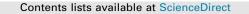
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# Clinical predictors of temporomandibular joint arthritis in juvenile idiopathic arthritis: A systematic literature review

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### ABSTRACT

*Aim:* To assess the level of evidence for subjective and objective parameters in clinical orofacial examination and determine if predictors for temporomandibular joint (TMJ) involvement in juvenile idiopathic arthritis (JIA) patients exist in the current literature.

*Method:* A comprehensive systematic electronic search strategy was performed in all major medical databases in June 2015. Studies were selected independently by two reviewers in accordance with a prespecified protocol and a risk of bias assessment for all included studies. Subjective examination outcome measures assessed were pain, decreased TMJ function, and TMJ sounds. The objective outcome measures assessed were maximal incisor opening, mandibular asymmetric opening, condylar translation, protrusion, myofascial pain on palpation, facial asymmetry, and micro- or retrognathism.

*Results:* The electronic database search identified 345 unique citations. After application of our strict, predefined inclusion and exclusion criteria, 21 articles were included and data extracted. The study heterogeneity did not allow for meta-analyses. No singular outcome measure can be suggested as a predictor of TMJ involvement in JIA, as sensitivity and/or specificity is too low compared to contrast-enhanced magnetic resonance imaging.

*Conclusion:* The current low level of evidence and study heterogeneity do not allow us to conclude on singular clinical outcome measures. To increase study comparability, we call for a standardized terminology and evidence-based guidelines for clinical orofacial examination parameters in JIA patients. © 2016 Elsevier Inc. All rights reserved.

#### Introduction

In juvenile idiopathic arthritis (JIA), the temporomandibular joints (TMJ) are often inflamed [1,2]. TMJ arthritis in the growing individual can affect dentofacial growth and development [3–5], as the mandibular condylar cartilage is an important mandibular endochondral growth site [6]. The growth site is situated within the intracapsular joint space, and inflammatory changes in the intracapsular environment and mandibular functional disturbances alter the local intercellular communication and biochemical functional demands, which may in turn disturb development in the growing patient [6–8].

Clinical diagnosis of TMJ involvement is challenging; clinical signs and symptoms vary considerably between studies. Limited

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correlation has been shown with the findings from gadoliniumbased, contrast-enhanced magnetic resonance imaging (Gd-MRI), which is currently the gold standard for detection of TMJ involvement in JIA [9,10]. Furthermore, an internationally accepted scoring system for TMJ diagnosis is pending, and clinical examination of the TMJs and associated structures has been validated for most temporomandibular disorders but not for JIA [11].

Stand-alone clinical orofacial examination of JIA patients has a low sensitivity and specificity for the diagnosis of TMJ arthritis. However, the current level of evidence remains unclear as to which parts of the clinical examination may be used as clinical predictors for positive imaging findings [12–15]. Additionally, MRI resources are limited and expensive, and sedation may be required, especially in small children. Consequently, there is a pressing need for supplementary diagnostic and prognostic procedures to aid early diagnosis and treatment of TMJ arthritis.



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In response hereto, we assessed and quantified what is currently known about the outcome measures in clinical orofacial examination by systematically evaluating the current literature to facilitate the highest level of evidence-based practice. The suggested clinical parameters for the diagnosis of TMJ involvement in JIA patients were evaluated, and the level of evidence for each of the parameters was determined.

# Material and methods

A comprehensive study protocol was designed outlining the research questions, the data search strategy, the data extraction procedures, and the methods used to assess the risks of bias. The protocol was designed on the basis of the Cochrane and PRISMA guidelines for systematic reviews [16,17]. The PICO table (population, intervention, comparison, and outcome) presents the outline and the search strategy (Table 1).

# Search strategy

The prespecified literature search was developed for a MED-LINE search and revised to comply with the syntaxes of the various databases. Additionally, a manual search was performed of the reference lists of included studies, and authors were contacted if clarification was needed. The primary literature search was conducted on December 9, 2013, and repeated on June 12, 2015, to include any new articles.

### Inclusion/exclusion criteria

The inclusion criteria were randomized clinical trials, cohort studies, observational studies, and case series with outcome measures involving clinical examination of the TMJ in JIA patients and with additional gadolinium-based contrast-enhanced magnetic resonance imaging (Gd-MRI) to assess soft-tissue changes and/or radiological examination with sagittal-corrected tomographic recordings, cone-beam computed tomography (CBCT), or medical CT to assess osseous changes. The exclusion criteria were (1) studies without measureable/objective outcome variables; (2) dual publications; (3) studies using insufficient imaging technigues to assess TMJ inflammation (MRI without contrast enhancement); (4) studies only using panoramic and/or cephalometric images; (5) non-peer-reviewed studies (e.g., conference abstracts); (6) articles mainly reporting on JIA patients older than 20 years of age; (7) use of clinical indices where no singular outcome measures can be extrapolated from a score [e.g., only the craniomandibular index (CMI) [18]; and (8) case series reporting

fewer than five JIA patients. No limits were defined regarding language.

We included both prospective and retrospective studies each of which is commented on separately in the results section.

#### Study selection

Two experienced clinicians and researchers specialized in clinical routine orofacial assessment of patients with JIA and treatment of TMJ arthritis (KDK and PS) extracted the data and independently assessed and coded the studies. Details of the data extraction are presented in the Figure. The first evaluation was based on titles only and the second on the abstracts of the included titles. Potentially eligible articles were then reviewed in full text. Any disagreement was resolved by consensus through discussion of the original article.

# Assessment of the risk of bias

Comprehensive predefined risk of bias criteria were established before undertaking the literature search. The criteria were designed according to the Cochrane guidelines, and due to the current low evidence level within this field, modified risk of bias criteria were developed also with reference to the Cochrane guidelines [16].

Each study was assessed in relation to the risk of bias at study level. The factors evaluated are presented in Table 2. Bias was defined as any factor with sufficient impact to have a notable effect on the results or conclusions of the study reviewed.

#### Reliability of risk of bias assessment

The two blinded reviewers independently assessed the individually included articles in compliance with the risk of bias criteria and the Oxford Centre for Evidence-Based Medicine Levels of Evidence (differential diagnosis/symptom prevalence study) [36]. This classification system ranks the evidence level creating a 5-point hierarchy where 1 is to the highest level of study evidence, while five represent the lowest level of study evidence. The criteria applied to establish the levels of evidence differ according to the type of studies (e.g., therapy, intervention, and prevention).

# Results

From a total of 345 unique citations, 21 articles complied with the inclusion and exclusion criteria were therefore included (Figure). The reasons for excluding full-text reviewed articles were

#### Table 1

PICO: Search terms were constructed for MEDLINE and modified to comply with the remaining databases

PICO

Databases included:

MEDLINE via PubMed, EMBASE, Cochrane Central Register of Controlled Trials, WEB IF SCIENCE, SCOPUS, and DATABASE of Abstacts of Reviews of Effect (DARE).

The MEDLINE search terms: ((juvenile idiopathic arthritis) OR (juvenile rheumatoid arthritis) OR (juvenile chronic arthritis) OR (juvenile idiopathic arthritides) OR (juvenile chronic arthritis) OR (Still\* disease) OR (still disease) OR JIA OR JCA OR JRA) AND ((temporomandibular joint) OR (temporomandibular joints) OR TMJ) AND ((risk factors) OR (risk factor) OR diagnosis OR diagnose OR predictors OR predictor OR prediction OR prevalence OR (clinical examination) OR (clinical examinations) OR (physical examination) OR (physical examination) OR (signs OR signs OR symptom OR symptoms) AND (imaging OR (magnetic resonance imaging) OR MRI OR radiography OR radiog

Patients: Patients with JIA receiving clinical and imaging examinations for assessment of potential TMJ involvement

Intervention: Clinical and imaging/radiological assessment of TMJ arthritis

Comparison: Imaging or radiological findings compared to clinical findings

Outcome: (1) Identify clinical predictors of positive imaging/radiological findings

<sup>(2)</sup> Identify the current level of evidence for these parameters

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