untersuchung war es, das Ausmaß und auch die klinische Bedeutung der Synovialitis beim Syndrom der kranio-mandibulären Dysfunktion zu untersuchen.

Material und Methoden Insgesamt 140 Kiefergelenks-MRTs wurden nach Untersuchung mit einem 3T-MR-System ausgewertet. Dabei wurde die synoviale Kontrastmittelaufnahme als entscheidendes Kriterium einer entzündlichen Gelenketeiligung quantitativ erfasst und in Relation gesetzt zu Arthrose, Diskusdegeneration, Diskusverlagerung, Gelenkerguss, Knochenmarködem und Einschränkung der Bewegungsexkursion.

Ergebnisse Es zeigte sich ein statistisch hochsignifikanter Zusammenhang zwischen den oben genannten bei CMD häufig vorzufindenden degenerativen Veränderungen einerseits und Zeichen der Synovialitis andererseits.

Schlussfolgerung Die Studie zeigt, dass die typischen MRT-Befunde bei CMD-Patienten häufig münden in bzw. überlagert werden von einer Gelenkentzündung, welche sich mani-

festiert in Form einer Synovialitis. Es ist davon auszugehen, dass sich diese entzündliche Komponente auswirkt auf das kli-

nische Beschwerdebild und die Prognose. Von Bedeutung ist diese Erkenntnis auch für die Wahl der Therapie.

Introduction

Craniomandibular dysfunction (or TMD – temporomandibular joint disease) is a general term for the clinical manifestations of temporomandibular joint dysfunction. Symptoms are clinically classified (if possible) as issues related to the mastication muscles, lesions of the intraarticular disc with restriction of motion and joint noises, and diseases of the articular skeletal segments or the cartilage in the narrower sense (as in osteoarthritis or arthritis).

Epidemiological examinations have shown a prevalence of temporomandibular pain syndrome of 8 – 15 % in women and 3 – 10 % in men. Therefore, symptoms caused by the temporomandibular joint and directly adjacent structures have a significant sociomedical and socioeconomic significance, especially since CMD is often associated with additional chronic pain syndromes [2]. A series of comorbidities like osteoarthritis, fibromyalgia, fatigue syndrome, depression, autoimmune diseases, and sleep apnea syndrome were described in a large US sample [3]. 40 % of the patients had already undergone one or more surgical interventions and almost all medication-based treatments [3].

The pathomechanism of craniomandibular dysfunction has not been fully clarified. Dysfunction of the temporomandibular joint capsule, articular disc, and mastication muscles primarily caused by degenerative changes is favored in the literature as a possible explanation. The lateral pterygoid muscle and particularly its attachment region play a key role in the occurrence of pain in CMD in the literature due to its anatomical relationship to the articular disc and the joint capsule [4]. MRI examination of the jaw joints with a dedicated coil is generally accepted as the method of choice for diagnosing CMD [5, 6].

Since persistent and difficult-to-treat pain syndromes play a central role in the indication for MRI diagnosis of the temporomandibular joint, both degenerative changes as well as the extent of (chronic) inflammatory processes in the temporomandibular joint are of particular interest in CMD.

While there is extensive literature regarding the manifestations of rheumatoid arthritis in the temporomandibular joint, there are no current MRI studies regarding (nonspecific) synovitis in CMD to our knowledge. Detection of an inflammatory component in CMD manifested as synovitis may be of importance for understanding symptoms and for selecting treatment.

Materials and Methods

A total of 72 MRI examinations of the temporomandibular joint (144 joints) in the years 2013 to 2018 were evaluated in a retrospective study. The patients were all referred by the Department of Oral and Maxillofacial Surgery with the diagnosis of craniomandibular dysfunction with pain symptoms. All patients were examined on the same 3.0 T MRI scanner (Philips Ingenia) using a dedi-

cated 4-channel temporomandibular joint coil (Philips D-Streamflex type S). The 3.0 T high-field MRI scanner is considered superior to the 1.5 T MRI scanner for imaging the temporomandibular joint because of the significantly better resolution of the anatomical structures, particularly of the shape, position, and internal signal of the articular disc [7].

The same examination protocol was used for all patients (► **Table 1**).

The examinations were all saved in the internal PACS system and were evaluated by two experienced radiologists in consensus.

2 patients (4 joints) were excluded from the analysis because they had verified chronic polyarthritis with significant signs of arthritis so that they did not meet the criteria for the selected target group.

The patient age was between 11 and 73 years with an average age of 39.3 years. In accordance with clinical experience, the majority of patients were female (69 %).

In the present MRI scans of the temporomandibular joint, the osseous structures were evaluated in a first step with respect to erosions and destruction as well as signs of osteoarthritis like narrowing of the joint space, bony appositions, sclerosis, and joint deformities and to edema in the bone marrow of the articular structures.

The shape, signal intensity and particularly the position of the intraarticular disc were evaluated. The conventional classification system according to Vogl was used to classify anterior disk dislocation with categorization as partial anterior disc dislocation grades 1 and 2 and as complete anterior disc dislocation with and without repositioning in a functional position [8]. Lateral and posterior disc dislocations were not included due to their rarity (lat. 4 %) and correspondingly difficult statistical application.

Special attention was given to the signs of synovitis in the present study. When diagnosing synovitis, increased synovial contrast enhancement is the most important criterion. However, a subjective semiquantitative analysis does not yield reproducible results and definitive differentiation from slight physiological contrast enhancement of the synovial membrane, as typically also seen in healthy temporomandibular joints, is not possible [9, 10]. A method that was initially developed for patients with idiopathic juvenile arthritis was used for quantification resulting in improved evaluation and reproducibility of synovial contrast enhancement [11]. The average pixel intensity (API) of the synovial membrane was measured in the coronal T1 post-contrast layer series at three locations (area 0.8 mm²) and this was used to form the mean value. This value is divided by the API in the muscle parenchyma of the longus capitis muscle. A value above the threshold of 1.55 (nondimensional) is considered a sign of synovitis. A sensitivity and specificity for the detection of synovitis of 91 % and 96 %, respectively, were specified in the publication mentioned above.

The thickness of the synovial membrane was not evaluated since there is no reproducible method or clearly defined measure-

► **Table 1** MRI examination parameters.

sequence	TR	TE	slice thickness [mm]	distance [mm]	FOV [mm]
PD SPAIR parasag	1978	40	2	2.2	80
T1 parasag	741	12	2	2.2	80
T1 parasag + contrast	741	12	2	2.2	80
T1 parasag + contrast max.	741	12	2	2.2	80
T1 cor + contrast	677	14	2	2.2	80
T1 cor + contrast max.	677	14	2	2.2	80
kinematic MRI	3.86	1.93	5	5	80

max. = maximum oral opening.

ment region. Evaluation of the present MRI scans of the temporomandibular joint also showed a significant range in this regard so that that is not a reliable criterion.

Statistical analysis was performed with the support of the Institute for Medical Statistics and Epidemiology, Technical University, München using the following method:

GEE models (generalized estimation equations) were used for the statistical analysis. Both the left and right sides were linked. The p-value was calculated as an expression of the significance and the coefficient estimate as an expression of the strength of a relationship. In particular the (possible causal) relationship between osteoarthritis, disc degeneration, and disc dislocation and synovitis and between joint effusion, bone marrow edema, restriction of motion and synovitis was of interest.

Results

A main result is that increased contrast enhancement that is typical for synovitis can be seen in 36 of 140 temporomandibular joints (= 25.7%) of CMD patients (with exclusion of a primary inflammatory arthropathy like chronic polyarthritis), i. e., a relatively high number in an unselected patient population with temporomandibular joint problems.

Osteoarthritis of the temporomandibular joint (► **Fig. 1**) was seen in 29 of these 36 cases (= 81%).

Degeneration of the articular disc was seen in 29 of the 36 synovitis patients (= 81%) (► **Fig. 2**).

Complete anterior disc dislocation (► **Fig. 3**) was seen in 18 of 36 synovitis patients (= 50%) and partial anterior disc dislocation was seen in 2 patients (= 5.6%).

Although there are overlaps, i. e., multiple presumed synovitis-promoting factors are simultaneously present, the relationships are so highly statistically significant that this is not decisive for the key message of the study.

Joint effusion was additionally present in 25 of the 36 synovitis cases (= 69%) and clear bone marrow edema in the capitulum in 9 of 36 (= 25%). In 31 of 36 synovitis patients (= 86%), the movement of the temporomandibular joint was limited, i. e., the man-

dibular condyle did not slide over the articular tubercle in the MRI examination in the maximum oral opening position.

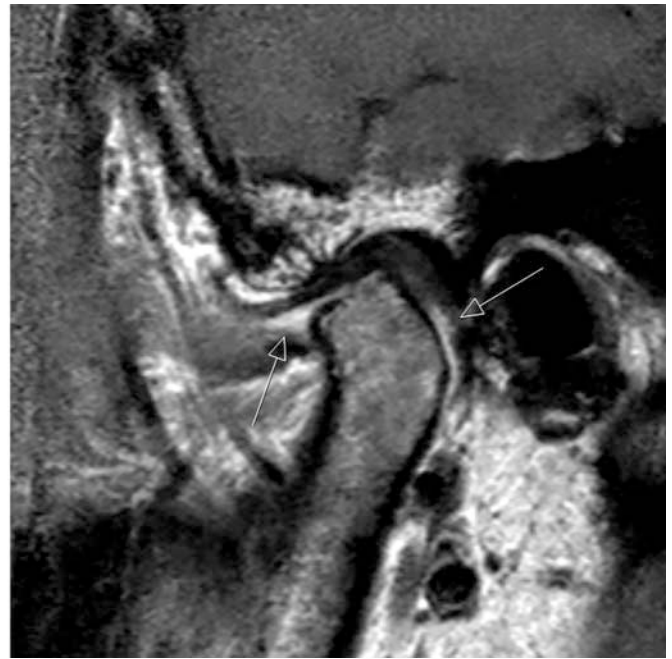
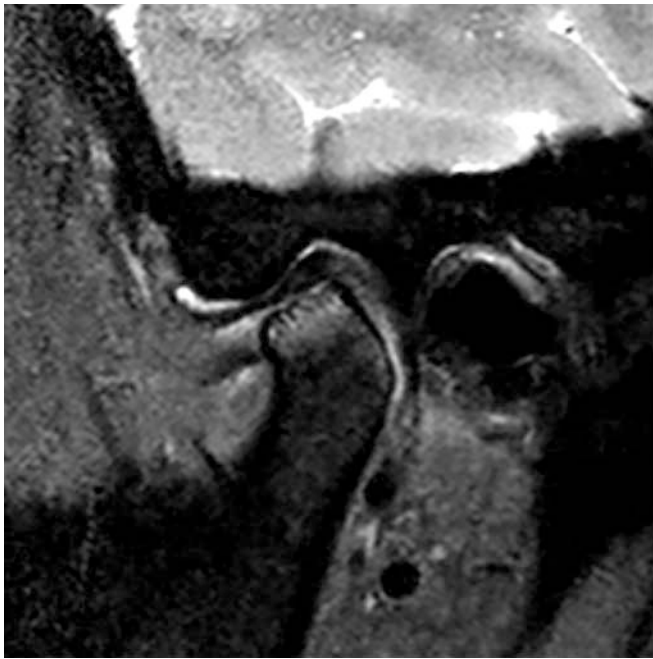
The relationship between synovitis and osteoarthritis of the temporomandibular joint, disc degeneration and complete anterior disc dislocation with all p-values less than 0.01 was highly significant in the statistical analysis (► **Fig. 4**). This also applies to the relationship between synovitis and joint effusion, erosion, bone marrow edema, and restriction of motion (► **Fig. 5**, ► **Table 2, 3**).

A notable partial result is that a pathological increase in synovial contrast enhancement and synovitis inflammation is seen in n = 20 or 49% of patients with an abnormal disc position. Joint effusion was seen in n = 26 or 63% of patients with an abnormal disc position.

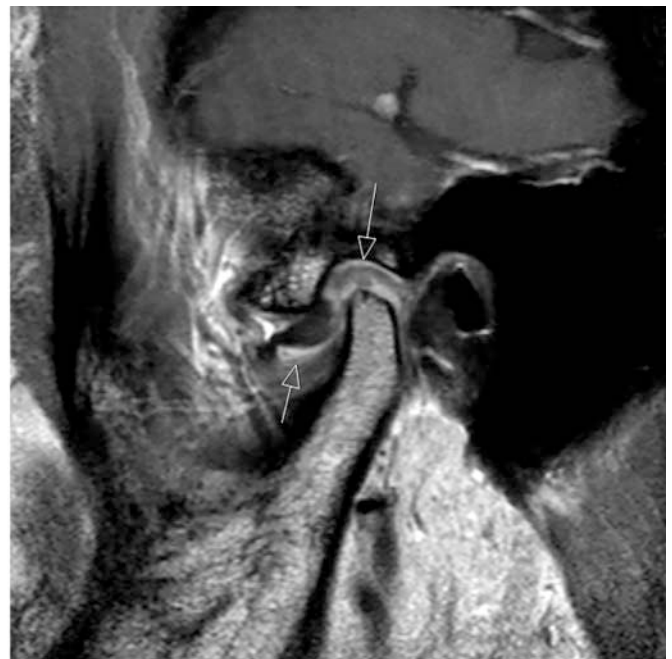
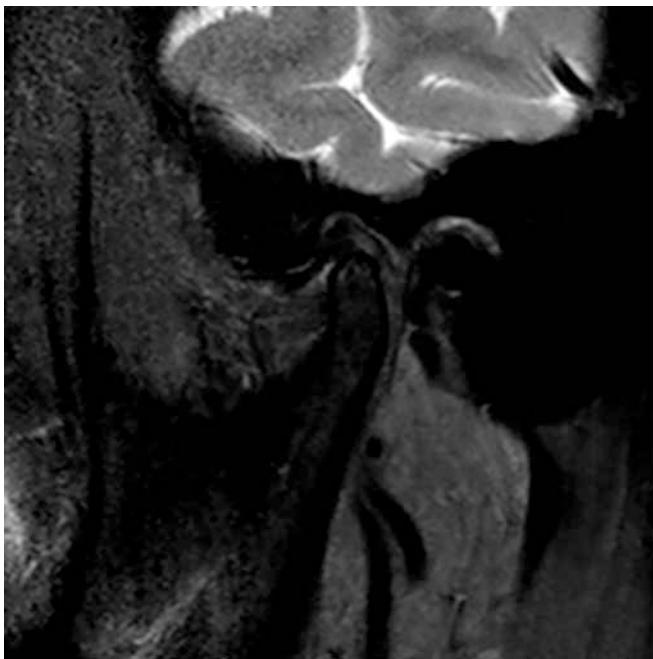
Discussion

The goal of the present study was to examine the significance of inflammatory processes in the temporomandibular joint in an unselected CMD patient population. Confirmed primary rheumatic diseases like rheumatoid arthritis were ruled out from the outset. The extent to which common CMD triggers that can be clearly diagnosed with MRI, such as osteoarthritis, disc degeneration, and disc displacement, can be complicated by or result in an (often chronic) inflammatory joint process was of particular interest. The increase in synovial contrast enhancement, which is an important criterion, was not only recorded qualitatively but was also quantified on MRI using a method developed for pediatric rheumatology [11 – 13]. MRI is considered the most reliable imaging method for diagnosing synovitis [10].

There was a highly significant relationship between osteoarthritis of the temporomandibular joint (and also bone marrow edema), disc degeneration, and disc displacement on the one hand and synovitis of the temporomandibular joint on the other hand. Therefore, according to our results, increased contrast enhancement and thickening of the synovial membrane is not only seen in primary inflammatory joint diseases like rheumatoid arthritis [14] but is also common in CMD syndrome.



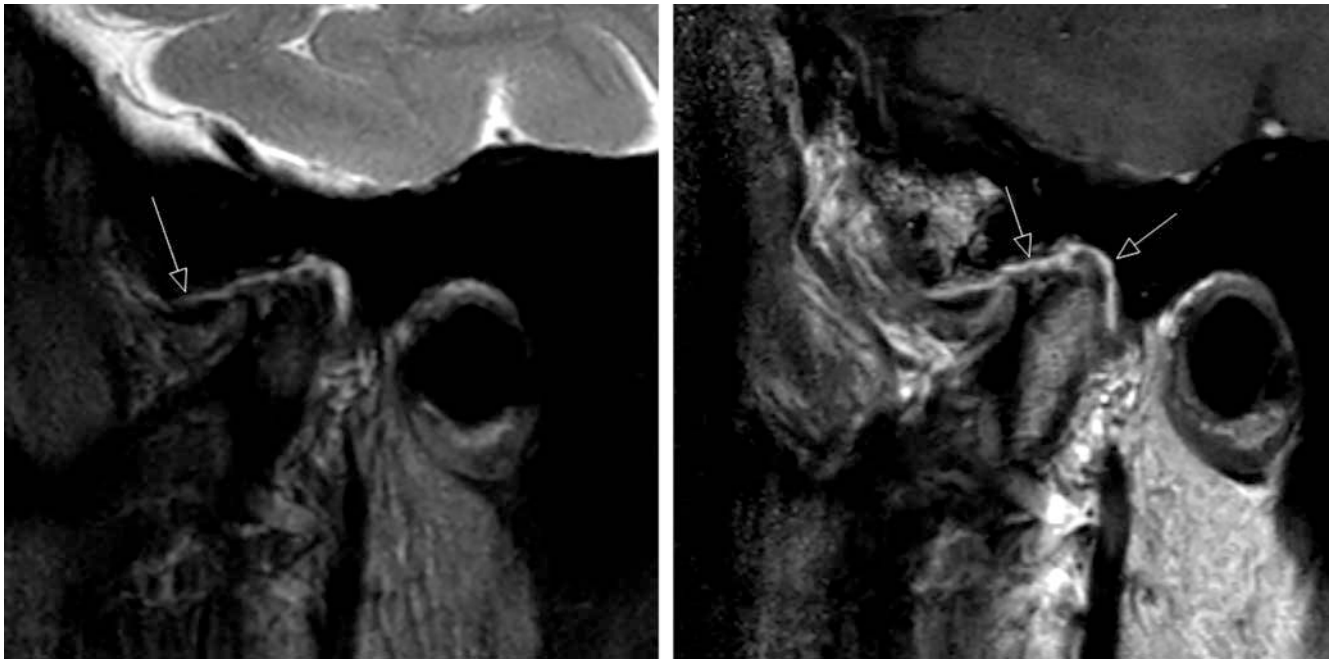
► **Fig. 1** PD SPAIR psag on the left, TI + contrast psag on the left: Osteoarthritis of the temporomandibular joint with bone marrow edema in the capitulum and increased synovial contrast agent uptake (arrows).



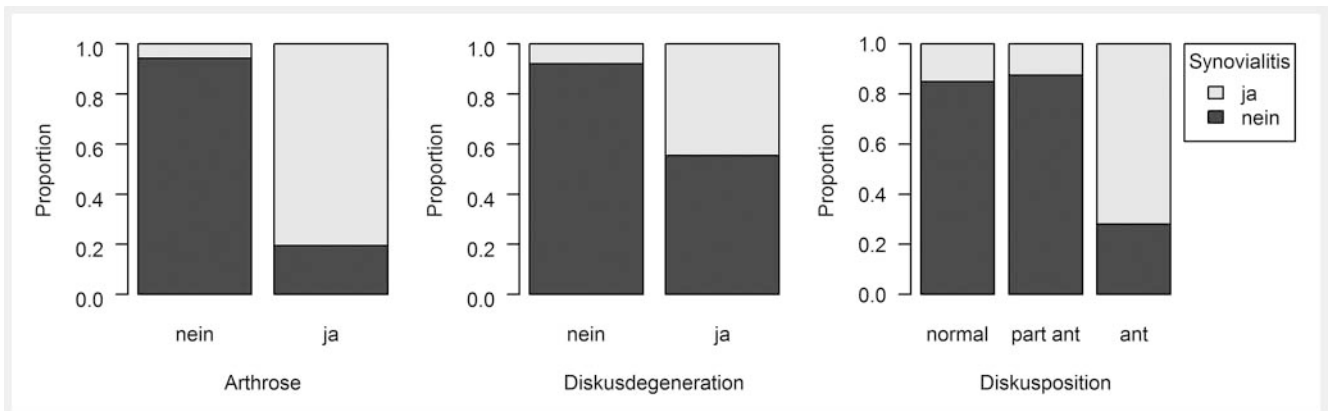
► **Fig. 2** PD SPAIR psag on the left, TI + contrast psag on the left: Significant disc degeneration with increased T2 signal intensity, distension, and lack of contour definition. Adjacent increased synovial contrast enhancement (arrows).

To our knowledge, there are currently no 3 T MRI studies regarding the frequency and extent of synovitis in CMD patients. Only one dynamic contrast-enhanced MRI study including patients whose main clinical symptom was temporomandibular joint pain showed significantly increased focal contrast enhancement in the retrodiscal zone, an indication that TMJ pain syndromes can be connected with increased vascularization and focal inflam-

mation [15]. However, a series of MRI studies addressed the importance of temporomandibular joint effusion and its connection to other pathological joint findings. A clear connection between joint effusion and osteoarthritis of the temporomandibular joint [16] and between joint effusion and disc displacement (particularly without repositioning in a functional position) was seen [17]. There was also a close connection between joint effusion and



► **Fig. 3** PD SPAIR psag on the left, TI + contrast psag on the left: Complete anterior disc dislocation (arrow) with increased synovial enhancement (arrows).



► **Fig. 4** s. Table 2.

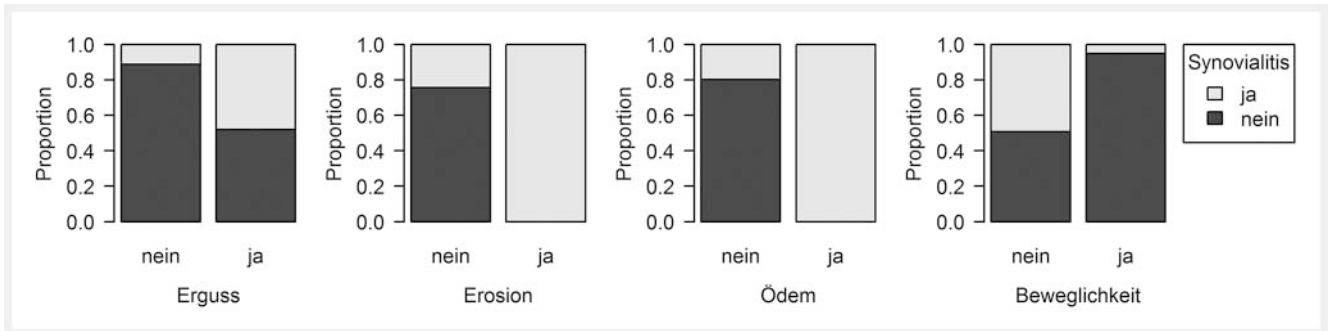
► **Table 2** Connection with synovitis.

	osteoarthritis	disc degeneration	disc displacement
p-value	<0.01	<0.01	<0.01
Estimate	e-4.247	e-2.928	e-2.835

bone marrow edema in the capitulum in clinical pain syndrome [18]. A further MRI study in CMD patients (unsurprisingly) showed a clear statistical relationship between anterior disc dislocation seen on MRI, osteoarthritis, bone marrow edema, and joint effusion and a clinically manifested pain syndrome [19].

Biochemical studies of concomitant joint effusion in patients with disc displacement were able to show changed composition with an increased protein level and signs of elevated inflammatory activity [20].

Synovitis is apparently a type of reaction of the joint resulting in various joint lesions as also seen in other joints in the periphery



► Fig. 5 s. Table 3.

► Table 3 Symptoms associated with synovitis.

	joint effusion	bone marrow edema	limited movement
p-value	<0.01	<0.01	<0.01
estimate	e-2.166	e-5.94	e-3.274

of the body. Therefore, for example, an MRI study in knee joints with osteoarthritis showed synovitis in up to 96% of cases at least in single compartments of the joint [21]. Histological findings in affected temporomandibular joints support this assumption with evidence of progressive cartilage damage, subchondral bone remodeling/destruction, and signs of chronic inflammation in synovial tissue, with inflammation and destruction of the subchondral bone playing a particularly important role in the initiation and progression of the disease process [22]. In addition, an imbalance between the joint capsule, articular disc and muscles of mastication, particularly the lateral pterygoid muscle, could be detected on a pathoanatomical basis [4].

Further biochemical analyses of the joint fluid recently provided information regarding the important role of inflammatory processes in the pathogenesis of CMD symptoms. In the case of joint effusion detected on MRI, a significantly elevated concentration of cytokines, i. e., inflammation mediators, was seen in the joint fluid [23]. A particularly clear relationship between an elevated concentration of tumor necrosis factor alpha and synovitis with destruction of cartilage and articular bone structures was able to be detected [24]. Biochemical analysis of synovial fluid in patients with CMD pain also showed an elevated level of a whole series of molecular pain biomarkers like metalloproteinase (MMP), vascular endothelial growth factor (VEGF), hyaluronic acid synthase that can be connected to chronic low-grade inflammation in particular [25]. Certain proteoglycans could be assigned to cells of degenerated temporomandibular joint discs on an experimental basis [26].

Of course, the clear MRI evidence of the role of synovitis in CMD symptoms is also relevant for treatment planning. However, the local intraarticular administration of corticosteroids as an anti-inflammatory measure had controversial effects. In juvenile rheumatoid arthritis, a clear improvement of the signs of arthritis was observed on MRI [27], an effect that can be not only statistically

proven but also quantified on MRI [11], but resorptive processes in the condyloid process of the temporomandibular joint were detected in an animal experiment as a side effect after only a single intraarticular administration of dexamethasone with histological verification of osteoclastic activity [28]. Arthrocentesis with mechanical distension and lavage had positive effects on inflammatory manifestations on MRI and on clinical pain syndrome [29, 30].

CLINICAL RELEVANCE

- In summary, the present study shows that the etiologically heterogeneous CMD syndrome with its MRI findings that are considered to be causative like osteoarthritis, disc degeneration and displacement, and joint effusion is associated with signs of synovitis on a highly significant basis.
- Clinical symptoms may be largely influenced by inflammatory processes even if a primary mechanical explanation initially seems likely.
- This should influence the clinical assessment and also the treatment of the often chronic CMD syndrome.

Conflict of Interest

The authors declare that they have no conflict of interest.

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