Long-term Outcomes of Temporomandibular Joints in Juvenile Idiopathic Arthritis:

17 years of follow-up of Nordic Juvenile Idiopathic Arthritis (JIA) cohort.

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Abstract:

Objective: To determine the prevalence of orofacial symptoms, dysfunctions, and deformities of the temporomandibular joint (TMJ) in juvenile idiopathic arthritis (JIA) 17 years after disease onset.

Methods: Drawn from a prospective, population-based Nordic JIA cohort with disease onset from 1997-2000, 420 consecutive cases were eligible for orofacial evaluation of TMJ involvement. The follow-up visit included demographic data, a standardized clinical orofacial examination, and full-face cone-beam computed tomography (CBCT). For comparison, 200 age-matched healthy controls were used.

Results: Of 420 eligible participants with JIA, 265 (63%) were included (mean age 23.5 ± 4.2 years) and completed a standardized clinical orofacial examination. Of these, 245 had a full-face CBCT performed. At least one orofacial symptom was reported by 33%. Compared to controls, the JIA group significantly more often reported TMJ pain, TMJ morning stiffness, and limitation on chewing. Furthermore, among participants reporting complaints, the number of symptoms was also higher in the JIA. The mean maximal incisal opening was lower in the JIA group ($p<0.001$), and TMJ pain on palpation was more frequent. Condylar deformities and/or erosions were observed in 61% as assessed by CBCT, showing bilateral changes in about 70%. Risk factors of condylar deformities were orofacial dysfunction or biologic treatment; enthesitis-related arthritis was protective.

Conclusion: This first study on long-term consequences of TMJ involvement in a population-based JIA cohort reports persistence of comprehensive symptoms, dysfunctions, and damage of the TMJ into adulthood. We suggest interdisciplinary follow-up of JIA patients also in adulthood.

Introduction:

Arthritis of the temporomandibular joint (TMJ) is a well-recognized entity in patients with juvenile idiopathic arthritis (JIA) with a prevalence of 40-86% (1-5) dependent on the cohort and imaging used (6). A prime concern in relation to childhood TMJ arthritis is the development of temporomandibular disorders (TMD) and dentofacial deformities. These deformities develop as TMJ inflammation impacts the condylar growth cartilage uniquely positioned intra-articularly (7). Retrognathia developing into micrognathia is a common finding, unilateral TMJ involvement may cause facial asymmetry (8-10), and arthritis-induced orofacial symptoms or dysfunctions may impair patients' quality of life (2, 3, 11).

Long-term (>10 years) outcomes of TMJ arthritis in JIA have been investigated in four cohorts (4, 12-14), all from the pre-biologic era. However, these cohorts have been small, selection biased, and difficult to compare because of different treatment approaches. Hence, long-term orofacial manifestations of JIA in a non-selected JIA cohort in the biologic era remain unknown.

In a population-based cohort with a 17-year follow-up the aims were to: 1) estimate the prevalence of orofacial symptoms and dysfunction in JIA compared to age-matched healthy controls, 2) estimate the prevalence of TMJ deformities assessed by cone-beam computed tomography (CBCT), 3) suggest predictors for developing radiological TMJ deformities.

Materials and Methods

Study design: We enrolled eligible JIA subjects from the Nordic JIA cohort 17 years after JIA onset. The cohort consists of consecutive cases with JIA diagnosed by experienced pediatric rheumatologists from particular geographical areas of Denmark, Finland, Norway, and Sweden. Characteristics of the cohort have previously been described (15, 16). The inclusion period was defined as disease onset from 1 January 1997 to 30 June 2000. Initially and during the inclusion period, letters were distributed to all referral institutions (primary care physicians, orthopedic surgeons, and pediatricians) in the catchment areas to ensure inclusion of all potential JIA candidates. The baseline visit took place 6 months (-1/+2 months) after disease onset. In the current study, disease onset was defined as the date of the first symptoms of arthritis described by the patient/parents or by a doctor. The date of diagnosis was the date the pediatric rheumatologist diagnosed JIA.

Registration of the active joints including the TMJs was done at baseline and prospectively (15, 16). To ensure a non-selected setting, all eligible patients were invited to participate regardless of their disease course. Last follow-up visit included an update on demographic data, standardized clinical orofacial examination according to consensus-based international recommendations (17), and a CBCT. In the original cohort, 510 JIA patients were included, but some centers had no access to CBCT. They were therefore excluded in the present study (Figure 1). Their exclusion did not hamper the population-based approach of the study.

Inclusion criteria: Participants fulfilling the International League of Associations for Rheumatology (ILAR) criteria of JIA (18) having had at least two follow-up visits. *Exclusion criteria:* Participants with cleft-lip-palate or other dentofacial and craniofacial anomalies unrelated to arthritis.

Disease activity: The validated Juvenile Arthritis Disease Activity Score (JADAS) was used to assess disease activity. JADAS71 includes a physician´s global assessment of disease activity (PhysGA)(0-10), the patient´s global assessment (PatGA) of general well-being (0-10), an active joint count assessed in 71 joints, and erythrocyte sedimentation rate (ESR) (19) with a range of 0-101 where ≤ 1 is equivalent to inactive disease (20). We applied the preliminary remission criteria by Wallace et al (21).

Definitions of TMJ involvement: We used the terminology of the standardized, consensus-based recommendations by the Temporomandibular Joint Juvenile Arthritis Work Group (*TMJaw* group) (22).

Assessment of orofacial symptoms: According to the international recommendations on orofacial examination in JIA (17), the participants completed a web-based questionnaire on orofacial pain frequency, intensity, location, and jaw function within the past two weeks. TMJ stiffness referred to morningstiffness in the jaw muscles and joints. Orofacial muscle pain was pain in the masseter and temporalis muscles and chewing limitations when the participants avoided hard or chewy foods because of pain in the face or jaw. Pain frequency was defined as pain from the jaw area within the past 2 weeks categorized as: 1) Never (0 points); 2) Not every week (1 point); 3) Several times a week (2 points); 4) Several times a day (3 points); 5) All the time (4 points).

WHO guidelines on cross-cultural translation (25), and questionnaire adaptation were used (23) for translation of the questionnaire to the four Scandinavian languages.

Assessment of dentofacial dysfunction: Standardized clinical examinations (17) were performed by eight specially trained investigators (five orthodontists, one orofacial pain specialist, one pediatric dentistry specialist and one oral maxillofacial surgeon).
The maximal incisal opening (MIO) was assessed as the distance between the lower and upper right incisal edge accounting for the vertical incisal overlap. Reduced mouth opening was defined as MIO $\leq$ -2 SD below the mean of age-related normative values of 17-year-olds (24). The same type of ruler was used in all centers. TMJ pain on palpation was documented on a closed and open mouth position with index finger placed on the TMJ. Asymmetric mouth opening was defined as a mandibular deviation $\geq$ 3 mm to either side in relation to the vertical midface reference line at maximum mouth opening.

Radiographic assessment: CBCT examinations were performed using the manufacturer's recommendation on details regarding doses, radiation time, and voxel size. Standardization was optimized using the following criteria: 1) Teeth in habitual occlusion with no protrusion of the mandible; 2) A large field of view, at least 12''.
The radiological appearance of the condylar head was scored as normal (condylar shape with smooth, intact outline) or abnormal, assessing CBCT volumes in the lateral, coronal, and axial planes. Abnormal condyles were subcategorized based on the predominant radiologic feature: 1) Deformity of the condyle with marked flattening or changes in shape with smooth and intact outline; 2) Erosion of the condyle with disruption of the outline due to cysts or erosions; 3) Deformity plus erosive changes. Importantly, this scoring system of the osseous deformities does not refer to a scale with gradual progression. The same observer (LHM), who is highly experienced in assessing CBCT, performed the evaluations of the condyles in the CBCT volumes. LHM was blinded to all clinical and demographic data.

Control group: Non-selected Danish age-matched individuals (N=200) between 18 and 30 years were used for comparison. The control group was composed of young healthy adults (dental students, members of a sports club and trainees within the retail industry) who voluntarily participated in the study. Inclusion criteria for the controls were healthy individuals with no history of arthritis, osteoarthritis, cleft-lip-palate, other craniofacial anomalies or ongoing orthodontic treatment. Orofacial symptoms were reported in the same web-based questionnaire as the JIA

group, and the same standardized orofacial examination was used (17). For ethical reasons, no CBCT examination was performed of the healthy controls.

Intra-observer variation in the assessment of the CBCT scans: 30 CBCT (60 TMJs) examinations were assessed twice with 6 months apart by the same observer (LHM) to test the intra-observer reliability.

Ethics: Approval was granted by national research committees in all the countries (1-10-72-280-13, 2012/2051, Dnr 2014/413-31, 174/13/03/03/2014), and the participants gave their written consent. Furthermore, Institutional Review Board approval was granted.

Statistics: Descriptive statistics of normally distributed data (mean±SD) and non-parametric data (median/interquartile range) were applied to assess the clinical characteristics of the cohort and disease activity. Chi square test was conducted to compare dichotomous data. Mann-Whitney test and standardized test statistics reported as a z score were used to compare medians on ordinal data. A logistic regression model was used to assess baseline predictors and predictors for the development of condylar changes. All candidate variables were dichotomized and odds ratios calculated using a multivariate logistic regression model. Age at onset and gender were included in the model, and the level of significance was $p<0.05$. Furthermore, to identify high-risk participants at the 17-year follow-up, we performed a logistic regression analysis of treatment, symptoms, dysfunctions, and JIA category.
Cohen´s kappa coefficient (κ) was analyzed to test the inter-rater agreement for categorical measurements.

Results:

Study population: Of 420 eligible participants from the JIA cohort, 265 (63.1%) were included in the present study (mean age 23.5 (SD ±4.2) years) (Figure 1). One patient was excluded because of fracture of a condyle. The mean follow-up time from JIA onset to orofacial examination was 17.3 years (SD ±1.3 years); 186/265 (70.6%) were girls. The distribution of JIA categories and other clinical data were as described in Table 1. We found no difference in gender, JIA category, number of active joints, or baseline JADAS values between included participants and those lost to follow-up. However, age at onset was lower in the included group (mean 6.0±3.9 vs. 7.6±4.3 years in those

lost to follow-up (p=0.003). Of the 265 participants completing the clinical orofacial examination, 245 had a full-face CBCT performed with 490 approved high-quality TMJ images.

The control group had a mean age of 23.6±2.9 years; 52.5% were girls.

Orofacial symptoms: In total, 87 of the 265 JIA participants (32.8%) reported at least one TMJ-related symptom at the follow-up visit, which was similar to the control group (p=0.11) (Table 2). Orofacial pain frequency and number of symptoms, TMJ pain, morning stiffness, and limitation of chewing were observed significantly more frequently in the JIA group and in all categories (Table 2). We found no inter-group difference in pain in the temporal (p=0.51) or masseter area (p=0.17) (data not shown). Overall, 89 (33.6%) participants with JIA reported jaw and/or facial pain within the past two weeks. Of the controls, 61 (30.5%) reported jaw and/or facial pain within the past two weeks, which was similar to the reports in the JIA group (p=0.48), but more controls reported pain less than once a week (71% versus 53%) and less reported pain several times per day or all the time (7% versus 27%) compared to the JIA group.

Dysfunction: In total, 136 (51.3%) participants with JIA had at least one clinical sign of orofacial dysfunction, not different from controls (p=0.12) (Table 2). The most frequent clinical findings were TMJ and orofacial pain on palpation in both groups (Table 2). Mean MIO was significantly lower in the JIA group (47.2±7.7 vs. 56.5±6.8 mm, p<0.001). The prevalence of participants with a MIO <-2SD was significantly higher among JIA participants than controls (p<0.001) (Table 2). TMJ pain on palpation was more frequent in the JIA group than in controls (p=0.03,Table 2). However, no inter-group differences were observed for "orofacial pain on palpation" or "asymmetric mouth opening".

Disease status and clinical findings: Inactive disease was found in 162 (61.1%) of the 265 participants with JIA, of whom 34 (12.8%) were in remission on medication, and 99 (37.4%) in remission off medication (21), while 29 (10.9%) had inactive disease without fulfilling the remission criteria. Of the participants with inactive disease or in remission on/off medication, 38/162 (23.5%) reported at least one orofacial symptom, and 70 (43.2%) had at least one clinical sign of dysfunction. In the same group, the frequencies of the reported symptoms were: 38/162 (23.5%) orofacial or jaw pain, 16 (9.9%) morning stiffness in the jaws, 11 (6.8%) limitation when chewing, and 7 (4.3%) locking of the jaw. Further, a reduced MIO was found in 22/162 (13.6%),

TMJ pain on palpation in 37 (22.8%), orofacial pain on palpation in 28 (17.3%), and asymmetric mouth opening in 26 (16.0%).

Radiologic findings: Normal CBCT of both TMJs was observed in 96/245 (39.2%) of participants with JIA (Table 3). Thus, the prevalence of at least one abnormal radiological TMJ appearance was 149/ 245 (60.8%) participants with JIA. Of these, 104/149 (69.8%) had bilateral TMJ deformities. Of 253 joints with CBCT changes, 119 (47.0%) had score 1 (deformity), 24 (9.5%) score 2 (erosion), and 110 (43.5%) score 3 (deformity and erosion). Abnormal condylar findings were most frequent in the RF-negative polyarticular group (76.5%) and least frequent in the ERA category (33.3%), but TMJ deformities were present in all JIA categories (Table 4).

TMJ pain on palpation doubled the odds of having an abnormal TMJ on the CBCT scan (OR 2.1; 95% CI 1.08-4.1), and there was a strong association with MIO < -2SD (OR 7.5; 95% CI 2.7-20.6) and abnormal TMJ on CBCT.

Of the 27 (10.2%) participants having at least one intra-articular TMJ injection during the disease course, all had abnormal condylar findings on CBCT, and 17 (63.0%) had erosions and deformities (data not shown).

Intra-observer reproducibility of the CBCT assessment: On 30 randomly selected CBCT examinations of 60 TMJs assessed twice 6 months apart, intra-observer agreement was found in 53 (88.3%) of the scans. Cohen´s κ=0.83, indicated an almost perfect intra-observer agreement (25).

Association between baseline predictors/clinical characteristics and abnormal radiologic condylar appearance at 17 years of follow-up: From the multivariate logistic regression analysis of the baseline predictors of condylar deformities/erosions, we found a positive association with an active joint count of >4 at baseline and a negative association with the presence of HLA-B27 (Table 5). At the 8-year follow-up, a cumulative joint count of >4 and the ERA category was associated with condylar changes (Table 5). Logistic regression analysis on age at onset and gender did not show any association with condylar deformity.

Treatment with biologics during the disease course and orofacial dysfunctions 17 years after onset were associated with a significantly higher risk of TMJ deformity ($p=0.02$ and $p<0.01$, respectively. The ERA category had a significant lower risk of developing TMJ deformities (Table 5).

Discussion:

This is the first study to report long-term data on temporomandibular symptoms, dysfunctions, and radiological findings in a population-based JIA cohort from the early biologic era compared to controls. The results showed higher prevalence of TMJ pain, TMJ morning stiffness, and chewing limitations in the JIA group. We found a higher prevalence of TMJ pain on palpation and a reduced MIO among the JIA participants; however, the prevalence of orofacial pain on palpation and asymmetric mouth opening was not different from that seen in the control group. The control group's complaints were mild and comparable to what has been reported in TMD unrelated to arthritis (26).

It is difficult to compare our results with previous long-term TMJ-related outcome studies from the pre-biologic era due to differences in study designs, terminologies, and definitions. In a questionnaire-based cohort study of 28 JIA patients, Engstrøm et al (13) documented a higher risk of TMJ pain and dysfunction in JIA patients than in healthy controls 15 years after diagnosis with 7% reporting limitation on chewing and 39% facial or TMJ pain, which is close to our findings. In 2001, Bakke et al (12) conducted a 26-year follow-up study on 42 women with JIA of whom 17% experienced orofacial pain. None of the 21 healthy controls reported orofacial pain. In a more recent cross-sectional 17-year follow-up study by Resnick and colleagues (4), 24% of the 21 JIA patients reported TMJ pain, which is consistent with our findings.

Our study showed no difference in self-reported orofacial muscle pain. Previous studies on TMD have consistently documented that orofacial pain is a common finding in healthy adults. The American OPPERA study (27) enrolled 4,346 adults and demonstrated a 4% annual incidence of painful TMD, and the prevalence of TMJ and/or facial pain was 19%. In comparison, the frequency of TMJ and/or facial pain in our control group was 33%. This difference may be explained by an older mean age in the OPPERA study considering a peak incidence of TMJ/facial pain in the age group 25-34 years (28).

It is not possible to differentiate JIA-associated TMD from other TMD etiologies based on clinical examination. We can only hypothesize that TMD symptoms and dysfunctions reported in the JIA group originate from TMJ involvement.

Few studies on long-term outcome of TMJ dysfunctions have been published, and dissimilarities in terminologies used hamper comparison. Prevalence of reduced MIO was 19-29% in two previous long-term studies (4, 12), which matches our findings. TMJ pain on palpation was demonstrated in

17% (12), which is lower than our prevalence (30%); however, their study was small and the methods used were not the same as ours.

Unexpectedly, we found the same rate of asymmetric mouth opening in the JIA and the control group. No previous long-term studies have reported an asymmetric mouth opening for comparison. Our findings can partly be explained by the high prevalence of bilateral CBCT-verified deformities in the JIA group, albeit such deformities do not necessarily lead to asymmetric mouth opening. Our findings could also suggest that asymmetric mouth opening can normalize over time. It is also well known that in clinical examinations, deflection can be misinterpreted as asymmetric mouth opening, leading to an uncertain measurement of the latter. The JIA participants and the control group were not evaluated by the same orthodontists, which can also influence the results.

A large number of patients experienced continued TMJ symptoms/dysfunctions despite inactive disease/remission indicating a need for continued, standardized orofacial monitoring (17).

CBCT is a well-established method to detect TMJ deformity and hard tissue changes. Recently, Kellenberger et al (29) suggested MRI for monitoring TMJ arthritis and published an additive scoring system to assess the osseous deformities. However, it was not published at the beginning of our study, and CBCT has previously been used for assessment of hard tissue changes (4, 30). In total, about 61% of the JIA participants had at least one condyle with abnormal CBCT findings, and about 70% of these subjects had bilateral changes. Importantly, the presence of radiographic condylar changes does not necessarily imply the presence of dentofacial deformity. The association between radiographic TMJ changes and dentofacial deformity will be established in a future study. Using a different CBCT scoring system, Resnick et al found TMJ abnormalities in 55% of their JIA patients at the age of 26 years, of whom 79% had bilateral changes. We found a slightly higher prevalence of radiographic TMJ changes. However, we have to acknowledge that some of the abnormal findings may not be directly attributable to the JIA disease since abnormal CBCT findings of the TMJ have been described in healthy individuals. Using a similar CBCT scoring system as used here, Stoustrup et al reported that 5/19 (26%) healthy controls had abnormal TMJ appearance (30); and Kellenberger et al (31) showed that anterior disk displacement in non-JIA adolescents most often is associated with osseous TMJ changes, mainly erosions, in non-JIA individuals. For ethical reasons, CBCT examinations of the TMJ were not performed in the healthy control group.

Study heterogeneity and small sample size have compromised previous studies of predictors of TMJ

involvement (32). However, our finding of a lower risk of condylar changes with the presence of HLA-B27 has also been observed in previous studies (2, 33). Likewise, an active joint count of more than four joints as a predictor of TMJ involvement is consistent with the findings in previous, smaller studies (33, 34). The protective effect of the ERA category for developing condylar deformities and/or erosions is a new finding. A high risk of developing condylar changes was associated with a severe disease course, indicated by the use of biologic treatment and a cumulative joint count of more than four. It is highly unlikely that there is a ~~Obviously, a~~ causal relationship between biologic treatment and development of condylar changes do not exist.

The strength of our study is the population-based setting, which qualifies it as a non-selected JIA cohort study. Furthermore, the generalizability of the study gains from the use of the consensus-based recommendations for clinical orofacial examination and the use of contemporary terminology regarding orofacial findings in JIA, which facilitates comparison of our findings with those of future studies. Our study is based on an ethnically homogenous Nordic cohort; still, the distribution of the JIA categories is consistent with other European and North American cohorts (35). However, several limitations must be acknowledged. Of the total cohort, 37% was lost to follow-up. Age at onset was lower in the included group, but we found no differences in gender, disease activity at baseline, and JIA category. Considering the fact that most of the participants are not attending pediatric clinics anymore, the response rate after 17 years was considered acceptable. The CBCT scans applied to evaluate condylar changes has also been used previously (30, 36), but does not discriminate graduation of severity. In addition, no knowledge about the time-related association between the development of the erosions and deformities can be provided. As MRI was not performed, we cannot conclude on TMJ arthritis activity at the last visit; however, this was not the aim of our study.

In conclusion, our findings underline the fact that extensive symptoms and dysfunctions are seen in JIA even 17 years after disease onset, and also in patients registered with inactive disease/remission. Individuals with substantial condylar damage were found in all JIA categories. We suggest including aspects of TMJ involvement in the general clinical decision-making by including orofacial symptom and dysfunction assessment an integrated part of general health assessment in JIA guided by recent consensus-based recommendations (17).

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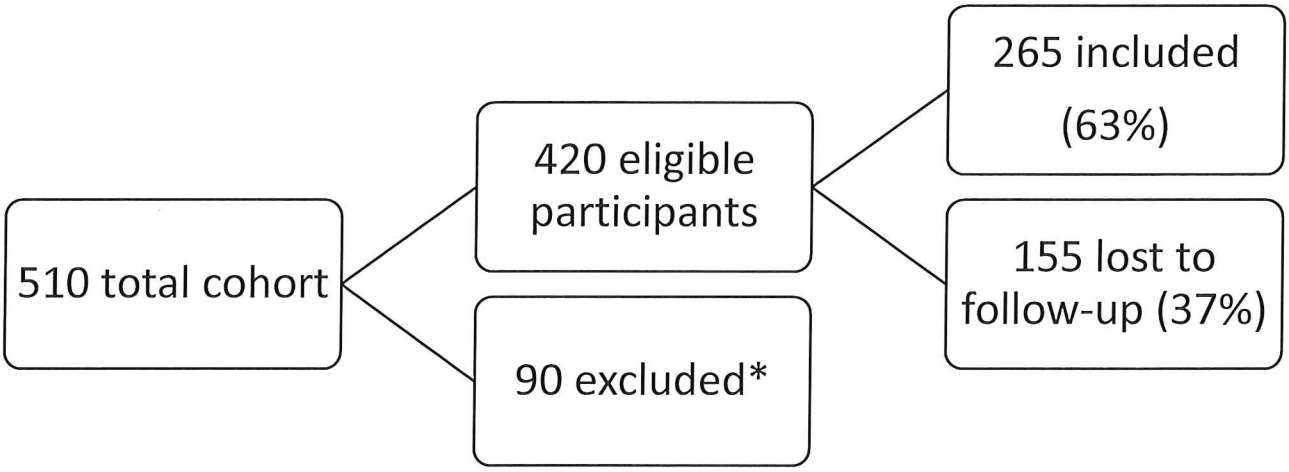
Figure legends

Figure 1 Flow-chart of the study population

* Excluded were six of the seven Swedish centers because of no access to CBCT.

Figure 1 Flow-chart of the study population



* Excluded were 6 of the 7 Swedish centers because of no access to CBCT.

Table 1 Demographic and clinical characteristics by JIA categories in the TMJ study of the Nordic JIA cohort at the 17-year follow-up visit.

	No of pati-ents	Total cohort (n=265)	sJIA (n=11)	Oligo persist (n=56)	Oligo ext (n= 58)	Poly RF- (n=52)	Poly RF+ (n=4)	Psoriatic (n=14)	ERA (n=27)	Undiff (n=43)
Females (%)	265	186 (70.6)	8/11 (72.7)	40/56 (71.4)	44/58 (75.9)	38/52 (73.1)	3/4 (75.0)	10/14 (71.4)	9/27 (33.3)	35/43 (81.4)
Age at onset mean±(SD)	265	6.2 (4.0)	5.0 (2.9)	5.5 (3.5)	4.9 (3.9)	5.9 (4.1)	11.1 (2.6)	6.4 (3.7)	9.0 (3.4)	7.3 (4.0)
Age at last follow up mean±(SD)	265	23.5 (4.2)	23.0 (3.1)	22.7 (3.5)	22.0 (4.0)	22.9 (4.3)	28.7 (2.6)	23.4 (4.2)	26.4 (3.5)	24.8 (4.5)
Disease duration mean±(SD)	265	17.3 (1.0)	17.9 (0.8)	17.3 (1.1)	17.2 (1.1)	17.2 (1.0)	17.6 (1.0)	17.0 (0.9)	17.4 (1.1)	17.3 (0.9)
ANA positive, n (%)	234	80 (34.2)	2 (25.0)	12 (21.4)	20 (34.5)	15 (28.8)	2 (50.0)	5 (35.7)	8 (29.6)	16 (36.4)
HLA-B27 positive, n (%)	264	57 (21.6)	0 (0.0)	6 (10.7)	7 (12.1)	8 (15.4)	1 (25.0)	3 (21.4)	21 (77.8)	11 (25.0)
CRP >10 mg/L, n (%)	257	14 (5.4)	0	1/53 (1.9)	2/55 (3.6)	3/52 (5.8)	0	2/14 (14.3)	4/27 (14.8)	2/42 (4.8)
ESR >20 mm/h, n (%)	218	15 (6.7)	0	2/48 (4.2)	2/48 (4.2)	3/47 (6.4)	0	3/14 (21.4)	2/22 (9.1)	3/33 (9.1)
PatPain VAS Median (IQR)*	260	1.0 (0-3.5)	0 (0-2.0)	0 (0-2.0)	1.0 (0-4.0)	1.0 (0-4.0)	5.0 (2.0-6.5)	1.5 (0-3.0)	1.0 (0.5-3.5)	2.0 (0.5-4.8)
PatGA VAS median (IQR)*	260	1.0 (0-3.0)	0 (0-1.0)	0 (0-1.0)	1.0 (0-2.5)	0.8 (0-2.8)	4.0 (1.3-7.8)	1.0 (0-2.0)	2.0 (1.0-4.5)	2.0 (0-4.5)
PhysGA VAS median (IQR)	265	0 (0-1.0)	0 (0-0.5)	0 (0-0)	0 (0-1.5)	0 (0-0.8)	1.0 (0-2.5)	0 (0-1.0)	1.0 (0-2.5)	0 (0-2.0)
JADAS 71 ≤1 n (%)	244	97 (39.8)	8 (80.0)	31 (63.3)	19 (36.5)	21 (42.0)	1 (25.0)	5 (38.5)	3 (11.5)	9 (22.5)

Values: Age at onset, age at last follow-up and disease duration: years, CRP =mg/L,ESR =mm/h, No = number. IQR =1st-3rd inter quartile range, Pat Pain VAS =patient´s intensity of pain on a 21-numbered circle visual analog scale (0-100). Pat GA VAS =the patient´s global assessment of the overall wellbeing on a 21-numbered circle visual analog scale. PhysGA VAS =the physician´s global assessment of disease activity on a 21-numbered circle visual analog scale. PhysGA is reported if a follow-up visit was performed. sJIA = systemic JIA, Oligo persist =oligo persistent JIA, oligo ext =oligo extended JIA, Poly RF- =polyarticular rheumatoid factor negative JIA, Poly RF+ =polyarticular rheumatoid factor positive JIA, ERA =enthesitis-related arthritis, Undiff =undifferentiated JIA. * =Statistical significance ($p \leq 0.05$) among the JIA categories.

Table 2 Prevalence of orofacial symptoms and dysfunction in the JIA group (n=265) and the control group (n=200)

	JIA group	Control group	Measures (95% CI)	p
Orofacial symptoms				
No symptoms	178 (67.2)	148 (74.0)		
≥ one symptom	87 (32.8)	52 (26.0)	OR[4]=1.4 (0.91-2.14)	0.11
TMJ pain	65 (24.5)	14 (7.0)	OR=4.32 (2.30-8.60)	<0.001*
TMJ morning stiffness	42 (15.8)	9 (4.5)	OR=4.02 (1.86-9.60)	<0.001*
Orofacial muscle pain	74 (27.9)	44 (22.0)	OR=1.07 (0.70-1.66)	0.74
Limitation on chewing	35 (13.2)	9 (4.5)	OR=3.24 (1.48-7.85)	0.001*
Locking of the jaw	20 (7.5)	17 (8.5)	OR=0.88 (0.42-1.84)	0.71
Orofacial pain intensity				
VAS pain>0; median (1st-3rd quartile)	25 (5;85)	19(6;60)	z[5]=0.63	0.53
Orofacial pain frequency				
Pain frequency>0; median (1st-3rd quartile)	1 (1;4)[1]	1 (1;3)[1]	z=2.61	<0.01*
Orofacial pain profile	30 (5;260)	20 (6;120)	z=1.53	0.13
Pain index>0[2]; median (1st-3rd quartile)				
Number of symptoms				
Per subject; median (1st-3rd quartile)	2 (1;5)	1 (1;3)	z=2.26	0.02*
Orofacial dysfunctions				
No dysfunctions	129 (48.7)	112 (56.0)		
≥ one dysfunction	136 (51.3)	88 (44.0)	OR=1.34 (0.91-1.97)	0.12
Reduced MIO[3]	51 (19.2)	3 (1.5)	OR=15.72 (4.94-79.69)	<0.001*
TMJ pain on palpation	79 (29.9)	42 (21.0)	OR=0.62 (0.40-0.95)	0.03*
Orofacial pain on palpation	67 (25.3)	50 (25.0)	OR=0.99 (0.64-1.50)	0.94
Asymmetric mouth opening	29 (10.9)	32 (16.0)	OR=0.65 (0.36-1.15)	0.11
Number of dysfunctions				
Per subject; median (1st-3rd quartile)	1(0;2)	0 (0;2)	z=2.34	0.02 *

Values indicate the number and percentage of patients. [1]Pain frequency =1 indicates not every week; 2 =several times a week; 3 =several times a day; 4 =all the time. [2]Pain index =pain frequency x pain intensity [3]MIO =maximal incisal opening <-2SD below mean of normative values (<40.9mm, ref (27)), [4]OR =odds ratio, [5]z =z score, *= Statistical significance ($p \leq 0.05$).

Table 3 CBCT appearance of the condylar head of the left and right temporomandibular joints in the Nordic JIA cohort at the 17-year follow-up visit (n=245).

	Left TMJ				
Right TMJ	Normal	Deformity	Erosion	Deformity and erosion	**Total n**
Normal	96 (39.2)	11(4.5)	6 (2.4)	4 (1.6)	**117 (47.3)**
Deformity	12 (4.9)	29 (11.8)	2 (0.8)	17 (6.9)	**60 (24.5)**
Erosion	4 (1.6)	3 (1.2)	3 (1.2)	1 (0.4)	**11 (4.5)**
Deformity/erosion	8 (3.3)	16 (6.5)	2 (0.8)	31 (12.7)	**58 (23.7)**
Total n	**120(49.0)**	**59(24.1)**	**13(5.3)**	**53(21.6)**	**245**

Values indicate the number and percentage of joints. Each TMJ was scored as normal/abnormal and the abnormal joints were subsequently scored with deformity/erosion or with a combination of the two possibilities. The scoring system does not refer to a scale with gradual progression.
Normal =normal condylar shape with smooth and intact outline/surface.
Deformation =deformity of the condyle, with marked flattening or other changes in shape with smooth and intact outline/surface. Erosion =erosion of the condyle, with disruption of outline or uneven surface due to cysts or erosion. Deformity and erosion =deformities plus erosive changes.

Table 4 Orofacial symptoms, dysfunctions and temporomandibular radiological appearance according to juvenile idiopathic arthritis (JIA) category (n=245)

No patients	Total cohort (n=245)	sJIA (n=10)	Oligo persist (n=52)	Oligo ext (n= 53)	Poly RF- (n=51)	Poly RF+ (n=4)	Psoriatic (n=13)	ERA (n=24)	Undiff (n=38)
TMJ-reported pain	65 (26.5)	2 (20.0)	8 (15.4)	14 (26.4)	12 (23.5)	1 (25.0)	4 (30.8)	10 (41.7)	14 (36.8)
TMJ morning stiffness	42 (17.1)	1 (10.0)	8 (15.4)	6 (11.3)	12 (23.5)	0 (0.0)	2 (15.4)	4 (16.7)	9 (23.7)
Chewing limitations	35 (14.3)	0 (0.0)	5 (9.6)	6 (11.3)	8 (15.7)	1 (25.0)	3 (23.1)	4 (16.7)	8 (21.1)
MIO<2 SD	51 (20.8)	0 (0.0)	5 (9.6)	14 (26.4)	13 (25.5)	1 (25.0)	2 (15.4)	5 (20.8)	11 (28.9)
TMJ pain on palpation	59 (24.1)	1 (10.0)	8 (15.4)	13 (24.5)	12 (23.5)	1 (25.0)	4 (30.8)	4 (16.7)	16 (42.1)
Normal bilateral radiological appearance	96 (39.2)	5 (50.0)	26 (50.0)	17 (32.1)	12 (23.5)	1 (25.0)	5 (41.7)	16 (66.7)	14 (36.8)
Radiological deformities and/or erosions	149 (60.8)	5 (50.0)	26 (50.0)	36 (67.9)	39 (76.5)	3 (75.0)	8 (61.5)	8 (33.3)	24 (63.2)

Values indicate the number and percentage of joints. sJIA = systemic JIA, Oligo persist =oligo persistent JIA, Oligo ext= oligo extended JIA, Poly RF- =polyarticular rheumatoid factor negative JIA, Poly RF+ = polyarticular rheumatoid factor positive JIA, ERA= enthesitis-related arthritis, Undiff = undifferentiated JIA.

Table 5 Associations between clinical characteristics at baseline, 8-year follow-up or at any time during the disease course and condylar deformities/erosions at the 17-year follow-up.

	Multivariate odds ratio (95% CI)	P-value
PREDICTORS EARLY IN DISEASE COURSE n=211		
Age at onset < 6 years	1.01 (0.52-1.97)	0.97
Female gender	1.08 (0.54-2.17)	0.84
Active joint count at baseline visit > 4 joints	2.14 (1.11-4.18)	0.02*
ESR > 20 at baseline	1.88 (0.95-3.70)	0.07
HLA-B27 positive	0.44 (0.20-0.98)	0.04*
Uveitis at baseline	1.54 (0.48-4.99)	0.47
PREDICTORS AT 8 YEARS OF FOLLOW-UP n=234		
Age at onset < 6 years	1.31 (0.73-2.36)	0.11
Female gender	1.31 (0.60-2.13)	0.36
Cumulative active joint count >4	2.07 (1.05-4.09)	0.03*
JADI-A >0	1.66 (0.94-2.93)	0.08
MTX	1.22 (0.62-2.41)	0.62
Biologics	2.10 (0.75-5.86)	0.16
ERA	0.35 (0.12-0.97)	0.04*
ASSOCIATIONS DURING THE DISEASE COURSE** n=244		
Age at onset < 6 years	1.18 (0.65-2.14)	0.47
Female gender	0.78 (0.40-1.53)	0.47
DMARDs during disease course	1.18 (0.59-2.36)	0.60
Biologics during disease course	2.37 (1.18-4.74)	0.02*
Cumulative active joints >4 at 17-year FU	1.94 (0.99-3.80)	0.06
Orofacial dysfunction at 17-year FU	3.13 (1.74-5.62)	<0.01*
ERA	0.17 (0.06-0.50)	0.01*

ESR= erythrocyte sedimentation rate; HLA-B27= Human leukocyte antigen B27; JADI-A= Juvenile Arthritis Damage Index- Articular; MTX= methotrexate; DMARDs= disease modifying anti-rheumatic drugs; ERA=enthesitis-related arthritis. *= Statistical significance ($p \leq 0.05$),** Associations between clinical characteristics at any time of the disease course and condylar deformities/erosions.