

Risk Factors for Temporomandibular Joint Arthritis in Children with Juvenile Idiopathic Arthritis

MATTHEW L. STOLL, TYLER SHARPE, TIMOTHY BEUKELMAN, JENNIFER GOOD, DANIEL YOUNG, and RANDY Q. CRON

ABSTRACT. Objective. To determine the prevalence and features of temporomandibular joint (TMJ) arthritis by magnetic resonance imaging (MRI) among children with juvenile idiopathic arthritis (JIA), and to identify risk factors for TMJ arthritis.

Methods. A retrospective chart review was performed on 187 patients with JIA who underwent a TMJ MRI at Children's Hospital of Alabama between September 2007 and June 2010. Demographic and clinical information was abstracted from the charts. Univariate and multivariate analyses were performed to identify risk factors for TMJ arthritis identified by MRI.

Results. MRI evidence of TMJ arthritis was detected in 43% of patients, with no significant difference among JIA categories. The number of joints with active arthritis (exclusive of the TMJ) and the use of systemic immunomodulatory therapies were not associated with TMJ arthritis. Multivariable analysis revealed a strong association between mouth-opening deviation and TMJ arthritis (OR 6.21, 95% CI 2.87–13.4). A smaller maximal incisal opening and shorter disease duration were also associated with an increased risk of TMJ arthritis.

Conclusion. TMJ arthritis was identified in a substantial proportion of children with JIA (43%) and affects all JIA categories. TMJ arthritis was present in some patients despite limited or otherwise quiescent disease and in the presence of concurrent systemic immunomodulatory therapy. Routine evaluation for TMJ arthritis by MRI is warranted for all children with JIA. (J Rheumatol First Release May 15 2012; doi:10.3899/jrheum.111441)

Key Indexing Terms:

TEMPOROMANDIBULAR JOINT
MAGNETIC RESONANCE IMAGING

JUVENILE IDIOPATHIC ARTHRITIS
RISK FACTORS

Juvenile idiopathic arthritis (JIA) is a chronic rheumatologic disease of childhood characterized by inflammatory synovitis that affects about 1 in 1000 children worldwide¹. One of the most clinically underrecognized arthritic joints is the temporomandibular joint (TMJ). While multiple case series of children with arthritis did not report on TMJ arthritis^{2,3,4}, studies that have prospectively evaluated for TMJ involvement with various imaging modalities have placed the prevalence of TMJ arthritis in children with JIA at around 50%^{5,6,7,8,9,10,11,12}. In several of these studies, medical history

and physical examination evidence suggestive of TMJ arthritis such as popping, pain, localized tenderness, and jaw asymmetry were shown to be insensitive for diagnosis^{5,9,11}; for example, Weiss, *et al* showed that 81% of JIA patients with active TMJ arthritis were asymptomatic¹¹. When untreated, TMJ arthritis can result in growth disturbances, pain, and longterm complications, prompting recommendations for routine evaluation of patients with JIA¹³. TMJ investigation by magnetic resonance imaging (MRI) with contrast is both highly sensitive^{5,11} and specific¹⁴ for the identification of TMJ arthritis among children with JIA.

The limitations of MRI are the availability and the expense, as well as the risks of sedation in some children. Moreover, addition of contrast adds extra expense to the study, requires intravenous (IV) access, and raises the risk of rare complications. Only 1 small study involving 15 children with JIA has evaluated whether contrast is dispensable in this setting, finding that precontrast fluid-sensitive sequences were insensitive for the detection of TMJ arthritis¹⁵. Additionally, it remains unknown whether screening should focus on high-risk children, as suggested by Cannizzaro, *et al*¹⁶. Studies have shown that the risk of TMJ arthritis varies by age and by JIA subtype, with younger children and those with polyarticular JIA generally found to be at higher risk than those with enthesitis-related arthritis in some but not all stud-

From the Department of Pediatrics and the Department of Radiology, University of Alabama at Birmingham, Birmingham, Alabama; and the Carolinas Oral and Facial Surgery Center, Wilmington, North Carolina, USA.

Dr. Cron was supported in part by the Arthritis Foundation, Alabama Chapter Endowed Chair in Pediatric Rheumatology.

M.L. Stoll, MD, PhD, MSCS, Department of Pediatrics; T. Sharpe, BS, Medical Student; T. Beukelman, MD, MSCE, Department of Pediatrics, University of Alabama at Birmingham; J. Good, DDS, MD, Former Resident, Department of Oral and Maxillofacial Surgery, University of Alabama at Birmingham, currently in private practice, Carolinas Oral and Facial Surgery Center; D. Young, MD, Department of Radiology; R.Q. Cron, MD, PhD, Department of Pediatrics, University of Alabama at Birmingham.

Address correspondence to Dr. M. Stoll, 210 Children's Park Place North, Suite 210, 1601 4th Ave. South, Birmingham, AB 35233-1711, USA.

E-mail: mstoll@uab.edu

Accepted for publication February 23, 2012.

ies^{7,8,9,10,16,17,18}. One recent study demonstrated an association with the overall severity of the arthritis¹⁶, but that study did not involve systematic screening for TMJ arthritis among children with JIA. To our knowledge, no other studies have evaluated whether the extent of synovitis exclusive of the TMJ is a risk factor, nor is it clear whether the use of biologics is protective.

We reviewed the charts of 187 children who underwent MRI of the TMJ, in which 185 of the scans were contrast-enhanced. We reviewed in detail the imaging findings resulting in the diagnosis of TMJ arthritis, and we evaluated for predictors of TMJ arthritis.

MATERIALS AND METHODS

Patients. This was a retrospective study conducted at a single center (Children's Hospital of Alabama, Birmingham, USA). We identified all children with JIA who underwent MRI of the TMJ between September 2007 and June 2010 by performing a search for patients meeting International Classification of Diseases-9th edition codes associated with JIA, limited to patients evaluated by a pediatric rheumatologist. Since the inception of the pediatric rheumatology center at the University of Alabama at Birmingham (UAB) in 2007, it has become our practice to routinely evaluate JIA patients with contrast-enhanced TMJ MRI regardless of symptoms, albeit with substantial variation among attending physicians; all of the studies are conducted at this hospital. Before the opening of the pediatric rheumatology center at UAB, children with JIA were managed here by an immunologist with experience in the diagnosis and treatment of this condition, including use of immunosuppressive therapies, although MRI of the TMJ were rarely obtained. Therefore, the year of diagnosis of the children in our study ranges from 1991 to 2010; the MRI were performed only between 2007 and 2010. Inclusion criteria were diagnosis of JIA according to the International League of Associations for Rheumatology (ILAR) criteria¹⁹ and completion of TMJ MRI. Exclusion criteria were any alternative diagnosis besides JIA. Institutional review board approval was obtained.

Data collection. The electronic medical charts were abstracted for relevant clinical, demographic, and imaging data. The date of the initial TMJ MRI was determined, and the clinic note from the immediately preceding visit was reviewed. Maximal incisal opening (MIO) was routinely measured using the Therabite Measuring Scale (Atos Medical, Hörby, Sweden); we did not use a standardized protocol to measure MIO. We did not take into account the incisal vertical overbite. For the purposes of our study, MIO was considered low if under 37.8 mm for children under age 8 years and under 40.6 mm for children age 8 years or older, because those values represent 2 SD below the mean for girls aged 7 and 10 years in the study by Ingervall²⁰. Presence versus absence of lateral deviation of the jaw at rest or with opening was documented at each visit; this was based solely on physical examination findings, and did not take into account other potential causative factors (e.g., posterior cross-bite.) The number of joints with active arthritis was determined by the attending pediatric rheumatologist; a joint count of zero in the absence of enthesitis or dactylitis was considered inactive arthritis. Results of routine laboratory studies and basic demographic information were documented, as well as total joint count exclusive of the TMJ, TMJ physical examination findings, and use of nonbiologic or biologic disease-modifying antirheumatic drug (DMARD) therapy.

Interpretation of TMJ MRI. The studies were performed as described²¹. Briefly, using a TMJ-specific head coil with the patient's mouth closed, we obtained 2–3 mm thick axial and coronal T1-weighted and fat-saturated (FS) T2-weighted images, followed by administration of gadolinium contrast and additional T1-weighted FS axial and coronal images. A normal TMJ is shown in Figure 1. Active arthritis was defined by the presence of synovial fluid or synovial enhancement (Figure 2), while chronic changes were defined by the

presence of erosive changes, condylar flattening, or disc displacement (Figure 3), although disc displacement was not observed in any patients in our study. Information about active or chronic arthritis was based upon the official radiology report. Eight different radiologists were involved in the interpretation of the studies.

Statistical analyses. Proportional data are reported as percentiles; continuous data as means \pm SEM and ranges. For the univariate analysis comparing children with and those without TMJ arthritis, differences in proportional data were evaluated with the chi-square or Fisher's exact test, and differences in continuous data with Student's t test (2 groups) or ANOVA (3 groups.) To evaluate the ability of MIO to discriminate between patients with and without subsequent abnormal MRI findings, we performed a receiver-operating characteristic (ROC) analysis. The area under the curve (AUC) in the ROC analysis represents the probability that for a randomly selected pair of patients with and without TMJ arthritis, the patient with TMJ arthritis had a smaller MIO. An AUC of 0.50 is equivalent to chance alone. To further evaluate predictors of abnormal MRI, we performed logistic regression analysis. Clinical predictors were presence versus absence of jaw asymmetry, MIO as a continuous variable, age at diagnosis (years), disease duration (years), joint count as a continuous variable, and ILAR subtype. Significant predictors in univariate analyses ($p < 0.1$) were further analyzed using stepwise backward selection multiple variable regression models with removal of covariates at the level of $p > 0.05$. Analyses were performed with Stata (version 10) and Predictive Analytics Software (version 17).

RESULTS

Patient population. We identified 382 subjects with JIA, of whom 187 (49%) underwent MRI of the TMJ. Of the 187, 2 refused IV contrast but were still included in our study. The clinical and demographic information of all 187 subjects is summarized in Table 1. At the time of the MRI, half the patients were taking either tumor necrosis factor (TNF) inhibitors or anakinra, and nearly 60% were taking methotrexate. A majority (67%) of patients was taking at least 1 nonbiologic or biologic DMARD. Overall, 43% were diagnosed with acute or chronic TMJ arthritis, based upon the MRI. There were no significant differences by JIA category; excluding the children with undifferentiated JIA ($n = 4$) and rheumatoid factor (RF)-positive polyarticular JIA ($n = 3$), incidences ranged from a low of 33% in children with systemic-onset arthritis and a high of 49% in children with RF-polyarticular JIA (Figure 4).

MRI findings of TMJ arthritis. MRI features of TMJ arthritis are shown in Table 2. For this analysis, we excluded the 2 subjects who refused IV contrast and used the individual TMJ joint as the unit of analysis, so there was a total of 370 TMJ studied. Of those, 135 (36%) showed evidence of active synovitis, either synovial fluid or synovial enhancement. Of those 135, only 14% showed synovial fluid alone, without abnormal enhancement, while nearly two-thirds showed abnormal enhancement without synovial fluid, and the remainder showed both. Thus, two-thirds of the TMJ with active synovitis would have been read as normal regarding active findings in the absence of IV contrast. Additionally, findings of chronic arthritis were rare in this group and typically accompanied findings of active arthritis. Changing the unit of analysis to the individual patient, 43% had evidence of active or chronic arthritis in at least 1 of their TMJ, with the vast majority of

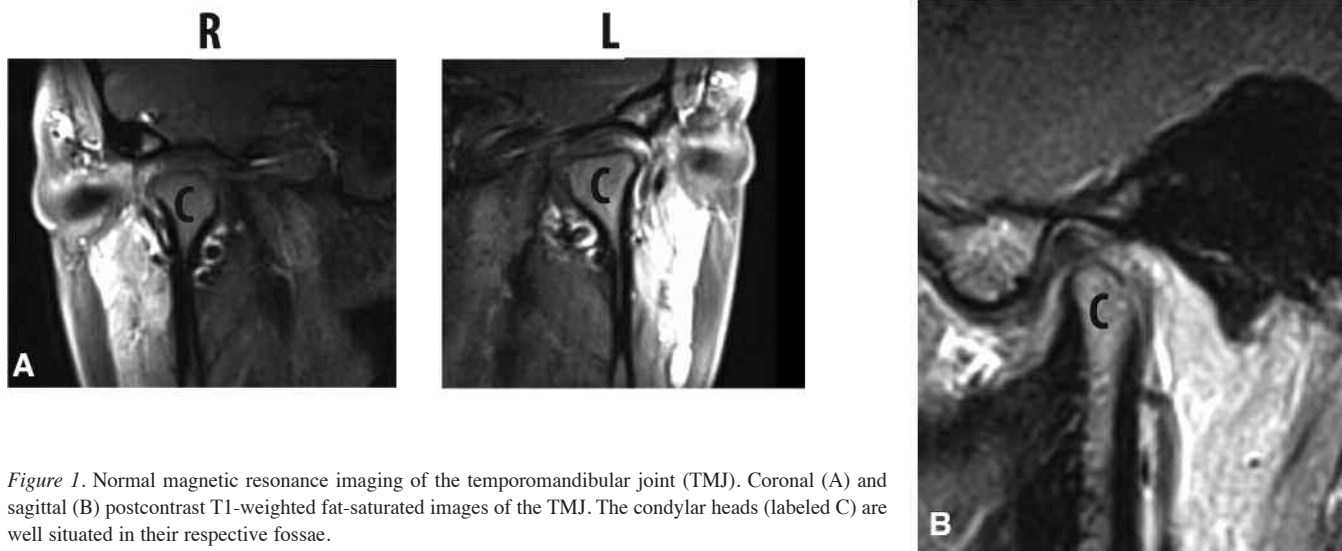


Figure 1. Normal magnetic resonance imaging of the temporomandibular joint (TMJ). Coronal (A) and sagittal (B) postcontrast T1-weighted fat-saturated images of the TMJ. The condylar heads (labeled C) are well situated in their respective fossae.



Figure 2. Active temporomandibular joint synovitis. Sagittal T2-weighted fat-saturated (FS) precontrast (A) and T1-weighted postcontrast FS (B) images show synovial fluid (A, arrows) and enhancement (B, large arrows). Erosive changes at the condylar head are also evident on B (small arrows).

those showing active arthritis with or without chronic changes. Arthritis was unilateral in 26% of cases and bilateral in 74%.

Because joint fluid in the absence of enhancement is not as specific a finding for inflammation, we evaluated whether such patients had other signs of TMJ arthritis. Seventeen TMJ representing 13 unique patients had a sole acute finding of joint effusion; of those, 3 had enhancement of the contralateral

TMJ, 8 had jaw asymmetry on examination, 1 had visible micrognathia, 3 had MIO below our cutoff for normal, and 1 had findings of chronic arthritis. Altogether, 9/13 had 1 or more abnormalities suggestive of TMJ arthritis in addition to the joint fluid on MRI.

MIO. Because MIO is easily quantifiable, and decreased oral opening appears to be predictive of TMJ arthritis⁵, we evalu-

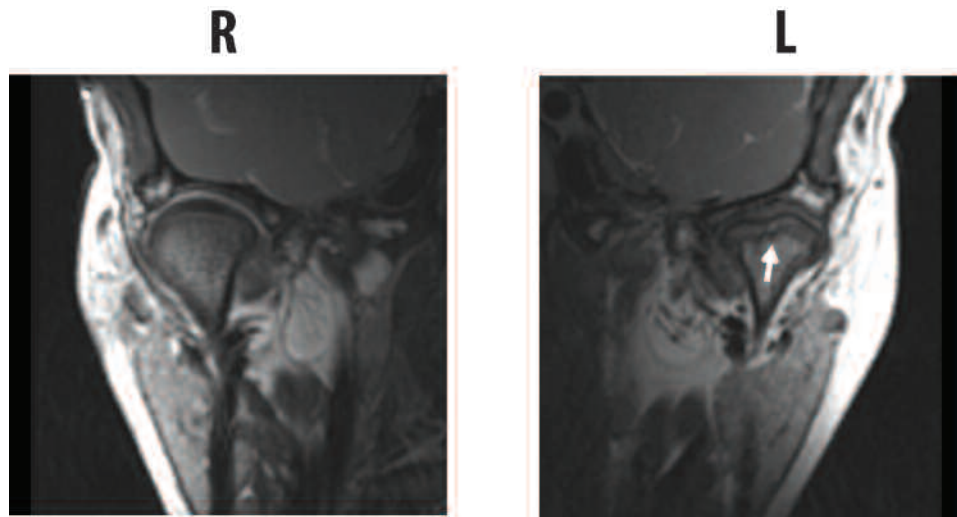


Figure 3. Destructive changes of the temporomandibular joint (TMJ). Coronal T1-weighted image of the TMJ shows flattening and erosive changes of the left condylar head (arrow); the right TMJ is normal.

ated whether MIO measurements can predict the risk of TMJ arthritis by comparing MRI results with MIO measurements obtained at the previous visit, which took place at a median of 1 month (range 0–6) prior to the MRI. MIO was obtained for 180/187 (96%) subjects. As expected, smaller MIO was associated with abnormal MRI findings (Table 1). Nevertheless, MIO measurements discriminated poorly between normal and abnormal MRI findings in an ROC analysis. The AUC for the ROC was 0.63, indicating that for a randomly selected pair of patients with normal and abnormal MRI examinations, the patient with the abnormal MRI will have a smaller MIO only 63% of the time (Figure 5). As a practical example, using a cut-off of 40 mm (or below) to obtain an MRI would result in a sensitivity of 32% and specificity of 75% to detect TMJ arthritis. To achieve 95% sensitivity for abnormal MRI findings would require obtaining MRI on everyone with MIO \leq 52 mm, which would also include 79% of normal subjects. Adjusting for patient age increased the AUC to 0.65 (data not shown).

Predictors of TMJ arthritis. Potential predictors of TMJ arthritis, including MIO, are shown in Table 1. The presence of mouth opening deviation on examination was highly predictive, with this finding noted in 49% of patients with arthritis, compared to 12% of patients without ($p < 0.001$). Because MIO increases with age²², we grouped patients according to age brackets of 0 to $<$ 8 years and 8 or older at the time of the MRI. Within each age bracket, children with normal TMJ had significantly higher MIO compared to those with arthritis ($p < 0.01$), with differences of 4.2 mm at both age brackets. The presence of any abnormality (mouth opening deviation or low MIO for age) was observed in 63% of patients with TMJ arthritis, compared to 31% of those without ($p < 0.001$). In contrast to indicators of TMJ arthritis, the presence and extent of arthritis exclusive of the TMJ was not predictive of TMJ arthritis. Further, TMJ arthritis often occurred in the context of inactive arthritis elsewhere; 36/73 (49%) of the patients without any

other active arthritis on examination had TMJ synovitis. In addition, there was no obvious association between use of DMARD and presence of TMJ arthritis, and 62% of the patients with TMJ arthritis were receiving at least 1 conventional or biologic DMARD. We did find that children with TMJ synovitis were older at diagnosis of JIA compared to those without (7.6 vs 6.0, $p = 0.006$), and had a shorter disease duration (1.6 vs 3.1 years, $p = 0.003$). We did not find an association between autoantibody (antinuclear antibody, RF, or citrullinated protein antibodies) or HLA-B27 status and TMJ arthritis.

Table 3 shows the results of the logistic regression analysis. Variables significant in the univariate analysis (left column) included mouth opening deviation, MIO, age at diagnosis, and disease duration; however, in the multivariable analysis (right column), only jaw deviation, MIO, and disease duration remained significant. As expected based upon the univariate analysis, the presence of mouth opening deviation was a positive risk factor for TMJ arthritis (OR 6.21, 95% CI 2.87–13.4), while MIO and disease duration were both protective (OR 0.94, 95% CI 0.90–0.99 and 0.87, 95% CI 0.78–0.97, respectively). That is, the higher the MIO and the longer the disease duration, the less TMJ arthritis was observed.

DISCUSSION

We evaluated 187 children with JIA followed at a single center for arthritis of the TMJ by MRI. Although it is our current typical practice to evaluate all patients early in the disease course, many of them had longstanding arthritis at the time of the study, reflecting the change in the management style with the opening of our pediatric rheumatology center in 2007. In addition, during the study period, only about half our patients were imaged, perhaps because of variations in practice patterns among the attending pediatric rheumatologists, engendering a possible source of bias. Overall, we identified evidence of TMJ arthritis in 43% of the cohort.

Table 1. Patient population. Statistically significant differences (p < 0.05) are depicted in bold type.

Feature	Entire Group, n = 187	TMJ Arthritis-negative, n = 106	TMJ Arthritis-positive, n = 81	p
Demographics				
Age at diagnosis, yrs; mean, SEM, range	6.7, 0.31, 1–15	6.0, 0.40, 1–15	7.6, 0.46, 1–15	0.006
Disease duration*, yrs; mean, SEM, range	2.5, 0.3, 0–17	3.1, 0.38, 0–14	1.6, 0.31, 0–17	0.005
Newly diagnosed (< 3 mo)	56, 30	28, 26	28, 35	0.228
Age at study, yrs; mean, SEM, range	9.1, 0.34, 1.7–21	9.1, 0.50, 1.7–2.1	9.2, 0.45, 2–18	0.794
Female, n, %	116, 62	63, 59	53, 65	0.402
Race, n (%)				0.981
White	162, 87	92, 87	70, 86	
African-American	23, 12	13, 12	10, 12	
Other	2, 1.0	1, 0.9	1, 1.2	
JIA subtype, n, %				0.251
Oligoarticular JIA	56, 30	31, 29	25, 31	
RF- polyarticular JIA	35, 19	18, 17	17, 21	
RF+ polyarticular JIA	3, 1.6	1, 0.9	2, 2.5	
Psoriatic JIA	37, 20	23, 22	14, 17	
Enthesitis-related arthritis	40, 21	25, 24	15, 18	
Systemic-onset JIA	12, 6.4	8, 7.5	4, 4.9	
Undifferentiated	4, 2.1	0	4, 4.9	
Laboratory studies				
Positive ANA	39/164, 24	23/92, 25	16/72, 22	0.678
Positive RF	6/118, 5.1	3/63, 4.8	3/55, 5.5	1.000
ACPA	4/50, 8.0	1/23, 4.3	3/27, 11	0.617
Positive HLA-B27	17/104, 16	11/54, 20	6/50, 12	0.249
Medications, n, %				
NSAID	125, 67	77, 73	48, 59	0.054
MTX	110, 59	68, 64	42, 52	0.090
Sulfasalazine	2, 1.1	0	2, 2.5	0.186
Leflunomide	2, 1.1	2, 1.9	0	0.506
Any anti-TNF	84, 45	50, 47	34, 42	0.479
Anakinra	9, 4.8	5, 4.7	4, 4.9	1.000
Combination DMARD	80, 43	49, 46	31, 38	0.276
MTX and anti-TNF	70, 37	42, 40	28, 35	0.479
MTX and anakinra	8, 4.3	5, 4.7	3, 3.7	1.000
Any DMARD	126, 67	76, 72	50, 62	0.150
Oral corticosteroids	32, 17	19, 18	13, 16	
Physical examination, n, %				
Mouth opening deviation	53, 28	13, 12	40, 49	< 0.001
MIO, mm; mean, SEM, range				
Age 0–7.9	41.3, 0.74, 23–54	43.1, 0.86, 34–54	38.9, 1.2, 23–49	0.004
Age 8+	45.8, 0.77, 30–65	47.8, 1.1, 31–65	43.6, 0.97, 30–62	0.005
Low MIO for age**	48, 27	21/99, 21	27/81, 33	0.067
Mouth opening deviation or low MIO	81, 43	30, 28	51, 63	< 0.001
Overall joint count†; mean, SEM, range	2.2, 0.32, 0–34	2.0, 0.31, 0–16	2.6, 0.61, 0–34	0.358
Joint count 0†	73, 39	37, 35	36, 44	0.185
Joint count 1 or lower†	115, 62	63, 59	52, 64	0.507
Joint count 4 or lower†	165, 88	94, 89	71, 88	0.829

* Elapsed time between diagnosis of JIA and the initial MRI. ** Defined as < 2 SD below norm for age²⁰. † Total joint count is exclusive of the TMJ itself. TMJ: temporomandibular joint; ANA: antinuclear antibody; ACPA: anticitrullinated protein antibodies; DMARD: disease-modifying antirheumatic drug (includes methotrexate, sulfasalazine, leflunomide, and biologic); JIA: juvenile idiopathic arthritis; MIO: maximal incisal opening; MTX: methotrexate; NSAID: nonsteroidal antiinflammatory drugs; RF: rheumatoid factor; TNF: tumor necrosis factor.

Several important conclusions can be drawn from our study. The first is that our data support previous findings that contrast-enhanced MRI is evidently superior to computed tomography and orthopantomogram in the evaluation of TMJ synovitis in children with JIA, in that it can detect early inflammatory changes that would otherwise be missed²³. Even noncontrast MRI would be insufficient, as two-thirds of

the abnormal studies lacked any evidence of excessive synovial fluid. In this respect, our findings corroborate those of a previous smaller study¹⁵.

Second, our study confirms that the physical examination based solely on MIO measurement and assessment of mouth opening deviation is not sensitive for diagnosis, confirming previous reports^{5,9,11}. Although mouth opening deviation was

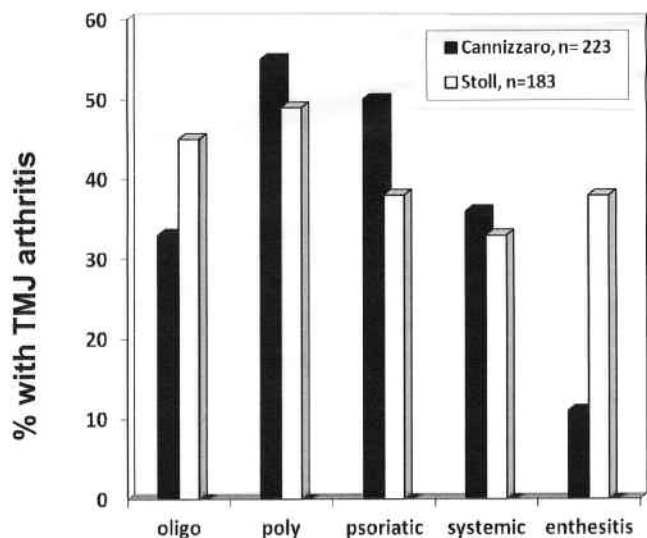


Figure 4. Percentage of patients with abnormal MRI of the TMJ, by JIA subtype. Current results are compared with those published by Cannizzaro, *et al*¹⁶. Oligo: oligoarticular JIA; poly: polyarticular JIA.

significantly more likely in children with compared to those without TMJ arthritis, 51% of cases with synovitis did not have this abnormality on examination. We did see lower MIO among children with compared to those without TMJ synovitis; that these differences were likely to be of clinical importance is emphasized by our studies and those of other groups showing increased MIO following intraarticular corticosteroid injection of the TMJ^{24,25}. However, since even those patients with abnormal MRI generally had MIO within the published age-matched normal ranges²⁰, reliance on an abnormal MIO as a screening tool would overlook the majority of cases, as illustrated by our ROC analysis.

Finally, we showed that TMJ arthritis can occur even in otherwise quiescent disease. Of the patients without active arthritis or enthesitis on examination, 36/73 (49%) had TMJ synovitis. Moreover, many of these patients were under treatment with immunosuppressive therapy: 62% of the patients with TMJ arthritis were under treatment with at least 1 conventional or biologic DMARD, often in combination. Findings of TMJ arthritis in otherwise quiescent disease raises the possibility that TMJ synovitis may be somewhat refractory to one or more systemic immunosuppressive therapies, analogous to the failure of conventional DMARD to treat sacroiliitis²⁶. Alternatively, it is possible that some of these subjects had subclinical arthritis in other joints that might have been identified with use of MRI²⁷.

An interesting finding was that patients with TMJ synovitis were, on average, imaged earlier in the disease course as compared to those with normal studies. The heterogeneity in time to perform the initial MRI may have reflected variation among the attending physicians, as well as the change in practice pattern upon the establishment of a formal pediatric rheumatology program, with some of our inherited patients having been diagnosed many years prior to our initial encounter with them. It may also have been the case that those patients perceived by their attending physicians to be at higher risk based upon history or examination were more likely to be imaged promptly. It is also possible that this observation suggests that systemic immunosuppressive therapy may be of benefit for TMJ arthritis; that is, some of the patients with normal studies may have had abnormal MRI had they been imaged earlier in their course. Although our data may suggest that the TMJ lags behind other joints with respect to response to immunosuppressive therapy, there is undoubtedly heterogeneity of response, at the level of the patient as well as indi-

Table 2. MRI findings of TMJ arthritis. Data are limited to patients with contrast-enhanced MRI (n = 185).

Finding	n	Percentage of Total	Percentage of Abnormal
By individual TMJ	370	NA	NA
Active or chronic arthritis	142	38	NA
Active arthritis, any	135	36	95
Synovial fluid alone	19	5.1	14
Enhancement alone	85	23	63
Synovial fluid and enhancement	31	8.4	23
Chronic arthritis, any	26	7.0	18
Erosions alone	12	3.2	46
Condylar flattening alone	12	3.2	46
Combination of findings of chronic arthritis	2	0.5	7.6
Acute arthritis without chronic changes	115	31	81
Chronic arthritis without acute changes	6	1.6	4.2
Acute and chronic changes	20	5.4	14
By individual patient	185	NA	NA
Any abnormality	81	43	NA
Active arthritis without chronic changes	59	32	73
Chronic arthritis without acute changes	2	1.1	2.4
Active and chronic changes	20	11	24

MRI: magnetic resonance imaging; TMJ: temporomandibular joint. NA: not applicable.

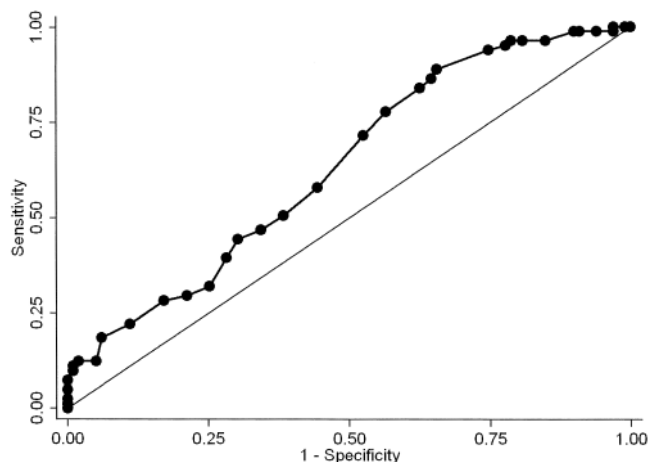


Figure 5. Receiver-operator curve analysis for the ability of maximal incisal opening to predict TMJ arthritis.

Table 3. Multivariable analysis of predictors of TMJ synovitis. Data are OR (95% CI).

Factor	Univariate OR	Multivariable OR
Mouth opening deviation	6.98 (3.38–14.4)	6.21 (2.87–13.4)
Maximal incisal opening	0.93 (0.89–0.97)	0.94 (0.90–0.99)
Age at diagnosis	1.10 (1.03–1.19)	NS
Disease duration	0.87 (0.79–0.96)	0.87 (0.78–0.97)

TMJ: temporomandibular joint; NS: not significant.

vidual therapy, such that the cumulative effect of longterm therapy with immunosuppressive medications may reduce inflammation in the TMJ in some patients. Clearly, there is no way to sort out these possibilities by this chart review; instead, future studies are indicated evaluating the effect of systemic immunosuppressive therapy on TMJ arthritis, as well as the role of adjunctive therapies including intraarticular administration of corticosteroids or even infliximab²⁸.

There were some differences between our results and those of other studies^{7,8,9,10,16,17,18}. We did not identify significant differences among JIA categories (Figure 4), and we reported that an older rather than a younger age of onset was a risk factor; we also did not report an association between extent of non-TMJ-related synovitis and the presence of TMJ arthritis, nor a protective effect of HLA-B27. The reasons for these differences are unclear but we did evaluate more patients than some previous studies. We also found that disease duration was protective against TMJ arthritis, also in contrast to previous reports^{10,12,18}. The difference here may reflect more aggressive use of immunosuppression compared to that available or used in the previous studies, as discussed above. Finally, we reported considerably fewer chronic changes than were reported in most of the other studies, particularly those that used plain or computed radiography, both of which would

detect only chronic changes^{7,8,17,29,30}. It may be argued that the low incidence of chronic changes suggests that some of the acute findings represented false-positive abnormalities. Importantly, however, Tzaribachev, *et al* performed a retrospective review of 96 children (192 TMJ) who underwent contrast-enhanced MRI of the head, evaluating the studies for evidence of TMJ arthritis; they reported abnormal fluid and synovial enhancement each in only 3% of imaged TMJ¹⁴. There was a retrospective study of children who underwent contrast-enhanced brain MRI, so they did not use the same TMJ coils that our radiologists used. Thus, it is possible that some of our findings could be false-positives; however, our findings of TMJ arthritis in 43% of subjects are consistent with other studies^{5,9,10,11,12,16,17,18,29,30}, so we do not suspect that there was a considerable number of false-positive studies.

It could also be argued that the low incidence of chronic changes reflects relatively early diagnosis; this explanation also seems unlikely, because patients with chronic changes had a shorter disease duration compared to those without chronic changes (1.4 vs 2.6 years; $p = 0.058$; data not shown), and a previous study showed a high incidence of chronic changes in newly diagnosed patients¹¹. Instead, we suspect that the low incidence of chronic changes may suggest that, at least in some patients, aggressive therapy can result in improvement of chronic changes, as has been reported in adults with rheumatoid arthritis³¹.

There are limitations to our study. For obvious ethical reasons, there was no histologic gold standard, so, like other investigators, we used the MRI as the gold standard. It is theoretically possible that contrast-enhanced MRI may lack specificity; indeed, studies of the pediatric wrist and adult sacroiliac joint have shown abnormalities in sizeable proportions of healthy control subjects^{32,33}. As discussed, however, TMJ fluid and enhancement appear to be rare findings in children without JIA¹⁴. There are, however, no prospective studies evaluating control pediatric subjects for TMJ arthritis. Additional limitations include the absence of a standardized method to measure MIO or evaluate for mouth opening deviation (including not taking into account the incisal vertical overbite), the retrospective and nonblinded assessments of the MRI, and the variability in the timing of the studies. Important strengths are the comprehensive procedure of our study, because we obtained MRI of the TMJ on nearly 50% of patients with JIA evaluated during the study time period by at least 1 of the staff pediatric rheumatologists; as well as the detailed clinical information available on these subjects.

Our study confirms previous reports that children with JIA regardless of category are at risk of TMJ arthritis, and that this can occur even in the context of immunosuppressive therapy and in the presence of a normal TMJ examination and in the absence of clinically evident arthritis outside the TMJ. Future studies are required to evaluate the risk of TMJ arthritis in an inception cohort of JIA, to compare the responsiveness of TMJ arthritis to systemic and local immunosuppressive thera-

py to that of more clinically accessible joints, and to identify longterm sequelae of persistent TMJ arthritis despite treatment with aggressive systemic immunosuppressive therapy.

ACKNOWLEDGMENT

We acknowledge the physicians and staff of the Department of Radiology at Children's Hospital of Alabama in Birmingham for their diligence and substantial contributions to the clinical assessment of TMJ arthritis in children with JIA.

REFERENCES

1. Schneider R, Passo MH. Juvenile rheumatoid arthritis. *Rheum Dis Clin North Am* 2002;28:503-30.
2. Ravelli A, Varnier GC, Oliveira S, Castell E, Arguedas O, Magnani A, et al. Antinuclear antibody-positive patients should be grouped as a separate category in the classification of juvenile idiopathic arthritis. *Arthritis Rheum* 2011;63:267-75.
3. Burgos-Vargas R, Vazquez-Mellado J. The early clinical recognition of juvenile-onset ankylosing spondylitis and its differentiation from juvenile rheumatoid arthritis. *Arthritis Rheum* 1995;38:835-44.
4. Calabro JJ, Marchesano JM. The early natural history of juvenile rheumatoid arthritis. A 10-year follow-up study of 100 cases. *Med Clin North Am* 1968;52:567-91.
5. Muller L, Kellenberger CJ, Cannizzaro E, Ettlin D, Schraner T, Bolt IB, et al. Early diagnosis of temporomandibular joint involvement in juvenile idiopathic arthritis: A pilot study comparing clinical examination and ultrasound to magnetic resonance imaging. *Rheumatology* 2009;48:680-5.
6. Hu YS, Schneiderman ED, Harper RP. The temporomandibular joint in juvenile rheumatoid arthritis: Part II. Relationship between computed tomographic and clinical findings. *Pediatr Dent* 1996;18:312-9.
7. Karhulahti T, Ylijoki H, Ronning O. Mandibular condyle lesions related to age at onset and subtypes of juvenile rheumatoid arthritis in 15-year-old children. *Scand J Dent Res* 1993;101:332-8.
8. Pedersen TK, Jensen JJ, Melsen B, Herlin T. Resorption of the temporomandibular condylar bone according to subtypes of juvenile chronic arthritis. *J Rheumatol* 2001;28:2109-15.
9. Billiau AD, Hu Y, Verdonck A, Carels C, Wouters C. Temporomandibular joint arthritis in juvenile idiopathic arthritis: Prevalence, clinical and radiological signs, and relation to dentofacial morphology. *J Rheumatol* 2007;34:1925-33.
10. Sidiropoulou-Chatzigianni S, Papadopoulos MA, Kolokithas G. Mandibular condyle lesions in children with juvenile idiopathic arthritis. *Cleft Palate Craniofac J* 2008;45:57-62.
11. Weiss PF, Arabshahi B, Johnson A, Bilaniuk LT, Zarnow D, Cahill AM, et al. High prevalence of temporomandibular joint arthritis at disease onset in children with juvenile idiopathic arthritis, as detected by magnetic resonance imaging but not by ultrasound. *Arthritis Rheum* 2008;58:1189-96.
12. Jank S, Haase S, Strobl H, Michels H, Hafner R, Missmann M, et al. Sonographic investigation of the temporomandibular joint in patients with juvenile idiopathic arthritis: A pilot study. *Arthritis Rheum* 2007;57:213-8.
13. Ringold S, Cron RQ. The temporomandibular joint in juvenile idiopathic arthritis: Frequently used and frequently arthritic. *Pediatr Rheumatol Online J* 2009;7:11.
14. Tzaribachev N, Fritz J, Horger M. Spectrum of magnetic resonance imaging appearances of juvenile temporomandibular joints (TMJ) in non-rheumatic children. *Acta Radiol* 2009;50:1182-6.
15. Kuseler A, Pedersen TK, Gelineck J, Herlin T. A 2 year followup study of enhanced magnetic resonance imaging and clinical examination of the temporomandibular joint in children with juvenile idiopathic arthritis. *J Rheumatol* 2005;32:162-9.
16. Cannizzaro E, Schroeder S, Muller LM, Kellenberger CJ, Saurenmann RK. Temporomandibular joint involvement in children with juvenile idiopathic arthritis. *J Rheumatol* 2011;38:510-5.
17. Twilt M, Moberg SM, Arends LR, ten Cate R, van Suijlekom-Smit L. Temporomandibular involvement in juvenile idiopathic arthritis. *J Rheumatol* 2004;31:1418-22.
18. Argyropoulou MI, Margariti PN, Karali A, Astrakas L, Alfandaki S, Kosta P, et al. Temporomandibular joint involvement in juvenile idiopathic arthritis: Clinical predictors of magnetic resonance imaging signs. *Eur Radiol* 2009;19:693-700.
19. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. *J Rheumatol* 2004;31:390-2.
20. Ingervall B. Range of movement of mandible in children. *Scand J Dent Res* 1970;78:311-22.
21. Cahill AM, Baskin KM, Kaye RD, Arabshahi B, Cron RQ, Dewitt EM, et al. CT-guided percutaneous steroid injection for management of inflammatory arthropathy of the temporomandibular joint in children. *AJR Am J Roentgenol* 2007;188:182-6.
22. Ingervall B. Positional changes of mandible and hyoid bone relative to facial and dental arch morphology. A biometric investigation in children with postnormal occlusion (Angle Class II, Div. I). *Acta Odontol Scand* 1970;28:867-94.
23. Kuseler A, Pedersen TK, Herlin T, Gelineck J. Contrast enhanced magnetic resonance imaging as a method to diagnose early inflammatory changes in the temporomandibular joint in children with juvenile chronic arthritis. *J Rheumatol* 1998;25:1406-12.
24. Arabshahi B, Dewitt EM, Cahill AM, Kaye RD, Baskin KM, Towbin RB, et al. Utility of corticosteroid injection for temporomandibular arthritis in children with juvenile idiopathic arthritis. *Arthritis Rheum* 2005;52:3563-9.
25. Ringold S, Torgerson TR, Egbert MA, Wallace CA. Intraarticular corticosteroid injections of the temporomandibular joint in juvenile idiopathic arthritis. *J Rheumatol* 2008;35:1157-64.
26. van der Heijde D, Sieper J, Maksymowych WP, Dougados M, Burgos-Vargas R, Landewe R, et al. 2010 Update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. *Ann Rheum Dis* 2011;70:905-8.
27. Gardner-Medwin JM, Killeen OG, Ryder CA, Bradshaw K, Johnson K. Magnetic resonance imaging identifies features in clinically unaffected knees predicting extension of arthritis in children with monoarthritis. *J Rheumatol* 2006;33:2337-43.
28. Alstergren P, Larsson PT, Kopp S. Successful treatment with multiple intra-articular injections of infliximab in a patient with psoriatic arthritis. *Scand J Rheumatol* 2008;37:155-7.
29. Svensson B, Adell R, Kopp S. Temporomandibular disorders in juvenile chronic arthritis patients. A clinical study. *Swed Dent J* 2000;24:83-92.
30. Larheim TA, Hoyeraal HM, Stabrun AE, Haanaes HR. The temporomandibular joint in juvenile rheumatoid arthritis. Radiographic changes related to clinical and laboratory parameters in 100 children. *Scand J Rheumatol* 1982;11:5-12.
31. Rau R, Herborn G, Wassenberg S. Healing of erosive changes in rheumatoid arthritis. *Clin Exp Rheumatol* 2004;5 Suppl 35:S44-9.
32. Muller LS, Avenarius D, Damasio B, Eldevik OP, Malattia C, Lambot-Juhan K, et al. The paediatric wrist revisited: Redefining MR findings in healthy children. *Ann Rheum Dis* 2011;70:605-10.
33. Marzo-Ortega H, Tanner SF, Rhodes LA, Tan AL, Conaghan PG, Hensor EM, et al. Magnetic resonance imaging in the assessment of metacarpophalangeal joint disease in early psoriatic and rheumatoid arthritis. *Scand J Rheumatol* 2009;38:79-83.