Clinical Orofacial Examination in Juvenile Idiopathic Arthritis: International Consensus-based Recommendations for Monitoring Patients in Clinical Practice and Research Studies

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ABSTRACT. ***Objective.*** To develop international consensus-based recommendations for the orofacial examination of patients with juvenile idiopathic arthritis (JIA), for use in clinical practice and research.

Methods. Using a sequential phased approach, a multidisciplinary task force developed and evaluated a set of recommendations for the orofacial examination of patients with JIA. Phase 1: A Delphi survey was conducted among 40 expert physicians and dentists with the aim of identifying and ranking the importance of items for inclusion. Phase 2: The task force developed consensus about the domains and items to be included in the recommendations. Phase 3: A systematic literature review was performed to assess the evidence supporting the consensus-based recommendations. Phase 4: An independent group of orofacial and JIA experts were invited to assess the content validity of the task force's recommendations.

Results. Five recommendations were developed to assess the following 5 domains: medical history, orofacial symptoms, muscle and temporomandibular joint function, orofacial function, and dentofacial growth. After application of data search criteria, 56 articles were included in the systematic review. The level of evidence for the 5 recommendations was derived primarily from descriptive studies, such as cross-sectional and case-control studies.

Conclusion. Five recommendations are proposed for the orofacial examination of patients with JIA to improve the clinical practice and aid standardized data collection for future studies. The task force has formulated a future research program based on the proposed recommendations. (J Rheumatol First Release January 15 2017; doi:10.3899/jrheum.160796)

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Temporomandibular joint (TMJ) inflammation and deformation are seen in a substantial number of patients with juvenile idiopathic arthritis (JIA). The reported prevalence of TMJ arthritis in JIA reaches 87% depending on the diagnostic criteria and methodology used[1,2,3]. TMJ inflammation may interfere with optimal joint function and may cause abnormal clinical symptoms, findings, and dysmorphic alterations in dentofacial growth and development[4-10,11-15]. Therefore, routine orofacial examinations constitute an important part of the general clinical assessment of patients with JIA, to ensure diagnosis of TMJ arthritis, evaluate treatment options, assess response to therapy, and provide ongoing monitoring of a patient with existing TMJ arthritis.

Within the past decade, increased attention has been paid to the consequences of TMJ arthritis in patients diagnosed with JIA. However, no standardized criteria for history-related items and functional clinical orofacial outcome measures have been established. Therefore, there are significant discrepancies in how clinical orofacial examinations are conducted. Recent systematic literature reviews have confirmed the need for standardized guidelines for the clinical orofacial examination to provide the opportunity for future interstudy comparisons[16,17].

The observed interstudy discrepancy in clinical orofacial examinations may be explained in part by differences in the professional training of the medical and dental practitioners conducting the studies. Specialists, including rheumatologists, maxillofacial surgeons, orthodontists, and orofacial pain specialists, use diverse methods and examination tools to perform orofacial examinations. Many of these techniques have not been validated in patients with JIA. Further, many published studies are retrospective, and extract non-standardized clinical data from charts, which may lead to biased conclusions. The objective of our present work is to develop international, interdisciplinary, consensus-based, and evidence-based recommendations for domains of importance, reflecting the minimum standard of care during routine clinical orofacial evaluations performed by rheumatologists and dentists. These domains may also be used as outcome measures in future clinical studies involving orofacial assessment in patients with JIA.

MATERIALS AND METHODS

Our study was conducted by members of the euroTMjoint network. The euroTMjoint group was founded in Oslo, Norway, in 2010 to establish an international, multidisciplinary research network to study TMJ arthritis in JIA. Today, the network is a multinational, independent, open research group representing a substantial number of the research groups who have published within this area[18].

This current work was initiated in 2012, when an international expert task force was established. The group consisted of 3 pediatric rheumatologists, 3 orthodontists, and 2 orofacial pain specialists. The members represent 6 international centers from Europe and North America.

Establishment of provisional recommendations for the clinical orofacial examination. Based on a systematic literature search[16] and expert-based consensus on clinical orofacial examination guidelines, the members of the task force identified and proposed 20 clinical outcome variables for the assessment of patient symptoms, and 12 clinical outcome variables for the assessment of TMJ arthritis-related signs. The primary goal was to recommend domains to monitor patients with existing TMJ arthritis, and to identify outcome variables within those domains to assess response of TMJ arthritis to therapy.

All members on the euroTMjoint mailing list (n = 83) were invited to participate in an online Delphi survey with the aim of rating the importance of each of the proposed outcome variables. The participants were encouraged to suggest additional outcome variables during each Delphi survey round, leading to 2 additional outcome variables for assessment of TMJ arthritis-related signs: effect of pain on orofacial function, and assessment of occlusion in the sagittal plane. The results from the first poll were summarized and were provided to the participants for the next iteration. The importance of each of the proposed outcome variables was assessed twice based on a numerical scale (0 = not important, 10 = of utmost importance). All proposed outcome variables were subcategorized based on their ratings of importance: "high importance" (score ≥ 8), "moderate importance" (6 ≤ score < 8), "low importance" (score < 6). The results of the Delphi survey were used as a guide to structure the discussions during the consensus meetings.

The task force was composed of 8 members who met for consensus meetings on 2 occasions: in April 2013 in Aarhus, Denmark, and in April 2014 in Tampere, Finland. Based on the outcome of the Delphi survey, the members established 5 general provisional recommendations by nominal group technique regarding monitoring patients with JIA who have TMJ arthritis.

Literature review. A second literature review was conducted to assess the strength and content validity of each of the 5 recommendations. We included all publications that dealt with diagnosis and monitoring of patients with JIA and TMJ arthritis. Four research questions (RQ) were established and applied to each of the 5 provisional recommendations.

The recommendations for monitoring patients with JIA who have TMJ arthritis were the following: (RQ1) What is the general validity of the recommendation? (RQ2) What is the level of evidence of the recommendation?

The recommendations for diagnosing TMJ arthritis were the following: (RQ3) What is the diagnostic validity of the recommendation? (RQ4) What is the level of evidence of the recommendation with respect to diagnostic validity?

The systematic literature search of relevant articles was performed on June 26, 2014. Two independent reviewers (PS and MT) screened titles and abstracts of the identified citations. Potentially relevant articles were reviewed in full text using predetermined inclusion and exclusion criteria (Supplementary Material 1, search strategy, and Supplementary Material 2, data extraction criteria, available with the online version of this article). The level of evidence (RQ2 and RQ4) was graded for each of the final recommendations in accordance with the quality of the included studies[19].

Final recommendations and level of evidence. Following the literature review, 12 experts within the field of TMJ arthritis in JIA were invited to assess the strength and content validity of the recommendations. Experts were identified based upon the following principles: clinical expertise, research activity, educational background, and general contribution to the field of TMJ arthritis in JIA. The identified group of experts consisted of pediatric rheumatologists (n = 4), orthodontists (n = 5), maxillofacial surgeons (n = 2), and orofacial pain specialist (n = 1). The invited experts were asked to assess the general validity and the diagnostic validity for each of the 5 recommendations by examining the results of the literature review

and scoring the perceived strength of the recommendation (SOR) for each of the 5 provisional recommendations using a 0–10 numerical scale (0 = do not recommend, 10 = highly recommend). In addition, they were invited to comment on the provisional recommendations and the literature review with suggestions for improvements in clarity or addressing redundancies. A final set of recommendations was proposed based on the consensus of the task force and invited experts. Ethical approval was not required for any parts of the study.

RESULTS

Forty members on the euroTMjoint mailing list participated in the Delphi study (48% response rate). The professional backgrounds of participants were orthodontists (17/40, 42.5%), orofacial pain specialists (11/40, 27.5%), pediatric rheumatologists (9/40, 22.5%), maxillofacial surgeons (2/40, 5%), and a radiologist (1/40, 2.5%). The participants' self-assessed median score of expertise in clinical TMJ examination was 8 (interquartile range 7–9) based on a numerical scale (0 = minimal experience, 10 = very experienced). The results of the Delphi survey revealed 17 outcome variables that were rated to be of "high" importance (median ≥ 8; Table 1); 10 were symptom-related and 7 were related to clinical findings. The residual outcome variables rated as "moderate" and "low" importance are presented in Supplementary Material 3 (available with the online version of this article).

The literature search resulted in 1144 citations, of which 495 were duplicates. After removal of duplicates, a total of 649 unique citations were included in the title and abstract screening process, which left 84 articles for full text review after exclusion of 565 unique citations (for search details, see Supplementary Material 4, available with the online version of this article). During the full-text review, 29 articles were excluded, leaving 55 articles for inclusion. An additional hand search of relevant articles identified 1 article, resulting in a total of 56 articles complying with the search criteria for research questions 1 and 2. The evidence from these articles was used to answer research questions 1 and 2 for each of the 5 recommendations. After applying data search criteria for the third and fourth research questions, 27 articles were included (Supplementary Material 4). Studies presenting with the highest level of evidence were given more consideration when answering the research questions. The number of articles identified for each of the recommendations is listed in Table 2 (for list of articles, see Supplementary Material 5).

Results from the literature review and suggestions from the invited group of TMJ experts led to minor changes in the 5 provisional recommendations. The 5 final consensus-based recommendations are listed in Table 2 together with the SOR and the associated level of evidence. A brief summary of the supporting evidence for each of the final recommendations is available below. A more detailed description of the supporting evidence for each of the 5 recommendations is available in Supplementary Material 6 (available with the online version of this article).

Recommendation 1. The medical history should include sex, age at time of examination, JIA category, disease duration, previous/current medications, previous/current orthodontic treatment, and disease activity.

The majority of all eligible articles included background information[1,6,7,8,12,13,14,20-58]. The information varied among the studies. The most consistently included items were age at time of examination, JIA category, and disease duration. Information about medication or disease activity level was

Table 1. Clinical outcome variables rated of "high importance" in the Delphi survey (median ≥ 8, on a numerical scale, 0 = not important, 10 = of utmost importance); presented together with second-round median scores and 25th/75th percentiles. First-round Delphi scores are reported in brackets.

Outcome Variables	Second-round Median Scores	25th/75th Percentiles
Symptom assessment variables		
Orofacial pain frequency	8 (8)	6–9 (5–8)
Orofacial pain intensity	8 (8)	5–9 (3–9)
Orofacial pain location	9 (8)	8–10 (7–10)
Effect of pain on orofacial function	8 (8)	7–9 (6–9)
Factors aggravating/alleviating orofacial symptoms	8 (7)	6–8 (5–9)
Effect of orofacial pain on chewing	8 (8)	8–9 (7–10)
Effect of orofacial pain on activities involving mouth opening (e.g., yawning)	8 (8)	8–9 (8–10)
Complaints associated with mouth opening	8 (8)	5–8 (5–8)
Improvement in symptoms after treatment (satisfaction score)	9 (9)	8–10 (8–10)
Improvement in function after treatment (satisfaction score)	9 (9)	8–10 (8–10)
Clinical examination variables		
Mouth opening pattern	9 (9)	8–10 (8–10)
Maximal mouth opening capacity	10 (10)	9–10 (9–10)
Mandibular laterotrusion capacity	8 (8)	7–9 (6–9)
Presence of extraoral muscle pain	8 (8)	7–9 (6–9)
Joint pain with palpation	9 (9)	7–10 (7–10)
Assessment of sagittal mandibular position (by visual inspection)	8 (8)	7–9 (7–9)
Assessment of facial frontal asymmetry (by visual inspection)	8 (8)	8–9 (7–10)

Table 2. Recommendations for the clinical orofacial examination of patients with juvenile idiopathic arthritis (JIA).

	Level of Evidence **	SOR, Median (IQR)
Executive principles		
a) The clinical orofacial examination is an important component in the general health assessment of individuals diagnosed with JIA		
b) The clinical orofacial examination should include an assessment of the following domains: medical history, orofacial symptoms, clinical orofacial signs of TMJ arthritis, orofacial function, and facial morphology		
Recommendations		
1) The medical history should include sex, age at time of examination, JIA category, disease duration, previous/current medications, previous/current orthodontic treatment, and general disease activity		
• General level of evidence of the recommended outcome measure (RQ2, n = 46)*	III	8.7 (7.3–9.7)
• Diagnostic level of evidence of recommendation (RQ4, n = 19)*	III	7.3 (6.3–8.2)
Symptom assessment		
2) The patient should be asked about the presence of orofacial symptoms. This should include location, intensity, frequency, character, and situations in which the symptoms occur		
• General level of evidence of the recommended outcome measure (RQ2, n = 41)*	III	8.5 (5.8–9.7)
• Diagnostic level of evidence of recommendation (RQ4, n = 21)*	III	6.9 (4.8–7.2)
Clinical examination		
3) The clinical examination of orofacial signs should include palpation of the TMJ (lateral pole) and masticatory muscles (masseter and temporalis muscles), assessment of pain on palpation, TMJ pain on mandibular movement, and assessment of joint sounds (listening or by auscultation)		
• General level of evidence of the recommended outcome measure (RQ2, n = 38)*	III	8.4 (5.8–9.7)
• Diagnostic level of evidence of recommendation (RQ4, n = 16)*	III	7.7 (6.8–8.2)
4) The clinical examination of orofacial function should include assessment of TMJ function; e.g., maximal mouth opening, mouth opening deviation, protrusion, laterotrusion, and condylar translation during opening		
• General level of evidence of the recommended outcome measure (RQ2, n = 50)*	III	9.6 (7.2–9.8)
• Diagnostic level of evidence of recommendation (RQ4, n = 24)*	III	8.2 (7.1–9.5)
5) The clinical examination should include assessment of facial morphology and symmetry; mandibular sagittal position (convexity of facial profile) and lower face asymmetry in the frontal plane		
• General level of evidence of the recommended outcome measure (RQ2, n = 24)*	III	8.8 (5.2–9.5)
• Diagnostic level of evidence of recommendation (RQ4, n = 13)*	IV	7.2 (5.1–9.2)

RQ: research question; SOR: strength of recommendations; IQR: interquartile range; TMJ: temporomandibular joint; JIA: juvenile idiopathic arthritis. * n = no. articles complying with the inclusion criteria for the specific research question. ** Level of evidence categorized according to Shekelle, *et al*[19]: III, evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies; IV, evidence from expert committee reports, or opinions or clinical experience of respected authorities, or both.

not consistently reported across the literature. A number of studies identified various demographic, clinical, and radiologic factors associated with the presence and severity of TMJ arthritis (Supplementary Material 5, available with the online version of this article). The task force therefore considers it important to standardize the medical history, and correlate this data with the orofacial examination findings. The level of evidence and strength of recommendation 1 is available in Table 2.

Recommendation 1 does not include imaging results in the medical history, because it is beyond the scope of this work to include recommendations on imaging modalities. However, the task force considers it important to assess clinical findings in the context of previous/current TMJ imaging results.

Recommendation 2. The patient should be asked about the presence of orofacial symptoms. This should include location, intensity, frequency, character, and situations in which the symptoms occur.

Forty of the eligible articles included some type of assessment of orofacial symptoms [6,8,9,12,13,14,20,21,23-26,32-45,47,52,54-65]. Extrapolated evidence from the literature indicates a significantly higher prevalence of orofacial symptoms in patients with JIA compared with non-JIA controls. Newly diagnosed patients with JIA and TMJ involvement are often asymptomatic but the prevalence of orofacial symptoms increases significantly with disease duration and age of the patient (Supplementary Material 6, available with the online version of this article). The level of evidence and strength of recommendation 2 is available in Table 2.

Orofacial symptoms such as pain are traditionally used as an important outcome measure in studies, even though pain is a poor predictor of the presence of TMJ arthritis. Nevertheless, the task force agreed on the importance of addressing orofacial symptoms in the clinical orofacial examination of patients with JIA because of a high reported prevalence of symptoms, and because there is a substantial effect of orofacial symptoms on daily activities reported in the literature[33]. However, in longitudinal studies including orofacial pain assessments, it is important to recognize that

pain reporting based on visual analog scales (VAS) is limited by reproducibility issues. This means that minor longitudinal changes in pain scores (< 10–14 mm on a VAS) cannot reliably be distinguished from random error within the assessment procedure[13]. In addition, it is important to recognize that orofacial signs and symptoms are regular findings in a nonarthritic adolescent population, with reported prevalence of 4%–7%[66,67,68]. The task force plans to develop a questionnaire to assess symptoms in JIA to achieve standardized collection of the important items represented in recommendation 2.

Recommendation 3. The clinical examination of orofacial signs should include palpation of the TMJ (lateral pole) and masticatory muscles (masseter and temporalis muscles); assessment of pain on palpation, TMJ pain on mandibular movement, and assessment of joint sounds (listening or auscultation).

More than half of the included studies (n = 37) that assessed the presence of clinical signs included palpation of the TMJ and masticatory muscles[6,7,12,14,20,21,22,23,26,27,29-37,39,40,41,42,44,45,46,47,52,54-59,61,62,64,65]. Extrapolated evidence from case-control studies shows that tenderness on palpation, crepitation, and clicking are observed with significantly more frequency in patients with JIA compared to healthy controls (Supplementary Material 6, available with the online version of this article). The level of evidence and strength of recommendation 3 is available in Table 2.

Despite the intermediate predictive value of orofacial palpation for TMJ inflammation, the task force agrees on the inclusion of these items because they provide useful information on the mechanical function of the TMJ, the function of the masticatory muscles, and interplay between the osseous parts and articular disc within the TMJ. Pain on palpation of the orofacial regions and presence of TMJ sounds are also common findings in patients with temporomandibular dysfunction (TMD). In fact, there can be a significant overlap in symptoms and clinical findings in patients with other TMD and JIA patients with TMJ arthritis[69]. It is therefore important for the clinician to recognize that findings of TMJ clicking and palpation-induced tenderness are not necessarily causally related to the joint inflammation seen in JIA and can occur in patients without JIA.

Recommendation 4. The clinical examination of orofacial function should include assessment of temporomandibular joint function; e.g., maximal mouth opening, mouth opening deviation, protrusion, laterotrusion, and condylar translation during opening.

Fifty of the eligible articles included assessment of the TMJ function and mobility[1,6,7,8,12,14,20,21,22,23,25,26,27,29-40,42,43,44,46-65]. The most consistently reported clinical outcome variables across the included literature were mouth opening capacity and mouth opening deviation. Based on the current literature, assessment of TMJ function seems to be extremely important. The evidence from a substantial number of the included articles indicates an increased prevalence of reduced TMJ function in patients with TMJ arthritis compared with healthy controls (Supplementary Material 6, available with the online version of this article). The level of evidence and strength of recommendation 4 is available in Table 2.

Diagnosis of TMJ arthritis based on TMJ function alone has poor sensitivity. Comparison of single measures of orofacial function to normative values are of limited diagnostic usefulness because of great variation in the normative values of TMJ function[70]. However, assessment of TMJ function traditionally constitutes an important outcome measure in longitudinal observational studies, or in studies dealing with intervention. Studies have typically used mouth opening capacity as an indirect outcome variable reflecting the current "functional status" of the TMJ, with increased posttreatment mouth opening capacities interpreted as a treatment-induced improvement in TMJ function. The task force finds the evaluation of TMJ function to be very important in the routine assessment of patients with JIA, as long as the variation within the assessment methods in the longitudinal assessment is factored into the interpretation of results, and conclusions drawn[53]. It remains unclear whether there is any diagnostic value in longitudinal assessment of orofacial function.

Recommendation 5. The clinical examination should include assessment of facial morphology and symmetry; mandibular sagittal position (convexity of the facial profile); and lower face asymmetry in the frontal plane.

For clarification purposes, the convexity of facial profile is defined as retrusion of the lower jaw in relation to the upper jaw. Lower face symmetry in the frontal plane is defined as the position of the mandible in relation to the vertical facial midline and the horizontal pupillary line.

Assessment of the facial morphology and symmetry was included in 24 of the eligible studies[1,14,21-24,26,33-35,37,39,41,44,45,47,48,51,54,57,60-63,65]. Extrapolated evidence from the literature indicates that facial asymmetry based on clinical examination is more prevalent in patients with JIA compared to healthy controls. Cross-sectional studies also reported a significantly higher prevalence of convex profiles in patients with JIA compared to controls (Supplementary Material 6, available with the online version of this article). The level of evidence and strength of recommendation 5 is available in Table 2.

Orofacial growth alterations and the development of dentofacial asymmetry are some of the primary complications in patients with JIA and TMJ involvement. The task force therefore agreed on the importance of regular clinical orofacial assessments for changes in facial symmetry and patient profile, although changes in dentofacial morphology is the outcome of longterm rather than short-term TMJ arthritis. The task force also recognizes that the presence of a convex profile and/or facial asymmetry is also a naturally occurring characteristic in a non-diseased population.

Combining the clinical outcome variables. Several papers

reported the use of standardized clinical orofacial assessment tools such as the Research Diagnostic Criteria for Temporomandibular Disorders[71], the Craniomandibular Index[72,73], and the Helkimo Index[74]. These criteria and indices were originally developed for diagnosis and assessment of dysfunction severity in the TMD patient population. Thus, they were not specifically intended or validated for the clinical orofacial examination in children and adolescents with JIA. In 2014, new diagnostic criteria for temporomandibular disorders were published[69]; however, to date these criteria have not been applied to the JIA population.

In studies dealing with JIA, the diagnostic value of the combination of clinical outcome measures was reported in few studies, but none were associated with more than a moderate diagnostic value of predicting TMJ inflammation[2,22,37,51]. Therefore, the task force did not consider it warranted to include combinations of outcome variables in the recommendations at this point.

Future research. The literature currently uses the term "TMJ involvement" without a standardized distinction between synovial inflammation and deformity of the joint. We will address this issue in our future work. Table 3 outlines our multiphased research program to develop, validate, and implement "evidence-based criteria" for the orofacial examination in patients with JIA.

DISCUSSION

These recommendations have been developed with the intention of standardizing and improving the clinical orofacial examination in JIA for clinical practice and for research studies. This is the first set of orofacial examination recommendations that exclusively applies to patients with JIA. The current recommendations do not include information on patient perception of disability or depression scores. The association between clinical orofacial findings and psychosocial aspects therefore constitutes a future research focus in patients with JIA.

Although extrapolated evidence from the literature clearly demonstrates a relationship between signs/symptoms and TMJ arthritis, these clinical findings are of insufficient magnitude to reliably predict the presence of TMJ inflammation. TMJ arthritis cannot be diagnosed by medical history and physical examination alone. Imaging and radiological techniques such as contrast-enhanced magnetic resonance imaging and cone-beam computerized tomography are required to rule out other causes of asymmetry or dysmorphic dentofacial development, and to help determine whether there is active inflammation or chronic structural changes caused by previous inflammation. This, however, should not undermine the importance of the clinical orofacial examination. Although the medical history and physical examination have limitations in diagnosing TMJ arthritis, they do play an important role in the longitudinal quantification of patient discomfort, orofacial dysfunction, and dysmorphic mandibular development. The regular clinical orofacial examination is therefore a critical part of the clinical assessment of patients with JIA because it documents the morbidity of TMJ arthritis regarding altered TMJ functions and dentofacial growth disturbances.

The level of evidence for all 5 recommendations was low, which underscores the lack of data from rigorous trials. The current literature revealed that insufficient description of outcome variables was a common finding during the review process. This highlights the importance of developing standardized outcome measures. It is our hope that the current recommendations will become part of standard clinical care, and will improve the quality of future studies. The authors recognize that revisions of these recommendations will be ongoing as our understanding of the pathophysiology of TMJ arthritis improves.

Table 3. Future research agenda as defined by the task force.

- Development of a standardized and evidence-based protocol for the minimum standard of care for the clinical orofacial examination of patients with JIA. This protocol will contain specifications for the clinical assessment of each of the proposed outcome measures
- Validity/reliability-testing of the proposed clinical outcome measures
- Assessment of the correlation between TMJ inflammation/hard tissue deformity and the clinical outcome measures proposed in the present recommendations
- Translation of the clinical examination items into multiple languages
- Dissemination of information to improve the knowledge and awareness of TMJ arthritis among the professionals who manage patients with JIA
- Implementation of the proposed standardized clinical orofacial examination in future multicenter observational and interventional studies

JIA: juvenile idiopathic arthritis; TMJ: temporomandibular joint.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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