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Temporomandibular joint damage in juvenile idiopathic arthritis: Diagnostic validity of diagnostic criteria for temporomandibular disorders

Roberto Rongo[1] | Per Alstergren[2,3,4] | Lucia Ammendola[1] | Rosaria Bucci[1] | Maria Alessio[5] | Vincenzo D'Antò[1] | Ambra Michelotti[1]

[1]School of Orthodontics, Department of Neurosciences, Reproductive Sciences and Oral Sciences, University of Naples "Federico II", Naples, Italy

[2]Faculty of Odontology, Malmö University, Malmö, Sweden

[3]Scandinavian Center for Orofacial Neurosciences (SCON), Malmö, Sweden

[4]Skåne University Hospital, Specialized Pain Rehabilitation, Lund, Sweden

[5]Department of Translational Medicine, University Naples Federico II, Naples, Italy

Correspondence
Roberto Rongo, School of Orthodontics, Department of Neurosciences, Reproductive Sciences and Oral Sciences, University of Naples "Federico II", Naples, Italy.
Emails: roberto.rongo@unina.it; roberto.rongo@gmail.com

Summary

Background: Diagnostic criteria reported in the expanded taxonomy for temporomandibular disorders include a standardised clinical examination and diagnosis (DC/TMD 3.B) of temporomandibular joint (TMJ) damage in patients with juvenile idiopathic arthritis (JIA); however, their validity is unknown.

Objectives: To assess the validity of DC/TMD 3.B for the identification of TMJ damage in JIA-patients, using magnetic resonance imaging (MRI) as gold standard, and to investigate the relation between clinical findings and TMJ damage.

Methods: Fifty consecutive JIA patients (9-16 years) were recruited. DC/TMD 3.B were compared with TMJs MRI (100 TMJs) performed maximum at 1 month from the visit. The severity of TMJ damage was scored in four grades. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), logistic regression models with odds ratio of DC/TMD 3.B and clinical findings respect to MRI were calculated.

Results: The DC/TMD 3.B were inadequate in the identification of TMJ damage (sensitivity = 0.15, specificity = 0.92, PPV = 0.85, NPV = 0.28, $P = 0.350$). Chin deviation and TMJ crepitus were associated with worse TMJ damage ($P = 0.006$; $P = 0.034$). Reduced mouth opening (OR = 3.91, $P = 0.039$) and chin deviation (OR = 13.7, $P = 0.014$) were associated with the presence of TMJ damage. Combining "pain" (history of pain, TMJ pain, pain during movements) and "function" (TMJ crepitus, reduced mouth opening, chin deviation) clinical findings, the sensitivity and the specificity were 0.88 and 0.54.

Conclusion: DC/TMD 3.B present a low sensitivity to diagnose TMJ damage. Chin deviation, reduced mouth opening and TMJ crepitus are associated with TMJ damage. We suggest combining "pain" and "function" findings for the evaluation of TMJ damage in JIA patients.

KEYWORDS

children, diagnostic criteria for temporomandibular disorders, diagnostic performance, juvenile idiopathic arthritis, magnetic resonance imaging, temporomandibular joint

1 | BACKGROUND

Juvenile idiopathic arthritis (JIA) represents the most common childhood rheumatic disease in the Western world, affecting approximately 1 per 1000 children, and it is an arthritic condition of unknown aetiology.[1] It is characterised by persistent inflammation of joints for at least six weeks with an onset prior to the age of 16 years.[2] The International League Against Rheumatism (ILAR) introduced new classification criteria for JIA, which currently is being used worldwide. The classification is based on a combination of clinical features, heredity and laboratory data. It includes systemic onset arthritis, oligoarticular and polyarticular subsets, psoriatic arthritis, enthesitis-related arthritis and undifferentiated arthritis.[3]

TABLE 1 Distribution of juvenile idiopathic arthritis (JIA) diagnoses, medication, pain history and magnetic resonance imaging (MRI findings) in 50 patients with JIA and good MRI and in 41 patients without MRI/good MRI hence excluded by the next analyses

	Participants with a good MRI		Participants without MRI/a good MRI	
	N	%	N	%
Number of patients				
#	50	100	41	100
Sex				
Boys	10	20	8	20
Girls	40	80	33	80
JIA diagnosis				
Oligoarticular	30	60	29	71
Polyarticular	15	30	11	27
Systemic	4	8	1	2
Psoriatic	1	2	0	0
Medication				
No	9	18	4	10
NSAIDs	3	6	12	29
Systemic steroids	1	2	0	0
DMARDs	14	28	15	37
Biologics	23	46	10	24
TMJs pain history				
Yes	4	8	1	2
No	46	92	40	98
Muscular pain history				
Yes	6	12	8	20
No	44	88	33	80
TMJ MRI score for severity of osseous deformity				
Grade 0	26	26		
Grade 1	30	30		
Grade 2	24	24		
Grade 3	12	12		
Grade 4	8	8		

N, number of observation; NSAID, non-steroidal anti-inflammatory drugs; DMARD, disease-modifying anti-rheumatic drugs.
Data are reported as frequencies and percentages.
TMJ MRI score is according to Kellenberger et al.[25]

Recently, there has been an increased research focus on the temporomandibular joint (TMJ) in JIA. The TMJ is among the most frequently affected joint in JIA patients. Prevalence of TMJ damage has been reported to be 30%-87%, depending on diagnostic criteria and on methodology.[4-6] Although TMJ damage in JIA is frequently asymptomatic, this joint may be affected both uni- and bilaterally, may be the first joint affected or may be affected during the course of JIA.[7]

The involvement of TMJ can occur in all JIA subtypes, in recent onset as well as long-standing disease.[8] The lacking to diagnose and treat this problem may have severe consequences such as pain, dysfunction,[9] cartilage and bone tissue destruction and mandibular growth alteration.[10] The main complaints reported by patients with TMJ involvement are reduced maximal opening capacity, pain during jaw movements, tiredness of the jaws, TMJ crepitus, chewing disabilities and neck pain.[11]

Based on current literature, magnetic resonance imaging (MRI) is considered the gold standard in detection of TMJ damage and diagnosis of ongoing TMJ arthritis in patients with JIA.[12] MRI allows assessment of osseous damage, disc localisation and configuration as well as effusion without exposure to ionising radiation. However, the disadvantages are high cost and the need of sedation in small children.[13] TMJ effusion is sometimes regarded as an early sign of TMJ inflammation and gadolinium-enhanced magnetic resonance (Gd-MRI) best elucidate the early stage of inflammation in the TMJ.[12] However, due to the fact that TMJ effusions can also be found in children without JIA and without TMJ damage,[14] the risk to overdiagnose TMJ damage is substantial. Several were the attempts to assess whether ultrasonic images could help the identification of early stage of TMJ inflammation but with scarce results, with very low sensibility as shown in a recent systematic review.[13,15]

Given the detrimental effect of bone destruction on TMJ, there is a need of clinical signs or symptoms that, by themselves or in combination with MRI, increase the diagnostic accuracy and performance for diagnosing TMJ damage and its inflammatory activity in JIA. The need is further emphasised by the apparent need for diagnosing, treatment and monitoring guidelines. There is now an international consensus-based recommendation for assessing and monitoring patients with JIA.[16] These recommendations include five domains: medical history, oro-facial symptoms, muscle and temporomandibular joint dysfunction, oro-facial function and dentofacial growth.

The diagnostic criteria reported in the expanded taxonomy for temporomandibular disorders (DC/TMD)[17] describe a standardised clinical examination[18] for diagnosis of joint inflammation resulting in pain or structural changes caused by a generalised systemic inflammatory disease such as JIA. The clinical examination includes four of the five domains discussed in the consensus-based recommendations (medical history, oro-facial symptoms, muscle and temporomandibular joint dysfunction, oro-facial function). However, in the

expanded taxonomy, the diagnostic criteria for JIA diagnosis were presented without known sensitivity and specificity values.

The main aim of this study was to investigate the diagnostic performance of the DC/TMD, as described in the expanded taxonomy, and to assess the diagnostic performance of other clinical variables for identification of TMJ damage in JIA patients. A second aim was to investigate the relation between clinical signs and TMJ structural changes as assessed by MRI.

2 | METHODS

This protocol was approved by the Ethical Committee of University of Naples "Federico II" of Naples (protocol 32617), in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.1 | Patients

The patients were recruited from the Clinic of Rheumatology of the Paediatric Department at the University of Naples "Federico II," Italy, between November 2015 and April 2017. Ninety-one patients with a diagnosis of JIA, according to the ILAR criteria,[3] were included in our study after informed consent was obtained. The patients were consecutively referred to the Temporomandibular Disorders and Orofacial Pain Clinic, University of Naples "Federico II," Italy, regardless of whether they had TMJ symptoms. The mean (SD) age of the patients was 11.8 (3.5) years, and the mean (SD) duration of disease since diagnosis was 5.5 (3.7) years. Most of the patients enrolled had a diagnosis of oligoarticular arthritis (60%), and many used biologic drugs (46%). Almost 90% did not report a history of TMJ or muscular pain in the last month (Table 1).

Inclusion criteria were JIA diagnosis according to the ILAR criteria (age at onset is under 16 years, disease duration is 6 weeks or greater, and other known conditions are excluded).[3]

Exclusion criteria were age less than 9 years or higher than 16 years; incomplete medical records; presence of congenital/acquired facial anomalies (eg, hemifacial microsomia, cleft lip/palate, Treacher-Collins syndrome, TMJ ankylosis); history of facial fractures; previous intra-articular TMJ interventions (eg, steroid injections, surgery); inability to verbalise or indicate pain or discomfort (eg, developmental delay); presence of medical comorbidities not allowing for a comprehensive clinical examination; and orthodontic treatment ongoing or within the past 12 months.

Table 1 shows the distribution of diagnoses among the patients as well as their medication and history of pains.

2.2 | Clinical examination

During the first visit, data regarding age, gender, subtype of JIA, disease onset date and systemic drug therapy were collected.

All patients underwent a clinical examination according to the DC/TMD protocol[19] by one calibrated examiner (LA). DC/TMD was developed by the International Network for Orofacial Pain and Disorders Methodology (INFORM) and is the evolution of the research diagnostic criteria for TMD (RDC/TMD)[20] that were validated in adults[21] and children.[22]

The examiner asked the patients about pain history according to the symptom questionnaire: oro-facial pain during the last month, pain at the TMJ or masticatory muscles, pain modifications (got better or got worse) with jaw movement, function or parafunction, joint noises (click or crepitus) and closed or opening locking jaw.

The DC/TMD protocol included opening pattern, opening movements, with the cut-off value for restricted mouth opening set to ≤40 mm,[23,24] lateral and protrusive movements, TMJ noises during jaw movements, muscle and TMJ pain with palpation.

The examiner (LA) collecting medical records was not informed of the findings of the MRI at the time of the first consultation.

Finally, an experienced orthodontist (VD) examined the patients using frontal facial photographs to evaluate the presence of chin deviation as sign of facial asymmetry. A picture, with a ruler for the calibration in the background, was taken with the patient in the upright sitting position with teeth in centric relation and lips at rest. For each patient, on the photograph, the facial midline (a line perpendicular to the interpupillary plane passing for the glabella) was identified, and the direction and severity of chin deviation was recorded. The orthodontist recorded a chin deviation when the chin shift from the facial midline was >2 mm to right or left side. The photographs did not present patient name and were recorded by an ID number; hence, the observer did not know patient name and did not know the findings of the clinical or MRI examinations. To evaluate the intra-observer reproducibility for the chin deviation, the observer (VD) analysed 20% of the frontal facial photographs (ten patients) twice and the Cohen's kappa was found to be 0.92 (SE: 0.06; CI 95% 0.80-1.00).

The diagnosis of TMJ damage due to JIA was derived according to the criteria suggested in the expanded taxonomy of DC/TMD systemic arthritides (3.B) criteria,[17] as shown in Table S1.

2.3 | MRI examination

Each patient underwent a MRI examination of the TMJ region in closed and open mouth positions within 1 month from the clinical examination. For the closed mouth position, the patient was asked to close the mouth with his or her teeth in light contact. For the open mouth position, the patient was asked to open the mouth as wide as possible. The MRI scans consisted of T1-weighted, T2-weighted, proton density images in the coronal, oblique and sagittal views. An orthodontist, expert in analysis of TMJ MRI (RR), assessed all the images blindly to clinical findings of the patients.

In the MRI, we assessed the TMJ bone damage as an indirect sign of an inflammatory process. Hence, "TMJ damage" was identified as a sign of a previous or ongoing inflammatory activity inside the TMJ.

TMJ damage was scored in four grades according to the severity of osseous deformity[25]: Grade 1: mild osseous deformity; mild flattening of the condyle and/or temporal bone; Grade 2: moderate osseous

TABLE 2 Diagnostic performance using the DC/TMD examination as well as combinations of clinical variables to diagnose to diagnose TMJ damage in JIA with MRI findings as reference standard

Examination	Criteria		Frequency (%)	Sensitivity	CI 95%		Specificity	CI 95%		PPV	CI 95%		NPV	CI 95%		P value Chi-square
DC/TMD	History of pain AND (TMJ pain OR TMJ crepitus)	No	13 (13)	0.15	0.80	0.25	0.92	0.75	0.99	0.85	0.57	0.96	0.28	0.25	0.31	0.350
		Yes	87 (87)													
PAIN	Presence of pain (pain at history OR TMJ pain OR pain during movements)	No	53 (53)	0.51	0.40	0.63	0.65	0.44	0.83	0.74	0.64	0.82	0.32	0.25	0.40	0.141
		Yes	47 (47)													
FUNCTION	Reduced mouth opening OR TMJ crepitus OR chin deviation	No	50 (50)	0.61	0.49	0.72	0.81	0.61	0.93	0.90	0.80	0.95	0.42	0.34	0.50	**<0.001**
		Yes	50 (50)													
TOTAL EXAMINATION	Pain at history OR TMJ pain OR pain during movements OR reduced mouth opening OR TMJ crepitus OR chin deviation	No	23 (23)	0.88	0.78	0.94	0.54	0.33	0.73	0.84	0.78	0.89	0.61	0.44	0.76	**<0.001**
		Yes	77 (77)													

PPV, positive predictive value; NPV, negative predictive value. PPV and NPV were calculated using the prevalence of TMJ damage found in the study (74%). Bold text indicates statistically significant values.

deformity; moderate flattening of the condyle and/or temporal bone; Grade 3: severe osseous deformity, severe flattening of the condyle with loss of height, and/or completely flat temporal bone and/or the presence of small erosions; and Grade 4: "destroyed" TMJ; presence of large erosions and/or fragmentation of the condyle, intra-articular ossifications, bone apposition on condyle or temporal bone.

Out of the 91 initial patients, 67 patients agreed to perform an MRI within 1 month; of this, 17 were excluded due to the low quality of the MRIs, leaving a total of 50 patients (100 TMJ scans, sum of right + left side) to be included in this study. To evaluate the intra-observer reproducibility for the MRI, the observer (RR) analysed 20% of the MRI (ten patients) twice and the Cohen's kappa was found to be 0.87 (SE: 0.07; CI 95% 0.73-1.00).

2.4 | Statistics

The power of the study was calculated a posteriori, based on the sample size of 100 TMJs and the prevalence of the TMJs arthritis of 74%. Considering a two-side binomial test ($\alpha = 0.05$), this study achieved a power with $\beta = 80\%$ to detect a change in sensitivity from 0.50 (maximum variability) to 0.68.

Data were reported as median with 25°-75° percentiles in case of ordinal data, frequency and percentage in case of nominal data, or mean and standard deviation in case of continuous data. The Spearman rho coefficient was used to calculate a possible relation between the duration of the disease and the degree of osseous deformity.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated together with the exact 95% confidence intervals (95% CI) for the 3.B DC/TMD diagnoses. Furthermore, the same parameters were investigated for the eight clinical findings assessed during the examination. Similarly, the diagnostic performance of pain-related variables, function-related variables and a combination of pain- and function-related variables were assessed. In all the analyses, the MRI scores were used as gold standard and each TMJ side was investigated independently. For the calculation of the PPV and NPV, we used the prevalence of TMJ damage found in the study.

Chin deviation and mouth opening deviation were analysed excluding the TMJs contralateral to the side of deviation. A Cochran-Mantel-Haenszel test was used to evaluate the association between the severity of the MRI and the presence of the clinical DC/TMD parameters. Univariate logistic regression model, with odds ratio (OR) calculations, was used to assess which of the single characteristics assessed during the clinical examination (muscle pain on palpation, TMJ pain on palpation, pain during movements, reduction of jaw opening, TMJ crepitus, chin deviation and mouth opening deviation) could be considered as a predictive value for TMJ damage.

Variables with a *P* value lower the 0.100 were inserted in a multivariate logistic regression model. After two weeks from the end of data collection, the MRI observer and the asymmetry observer repeated the evaluation for the 20% of patients and the reproducibility of the assessments was evaluated by Cohen's kappa.

TABLE 3 Sensitivity and specificity for single clinical variables to diagnose TMJ damage in JIA with MRI findings as reference standard

Examination		Frequency (%)	Sensitivity	CI 95%		Specificity	CI 95%		PPV	CI 95%		NPV	CI 95%		*P* value Chi-square
Uncorrected deviation on mouth opening	No	50 (67)	0.37	0.24	0.51	0.76	0.53	0.92	0.80	0.63	0.90	0.32	0.26	0.39	0.275
	Yes	25 (33)													
Reduced mouth opening	No	72 (72)	0.34	0.23	0.46	0.88	0.70	0.97	0.89	0.73	0.96	0.32	0.27	0.37	**0.030**
	Yes	28 (28)													
History of pain	No	85 (85)	0.16	0.09	0.27	0.88	0.70	0.97	0.80	0.55	0.93	0.27	0.24	0.30	0.566
	Yes	15 (15)													
TMJ pain	No	65 (65)	0.38	0.27	0.50	0.73	0.52	0.88	0.80	0.67	0.89	0.29	0.23	0.35	0.315
	Yes	35 (35)													
Muscular pain	No	38 (38)	0.62	0.50	0.73	0.38	0.20	0.59	0.74	0.67	0.80	0.26	0.17	0.39	0.955
	Yes	62(62)													
Pain during movements	No	87 (87)	0.15	0.08	0.25	0.92	0.74	0.99	0.85	0.56	0.96	0.27	0.25	0.30	0.350
	Yes	13 (13)													
Chin deviation[a]	No	48 (65)	0.45	0.31	0.58	0.94	0.73	1	0.96	0.78	0.99	0.35	0.30	0.42	**0.003**
	Yes	26 (35)													
TMJ crepitus	No	86 (86)	0.19	0.11	0.30	1.00	0.87	1.00	1.00	0.73	1.00	0.30	0.28	0.33	**0.017**
	Yes	14 (14)													

PPT, positive predictive value; NPV, negative predictive value. PPV and NPV were calculated using the prevalence of TMJ damage found in the study (74%). Bold text indicates statistically significant values.

[a]To avoid underestimating the reliability of these parameters in the statistical analysis, the joint contralateral to the deviation (skeletal and opening) was excluded in the statistical analysis.

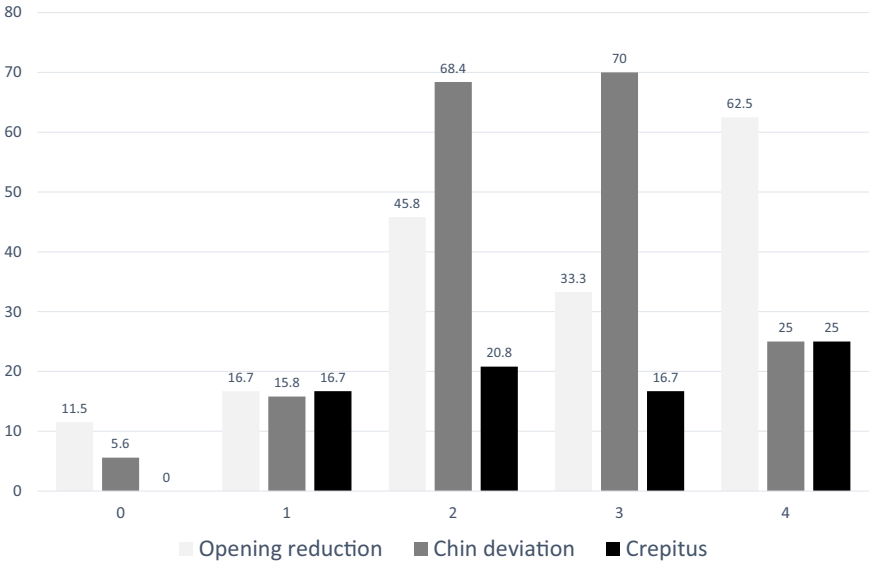

FIGURE 1 Association between severity of TMJ damage and single clinical findings, only statistically significant association, was reported. Percentages of presence of reduced mouth opening, chin deviation and TMJ crepitus are shown on the Y-axis, while severity of TMJ damage is shown on the X-axis. Reduced mouth opening, $P = 0.030$; chin deviation, $P = 0.003$; TMJ crepitus, $P = 0.017$

All statistical tests were two-sided. *P* values less than 0.05 were considered significant. Statistical analysis was performed using SAS (SAS 9.2; Statistical Analysis Software, Cary, NC, USA).

3 | RESULTS

Table 1 shows the results from the MRI scoring. Of the 100 joints examined with MRI, 74 (74%) showed MRI changes that were not within the normal range. The median (25/75 percentiles) score for severity of osseous deformity was 1 (0/2; n = 100). The disease duration was not significantly related to TMJ damage severity ($r_s = 0.062$; n = 100; $P = 0.537$).

No significant differences were found for number of painful mandibular movements or number of jaw muscles with palpation pain between the two groups of children with JIA with or without TMJ damage, and the same was for the range of mandibular movements (Table S2).

Table 2 shows the sensitivity, specificity, PPV and NPV for the DC/TMD diagnosis as well as the combinations of clinical findings. Diagnosis of TMJ damage according to the DC/TMD criteria showed a sensitivity of 0.15 and a specificity of 0.92, as compared to the MRI findings ($P = 0.350$). The PPV was 0.85 and the NPV was 0.28 (Table 2).

The results related to single clinical variables are shown in Table 3. In particular, TMJ crepitus showed the highest specificity and PPV (1.00), while muscular pain showed the highest sensitivity (0.62). Figure 1 shows the proportion of patients with reduced mouth opening, TMJ crepitus and chin deviation in the five degrees of TMJ damage according to MRI. Chin deviation, reduction in mouth opening and TMJ crepitus were significantly associated with TMJ damage ($P = 0.003$; $P = 0.030$; $P = 0.017$, Figure 1).

Clinical findings were grouped in PAIN -related clinical variables (history of pain, TMJ pain, pain during movements), FUNCTION -related clinical variables (TMJ crepitus, reduced mouth opening, chin deviation) and TOTAL EXAMINATION (PAIN + FUNCTION). The TOTAL EXAMINATION showed the highest sensitivity 0.88 and the highest NPV 0.61; all the data referred to the diagnostic performance of these three groups are shown in Table 2.

The logistic regression models (Table 4) showed that the presence of TMJ damage could be predicted by both reduced jaw opening (OR = 3.91, 95% CI 1.07-14.3, $P = 0.039$) and chin deviation (OR = 13.7, 95% CI 1.7-110.2, $P = 0.014$) and two combinations of clinical findings FUNCTION (OR = 6.52, 95% CI 2.21-19.2, $P = 0.015$) and TOTAL EXAMINATION (OR = 8.43, 95% CI 2.98-23.8, $P = 0.015$). In the multivariate logistic regression model, TMJ damage could be predicted by the suggested clinical examination (TOTAL EXAMINATION, OR = 4.44, 95% CI 1.34-14.8, $P = 0.015$).

4 | DISCUSSION

This study indicates that diagnostic performance of the DC/TMD criteria, as described today, is insufficient to identify all JIA patients with TMJ damage. However, when the DC/TMD 3.B criteria are positive, there is the 85% of chance (PPV) that the patient has a TMJ damage, but they are not able to detect more than the 15% of cases. The same goes for chin deviation that is strongly associated with severity of TMJ damage as a clear and late sign of TMJ damage or growth disturbance. It may be considered as important for assessment in these patients as well as evaluating the progress of the disease in relation to treatment. In addition, this study suggests combining pain-related variables with function-related variables in order to achieve a higher diagnostic performance to diagnose JIA patients with TMJ damage.

We used MRI as the reference standard to decide whether a TMJ had damage or not. Although MRI is not a perfect reference standard, it is still considered the prime diagnostic non-invasive modality for patients with clinical symptoms of TMJ soft tissue disease.[26-28]

This study investigated, primarily, sensitivity and specificity of the DC/TMD for the identification of TMJ damage in JIA, using the

TABLE 4 Results from the univariate and multivariate logistic regression analyses for factors that may predict TMJ damage in JIA patient

	Odds	OR	CI 95%	*P* value	Multivariate regression analysis	CI 95%	*P* value
Uncorrected deviation on mouth opening							
No	2.12	1.88	0.6-5.92	0.279	-	-	
Yes	4						
Reduced mouth opening							
No	2.13	3.91	1.07-14.3	**0.039**	0.83	1.27-5.48	0.850
Yes	8.3						
TMJ pain							
No	2.42	1.65	0.62-4.43	0.318	-	-	
Yes	4						
Muscular pain							
No	2.8	1.02	0.41-2.57	0.955	-	-	
Yes	2.87						
Pain during movements							
No	2.62	2.10	0.43-10.1	0.358	-	-	
Yes	5.5						
History of pain							
No	2.69	1.48	0.38-5.73	0.567	-	-	
Yes	4						
Chin deviation[a]							
No	1.83	13.7	1.7-110.2	**0.014**	-	-	
Yes	25						
TMJ crepitus							
No	2.30	-	-	-	-	-	
Yes	-	-					
PAIN							
No	2.11	1.99	0.79-5.04	0.145			
Yes	4.22						
FUNCTION							
No	1.38	6.52	2.21-19.2	**0.001**	3.5	0.65-18.9	0.146
Yes	9						
TOTAL EXAMINATION							
No	0.64	8.43	2.98-23.8	**<0.001**	4.44	1.34-14.8	**0.015**
Yes	5.41						

Odds, odds for having TMJ damage; OR, odds ratio; CI 95%, 95% confidence interval. Bold text indicates statistically significant values.
[a]To avoid underestimating the reliability of these parameters in the statistical analysis, the joint contralateral to the deviation (skeletal and opening) was excluded in the statistical analysis.

recommendations of the expanded taxonomy for TMD.[17] It investigated sensitivity and specificity of other clinical variables collected during the clinical examination, alone or in combinations. Using solely the DC/TMD criteria, the sensitivity was too low to be considered useful for identifying TMJ damage in JIA patients. These criteria thus did not achieve a sufficient level of sensitivity to be valid for the diagnosis of TMJ damage in JIA patients. The DC/TMD criteria, however, showed a fairly high specificity, which means that the test identifies 92% of JIA patients without TMJ damage. Theoretically, these criteria may therefore be of certain value as a test to identify JIA patients without TMJ damage, which would be useful for screening in paediatric care. This must be further tested before it has a possibility to be of clinical usefulness.

DC/TMD describe criteria for a series of TMD pathologies[19] and have been validated from the age of 18 years. It has not yet been validated for TMJ damage diagnosis in JIA patients, and this study is the first attempt to do so. Several studies have evaluated different protocols for diagnosis of TMJ damage in JIA. Helkimo's dysfunction

index[29] was one of the first index to be used for TMD diagnosis, but it has low reproducibility and no established validity when used in patients with JIA.[30] Also, the validity of RDC/TMD[20] used in several studies to assess the presence of temporomandibular disorders in JIA patients[31] has not been established.[32]

Arthritic inflammatory process in TMJ may cause pain, cartilage and bone tissue destruction as well as growth disturbances. After severe damage or growth disturbance, clinically detectable changes such as occlusal changes and micrognathia may occur but that is usually late in the disease process. It is therefore very difficult to identify early TMJ involvement and to treat it in its early form to prevent damage. Also, signs and symptoms are very variable between and within patients; the patient might present from no signs or symptoms to any combination of pain, swelling/exudate, tissue degradation and growth disturbance.[33,34] Indeed, pain is not always predictive of TMJ arthritis or TMJ damage, as confirmed also by Allen et al[35] and Alstergren et al[36] Given the unreliable presence of pain in patients with arthritis and limited sensitivity of DC/TMD criteria (that are based on pain), we investigated the sensitivity and specificity of other signs, as single variables or combination, obtained from the clinical examination.

First, we considered *TMD pain*. Ninety-four percentage of the patients were considered to show signs of TMJ damage according to the MRI. On the other hand, history of joint pain and familiar pain on palpation were seldom reported. Similarly, only few patients fulfilled criteria for arthralgia or myalgia. This may explain the low sensitivity of the DC/TMD criteria. We also combined data on "familiar" and "not familiar" pain. Hence, TMJ pain on palpation was found in less than half of the patients, whereas masseter muscular pain on palpation was found in a majority. Some patients reported pain during mandibular movements. Indeed, the prevalence of self-reported joint and muscular pain was lower than that assessed during the clinical examination and the prevalence of muscle pain on palpation was high consistently with other studies.[37,38] When the pain variables were combined, the sensitivity increased but not to an acceptable degree. At the same time, the specificity decreased. Due to these shortcomings, pain alone cannot be considered as an useful tool to diagnose TMJ damage in JIA patients.

Second, we considered *mandibular movements*. Reduced mouth opening had a sensitivity of 0.34 and a specificity of 0.88, meaning that almost 9 of 10 JIA-patients had no reduced mouth opening and thus did not have TMJ damage. Moreover, we found that reduced mouth opening had a predictive value for TMJ damage with an OR of 3.91, which must be regarded as a high risk. The association between reduced mouth opening and TMJ damage has been found in previous studies,[24,39] suggesting that reduced mouth opening is an important factor to be include in the clinical examination for assessment and to follow-up of these patients. Assessment of mouth opening capacity over time may in the future be of value to find early TMJ damage.

In this study, reduced mouth opening capacity was defined as a mouth opening capacity of ≤40 mm. This is according to DC/TMD, which are validated in adults. However, in children and adolescents, this definition may need to be adjusted.[40]

Third, we considered *joint noise*. Crepitus presented a low sensitivity (0.19) and a very high specificity (1.00). It was more frequent in TMJs with a higher grade of damage. This means that if a patient has a crepitus, it is highly likely that he or she has a TMJ damage.

Finally, we considered *functional and skeletal asymmetries*. Chin deviation and an opening pattern with uncorrected deviation were able to predict TMJ damage on the affected side or to detect the most damaged joint. To avoid underestimating the validity of these parameters, we decided to exclude in the statistical analysis the joint contralateral to the deviation. In particular, we found uncorrected deviation in mouth opening in 42% of patients with TMJ damage with a sensitivity of 0.37 and specificity of 0.76. This clinical parameter was the best predictor of TMJ inflammation in both Stoll et al[8] and Koos et al,[6] who found 49% and 62% of mouth opening uncorrected deviation in JIA patients with MRI-confirmed TMJ inflammation, compared to 12% and 16% of JIA patients without TMJ inflammation. However, opening pattern with uncorrected deviation, especially in young patients, is largely variable between studies (3%-78% of populations).[2] Deviation during mouth opening could be caused also by muscular or articular pain problem, which could account for our low sensitivity value (sensitivity = 0.37). Hence, in accordance with Billiau et al[10] and given the inconsistent findings, this single clinical parameter cannot be considered as a valid screening tool.

The evaluation of asymmetry was made on facial photographs, and chin deviation was significantly associated with TMJ damage with a specificity of 0.94. This is supported by other studies[41,42] on the effects on TMJ damage on facial growth and development. Chin deviation was also associated with the severity of the TMJ damage with a high OR of 13.7. This means that a deviated chin is a clear and late sign of TMJ damage or growth disturbance and must be considered as important for assessment of these patients as well as evaluating the progress of the disease in relation to treatment.

The analysis of the current literature and our results shows that the use of single clinical TMJ findings limits TMJ diagnosis. For example, no one of the variable analysed had NPV higher than 0.35, meaning that a single clinical finding is not useful to exclude the TMJ damage. Combinations of clinical features were tested in several studies. Koos[6] compared clinical examination and early synovitis assessed on MRI in JIA patients and found that a combination of clicking, TMJs and muscles tenderness, and mouth open capacity showed a sensitivity of 0.73 and a specificity of 0.42. Similarly, Abramowicz et al,[43] using limited maximal incisal opening and deviation on opening, found a high specificity (86% and 94% respectively) as predictors of synovitis. A new "3 minutes protocol" including impairment or pain during chewing, limited, deviated or painful mouth opening, crepitus, asymmetry and retrognathia was tested by Steenks et al[44] They conceptualised at least one positive score as indication of potential TMJ damage with specificity and sensitivity respectively of 0.77 and 0.57. The validity of this protocol was investigated against a disease activity score (JADAS-27) and not against MRI as gold standard; this could represent a limit since there is no relationship between condylar lesions and disease activity score.[10] Finally, in a recent systematic

review, the authors evaluated as clinical parameters for the diagnosis of TMJ arthritis in JIA patients subjective pain, TMJ sounds, maximal incisal opening, myofacial pain on palpation and facial asymmetry. They concluded that the low level of evidence does not allow selecting clinically relevant outcome measurements.[39]

Based on the diagnostic performance of the analysed parameters and the regression analysis, we proposed to associate clinical findings related to pain and to function. In particular, "pain" included positive response to pain at history, even more than 30 days before, and/or pain at movements and/or pain at TMJ palpation. We suggest merging reported and recorded pain because the discrimination of TMJ pain in children could be difficult.[45] "Function" included crepitus and/or reduction in mouth opening capacity and/or chin asymmetry which had a high specificity. However, in pathologies that worsen quickly and severely with irreversible changes, preferred diagnostic tests are tests with high sensitivity and high NPV. We therefore decided to combine clinical variables related to "pain" and "function," which showed a sensitivity of 0.88 and a NPV of 0.61. This examination allows to identify almost 9 of 10 patients with TMJ damage; however, the diagnostic performance of clinical examination is still insufficient to identify JIA patients with or without TMJ damage or early signs of TMJ arthritis.

Consistently with Ringold and Cron,[7] we did not find any correlation between the disease duration and the severity of TMJ destruction (Spearman's rho = 0.062; $P = 0.537$). In contrast, Pedersen and colleagues reported that children with longer disease duration were more likely to have extensive damage.[5]

5 | CONCLUSIONS

TMJ is one of the most involved joint in JIA patients. On the 50 patients examined in this study, 94% showed at least one affected joint. However, more than the 90% did not report history of TMJ pain in the last 30 days.

This study indicates that diagnostic performance of the 3.B DC/TMD criteria, as described today, is insufficient to identify JIA patients with TMJ damage.

Chin deviation, TMJ crepitus and reduction on mouth opening are associated to a high risk of TMJ involvement and are more frequent when the damage of the TMJ is more severe. They may be considered important for assessment in these patients as well as evaluating the progress of the disease in relation to treatment.

In addition, this study suggests combining pain-related variables with function-related variables to achieve a higher diagnostic performance to diagnose JIA patients with TMJ damage.

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CONFLICT OF INTEREST

The authors of this manuscript declare that they have no conflict of interest.

ORCID

Roberto Rongo https://orcid.org/0000-0002-9741-794X

Rosaria Bucci https://orcid.org/0000-0002-2588-2949

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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