

Prevalence, Course, and Associated Factors of Pain in the Temporomandibular Joint in Early Rheumatoid Arthritis: Results of a Longitudinal Cohort Study

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Aims: To assess the prevalence, 3-year course, and associated factors of temporomandibular joint (TMJ) pain in patients with newly diagnosed rheumatoid arthritis (RA). **Methods:** A total of 264 patients with newly diagnosed RA were included. Patients were assessed after 3 months, 6 months, 9 months, 1 year, 1.5 years, 2 years, and 3 years. TMJ pain was scored by manual palpation, and the prevalence of TMJ pain was calculated at baseline and at all seven follow-up intervals during 3 years. Factors assessed for a potential association with TMJ pain at baseline included: demographic factors (gender and age), disease-related factors (symptom duration, rheumatoid factor [RF], anti-cyclic citrullinated protein [anti-CCP], C-reactive protein [CRP], and Disease Activity Score 28 [DAS28]), and functional factors (Health Assessment Questionnaire [HAQ] and European Quality of Life 5 Dimensions Questionnaire [EQ5D]–anxiety/depression). A stepwise logistic regression model was used to determine factors associated with TMJ pain in patients with RA. **Results:** The prevalence of TMJ pain in patients with RA was 10.6% at baseline, which decreased to 3.6% in the first year after inclusion and remained stable thereafter. Disease activity as determined by the DAS28 was significantly associated with TMJ pain (odds ratio [OR] = 1.51; 95% confidence interval [95% CI] = 1.12–2.05; $P = .009$) at baseline. A second logistic regression analysis was performed with the following variables of the DAS28: erythrocyte sedimentation rate (ESR), tender joint count, swollen joint count, and global health. Tender joint count (OR = 1.06; 95% CI = 1.01–1.12; $P = .03$) and global health (OR = 1.02; 95% CI = 1.00–1.03; $P = .03$) were significantly associated with TMJ pain at baseline. The remaining factors included in the analysis were not significantly associated with TMJ pain at baseline. **Conclusion:** The prevalence of TMJ pain in patients with newly diagnosed RA is approximately 10% and decreases during follow-up, especially in the first year. Disease activity is a risk factor for TMJ pain in patients with newly diagnosed RA. *J Oral Facial Pain Headache* 2017;31:233–239. doi: 10.11607/ofph.1606

Keywords: associated factors, course, early rheumatoid arthritis, prevalence, temporomandibular joint pain, TMD

Rheumatoid arthritis (RA) is an autoimmune disease that causes pain, swelling, and stiffness of the synovial joints.¹ The 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria are currently used to diagnose RA.¹ Its prevalence ranges from 0.1% to 2% of the world population and is higher in females and elders.^{1,2,3} In its early stage, the joints in the hands and feet are most often affected, and the stiffness is worst in the morning.¹ As there is no cure yet, the aim of RA treatment is to improve function and relieve symptoms, and research has shown that patients benefit the most from early treatment.⁴ Clinical outcomes have a better prognosis with early intervention, since joint destruction may be prevented.^{4,5}

The temporomandibular joint (TMJ) can also be affected by RA. Using self-report questionnaires, Wolfe et al found a jaw pain prevalence of 19% in a study population of 17,683 patients with RA.⁶ This is the largest study on this topic performed to date, but the disease duration of the RA patients was not described. In a study by Yi-Chun Lin et al, a

Table 1 Number of Potential Patients, Number of Patients Assessed During Follow-up, and the Participation Rate (ie, the Ratio of the Number of Patients Assessed to the Number of Potential Patients)

Time	Number of potential patients	Number of patients assessed	Participation rate
Baseline	264	264	100
3 mo	260	252	97
6 mo	255	240	94
9 mo	242	217	90
1 y	216	196	91
1.5 y	188	154	82
2 y	134	115	86
3 y	80	50	63

prevalence of tender TMJs of 20% was found in 56 patients with RA.⁷ The mean disease duration prior to inclusion was 6.9 years. Bono et al investigated a study population of 100 RA patients with a preinclusion mean symptom duration of 10 years and found a TMJ pain prevalence of 58%.⁸ This wide variation in the reported prevalence of TMJ involvement in RA may be due to the various diagnostic criteria that have been applied for the recognition of TMJ pain and the different RA disease stages.

TMJ pain in the early stages of RA has not been investigated; however, early diagnosis is important because it enables early intervention, which in turn yields a better prognosis for the possible clinical consequences of RA of the TMJ, such as condylar degeneration.⁷ Therefore, further research is needed to investigate the prevalence of TMJ pain in the early stages of RA. There is also no consensus about the factors associated with TMJ pain in patients with RA, and this also requires further investigation.^{7,9,10}

The aim of this study was to assess the prevalence, 3-year course, and associated factors of TMJ pain in patients with newly diagnosed RA.

Materials and Methods

Study Design and Patient Population

The study population consisted of patients who were included in the Early Arthritis Cohort (EAC) of Reade in Amsterdam, the Netherlands, from 2008 to 2012 (ie, from 2008 and onwards, the TMJ was assessed). The EAC started in 1995 to investigate a wide variety of topics related to the signs and symptoms of arthritis. The inclusion criteria of the EAC were: patients older than 18 years who had less than 3 years of complaints, did not receive disease-modifying antirheumatic drug (DMARD) treatment during the past 6 months, and had a minimum of two swollen joints or

one swollen joint with positive anti-cyclic citrullinated peptide (anti-CCP). The exclusion criteria were: patients who did not receive DMARDs, prednisone treatment less than 6 months ago, and patients who had gout, arthritis due to a bacterial infection, reactive arthritis, sarcoidosis, or an auto-immune disease other than RA.

For the present study, the patients with an RA diagnosis at baseline (2008) were selected. RA was diagnosed according to the ACR/EULAR criteria.¹ The ACR criteria are based on the following variables: joint involvement (number of large or small joints), serology (rheumatoid factor [RF] anti-CCP, acute-phase reactants [ie, C-reactive protein (CRP)], and erythrocyte sedimentation rate [ESR]), and duration of the symptoms. Each variable is scored, and the total added score (ranging from 0 to 10) determines the RA classification.¹ A score higher than 5 is indicative of the presence of definite RA.¹

At baseline, sociodemographic factors (gender and age) and blood samples (analyzed for RF, anti-CCP, CRP, and ESR) were collected, and questionnaires (on daily functioning and anxiety/depression) were completed by the patients (for details, see below). A total of 264 RA patients were included from 2008 through 2012. Patients had a variable follow-up duration, and so not all data from the 3 years could be collected for the total study population—for example, patients who were included in 2011 could only have a follow-up duration of 1 year. Table 1 presents the total number of potential patients and the number of patients assessed. Patients who dropped out because of moving ($n = 18$) or because they passed away ($n = 3$) were extracted from the number of potential patients from the measurement moment at which they were lost. The most common reasons for dropout were lack of time ($n = 23$) and remission of the disease ($n = 8$). None of the patients received any treatment that was specifically aimed at alleviating possible TMJ pain.

All patients provided written informed consent according to the Declaration of Helsinki. Approval for the EAC study was obtained by the Medical Ethical Review Board of Reade/Slotervaart General Hospital in Amsterdam.

TMJ Pain

Patients were examined by thoroughly trained clinical research assistants (medical doctors with specialist training in the diagnosis of rheumatic diseases) using the Disease Activity Score 44 (DAS44) at baseline and at several follow-up visits (3 months, 6 months, 9 months, 1 year, 1.5 years, 2 years, and 3 years after baseline). Several research assistants were involved in this study; the one on call performed the examination. The DAS44 provides a score for disease activity

and is based on assessment of 44 joints, the ESR (in mm/hour), and the patients' self-assessment of disease activity as assessed on a 100-mm visual analog scale (VAS). The DAS44 includes the assessment of the tenderness of the TMJ, which was the main parameter of interest in the present study. TMJ pain was scored by manual palpation on a 4-point scale (0 = no pain, 1 = pain, 2 = pain with a grimace, and 3 = pain with a grimace and withdrawal). The presence of TMJ pain was dichotomized as no pain (score 0) or pain (scores 1–3). Palpation force was determined as pressing hard enough to see the white of one's nailbed. No data on self-assessed general or local pain were collected.

The following factors at baseline were selected as possible factors associated with TMJ pain.

Demographic Factors

- Gender: Gender could potentially be associated with TMJ pain. In Visscher et al, women reported TMD pain complaints more often than men.¹¹
- Age: Age was measured in years. Older age might be associated with more TMJ pain.

Disease-Related Factors

- Symptom duration: During the first visit, patients were asked when the symptoms started. This involved a self-report of the maximum duration of the signs or symptoms of synovitis in any joint that was clinically involved at the time of first assessment. Symptom duration was measured in years. The longer the duration, the more damage can be expected in the joints, possibly leading to more TMJ pain.¹
- Auto-antibodies: RF and anti-CCP antibodies are indicators of RA disease severity and can be found in the body many years before the first clinical manifestation of RA.¹² Higher levels of auto-antibodies might be related to more TMJ pain.
- Inflammation activity: CRP is measured to prove or rule out an infection or inflammation in the body. During an infection, the liver produces CRP (which is measured in mg/L). The amount of inflammation might be positively correlated with TMJ pain.
- Disease activity: This was measured using the Disease Activity Score 28 (DAS28).¹³ This index is widely used to discriminate between high and low disease activity in RA patients. The DAS28 was developed to simplify the use of the DAS44, but does not include the TMJ. To calculate the DAS28, 4 items are included: the number of tender joints (0–28), the number of swollen joints (0–28), ESR (mm/hour), and the patient's general health or global disease activity during the past

week, measured on a VAS (0–100). The formula is as follows:

$$(DAS28 = 0.56 * \sqrt{tender28} + 0.28 * \sqrt{swollen28} + 0.70 * \ln(ESR) + 0.014 * GH)$$

- The DAS28 indicates the current RA disease activity (remission: DAS28 ≤ 2.6; low disease activity: 2.6 ≤ 3.2; moderate disease activity: 3.2 ≤ 5.1; high disease activity: > 5.1). It is expected that patients with a higher disease activity have more TMJ pain.¹⁴

Functional Factors

- Daily functioning: The Health Assessment Questionnaire (HAQ) was used to evaluate functional impairment and work disability. This questionnaire includes 20 items in 8 dimensions about difficulties in dressing, rising, eating, walking, personal hygiene, reach, grip, and usual activities. For each category, patients can assign a value from 0 to 3 (0 = without any difficulty, 1 = with some difficulty, 2 = with much difficulty, and 3 = unable to perform the task). The highest scores of each dimension are summed and divided by 8, resulting in an index.¹⁵ It can be expected that a higher HAQ is associated with more TMJ pain.¹⁰
- Anxiety/depression: This was measured by one question of the European Quality of Life 5 Dimensions (EQ5D) questionnaire.¹⁶ The EQ5D–anxiety/depression was dichotomized as no problems (score of 0) and problems (score 1 or 2). Anxiety and depression are considered risk factors for TMJ pain.¹⁷

Statistical Analyses

Means and medians of the baseline characteristics were calculated. Student *t* test (for normally distributed variables), Mann-Whitney *U* test (for not normally distributed variables), and chi-square test were used to compare the patients with a full follow-up (*n* = 50) with patients without a full follow-up (*n* = 214). The difference was considered statistically significant if *P* < .05. The baseline variables that were used to compare the two groups were gender, age, RF, DAS28, and HAQ. The prevalence of TMJ pain was calculated at baseline and for all seven follow-up measurements during 3 years and visualized in a graph.

A stepwise logistic regression model was used to analyze possible associated factors of TMJ pain in patients with RA. Collinearity of all possible baseline predictors was analyzed using Spearman and Pearson tests. First, single regression analysis was used to determine the association between TMJ pain

Table 2 Baseline Characteristics of Patients with Rheumatoid Arthritis in the Early Arthritis Cohort (n = 264)

Characteristics	Mean ± SD	Median (IQR)	n (%)
Gender			
Females			197 (74.6)
Males			67 (25.4)
Age (y)	53.6 ± 13.0		
TMJ pain			28 (10.6)
Symptom duration (y)		0.2 (0.1–0.3)	
RF-positive			158 (59.8)
Anti-CCP-positive			197 (74.6)
CRP (mg/L)		10 (3–22)	
DAS28	5.0 ± 1.4		
ESR (mm/h)		23.0 (11.8–43.0)	
Tender joint count		5 (3–10)	
Swollen joint count		6 (4–10)	
Global health (100-mm VAS)		60.0 (39.2–78)	
HAQ		1.3 (0.6–1.6)	
EQ5D—anxiety/depression problems			97 (40.6)

SD = standard deviation; IQR: interquartile range; RF = rheumatoid factor; Anti-CCP = anti-cyclic citrullinated peptide antibodies; CRP = C-reactive protein; DAS28 = Disease Activity Score; ESR: erythrocyte sedimentation rate; VAS = visual analog scale; HAQ: Health Assessment Questionnaire; EQ5D: European Quality of Life 5 Dimensions Questionnaire.

and the possible associated factors. The dependent variable was TMJ pain at baseline and the independent variables were demographic factors (gender and age), disease-related factors (complaint duration, RF, anti-CCP, CRP, and DAS28), and functional factors (HAQ and EQ5D—anxiety/depression) at baseline. The independent variables that showed at least a weak association with TMJ pain (as indicated by a *P* value < .10 in the single logistic analysis) were entered in the multivariate regression model. Then, in a backward stepwise manner, the independent variable with the weakest association was removed from the regression model until all variables included were statistically significant (*P* < .05). For each removed predictor variable, the *P* value upon exit was noted, and odds ratios (OR) and 95% confidence intervals (CI) are reported for the predictors. All analyses were performed with the IBM SPSS Statistics, version 21.0.

Results

Descriptive Variables

Patient characteristics at baseline are presented in Table 2. The study sample consisted of 264 patients (74.6% female, 25.4% male) with a mean ± standard deviation (SD) age for all participants of 53.6 ± 13.0 years. The mean symptom duration was 0.2 (interquartile range [IQR] 0.1 to 0.3) years. Patients with a full follow-up (n = 50) were not statistically different in baseline characteristics compared to the patients without a full follow-up (n = 214). The percentages, means, and medians of the baseline characteristics of the patients with a full follow-up and without a full follow-up, respectively, were as follows: females: 76.2% vs 68.0% (*P* = .23); age: 53.6 years vs 53.6 years (*P* = .99); RF-positive: 60.7% vs 56% (*P* = .54); DAS28 mean score 5.1 vs 5.0 (*P* = .51); HAQ median score: 1.3 vs 1.3 (*P* = .83).

Course of TMJ Pain

At baseline, the prevalence of TMJ pain in patients with RA was 10.6%. The prevalence decreased over 3 years. The course of TMJ pain in patients with RA is shown in Fig 1. In the first year, the prevalence decreased from 10.6% to 3.6%, and after 3 years it remained stable, around 4.0%.

Factors Associated with TMJ Pain at Baseline

In the single regression analysis, disease activity measured by the DAS28 was positively associated with TMJ pain, while anti-CCP showed a negative association with the presence of TMJ pain. In the multivariate regression model, the only predictor for TMJ pain that was retained in the model was DAS28 (OR = 1.51; 95% CI = 1.12–2.05; *P* = .009) (Table 3).

To determine which of the variables of the DAS28 were responsible for the positive association with TMJ pain at baseline, a second logistic regression analysis was performed with the four items of the DAS28: ESR, tender joint count, swollen joint count, and global health. In the single regression analysis, tender joint count (OR = 1.06; 95% CI = 1.01–1.12; *P* = .03) and global health (OR = 1.02; 95% CI = 1.00–1.03; *P* = .03) were significantly associated with TMJ pain at baseline. In the multiple regression analysis, the two variables showed a similar, nonsignificant association with TMJ pain (tender joint count: OR = 1.06; 95% CI = 0.98–1.10; *P* = .14; global health: OR = 1.01; 95% CI 0.99–1.03; *P* = .11). In other words, TMJ pain at baseline was equally associated with both variables, and the prediction of TMJ pain based on one of the variables was not improved by adding the outcomes of the other variable.

Table 3 Multiple Logistic Regression Analysis of Possible Associated Factors at Baseline for TMJ Pain in Patients with Rheumatoid Arthritis

	n	Single regression model			P-to-exit	Multiple regression model		
		P value	OR	95% CI		P value	OR	95% CI
Demographic factors								
Gender (female)	264 (197)	.39	0.69	0.3–1.6				
Age (y)	264	.63	1.01	0.98–1.0				
Disease-related factors								
Symptom duration (y)	222	.29	1.78	0.61–5.25				
Rheumatoid factor (positive)	264 (158)	.48	0.75	0.34–1.65				
Anti-CCP (positive)	264 (197)	.028	0.41	0.18–0.91	0.12			
CRP (mg/L)	254	.64	1	0.99–1.01				
DAS28	259	.009	1.51	1.12–2.05		.009	1.51	1.12–2.05
Functional factors								
HAQ	251	.36	1.91	1.04–3.49				
EQ5D–anxiety/depression (problems)	239 (97)	1.0	0.99	0.44–2.26				

OR = odds ratio; 95% CI = 95% confidence interval; Anti-CCP = anti-cyclic citrullinated peptide antibodies; CRP = C-reactive protein; DAS28 = Disease Activity Score; HAQ: Health Assessment Questionnaire; EQ5D: European Quality of Life 5 Dimensions Questionnaire.

Discussion

The purpose of this study was to investigate the prevalence and 3-year course of TMJ pain in patients with newly diagnosed RA. In addition, the study explored which factors were associated with the presence of TMJ pain in patients with RA.

At the first visit to the rheumatologist, a prevalence of TMJ pain of 10.6% was found in the patient population with RA diagnosed according to the 2010 ACR/EULAR criteria. These percentages are lower than those found in previous studies.^{6,7,8} This may be due to variations in patient selection, the method of establishing the presence of TMJ pain, and the differences in symptom duration. In Wolfe et al, a prevalence of TMJ pain of 19% in patients with RA was found.⁶ In that study, patients with RA were included, but no information about the diagnostic criteria for RA nor complaint duration were reported. Furthermore, jaw pain was considered to be present according to self-report of pain. Lin et al included RA patients in their study according to the 1987 ACR/EULAR criteria, and TMJ tenderness was assessed by palpation.⁷ They found a prevalence of tender TMJs of 20%. Bono et al also used a population of RA patients diagnosed with the 1987 ACR/EULAR criteria, and TMJ pain was assessed by palpation and active mouth opening.⁸ They found a 58% prevalence of TMJ pain. In the present study, the population included patients with RA with a median complaint duration of only 0.2 years, while in the studies of Lin et al and Bono et al it was 5.9 years and 10 years, respectively.^{7,8} This could indicate that patients with RA are more likely to develop TMJ pain later on in the disease process, which may be the result of joint damage and deformities of the TMJ. However, the present results

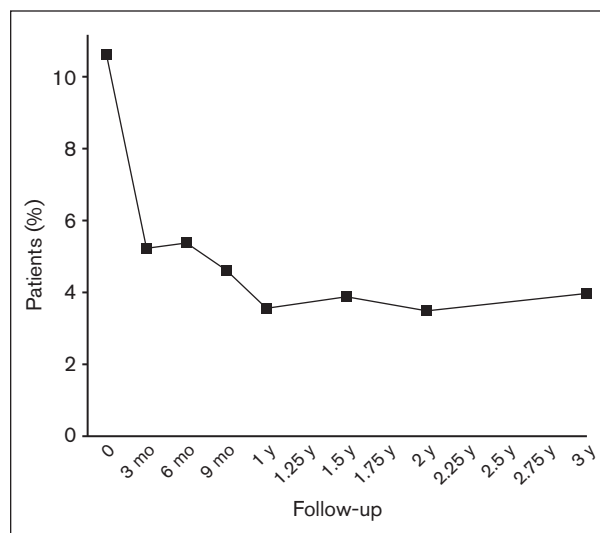


Fig 1 Course of TMJ pain during 3 years of follow-up of patients with rheumatoid arthritis in the Early Arthritis Cohort (Percentage of TMJ pain in patients with rheumatoid arthritis in the cohort per time point).

showed the most pronounced decrease in TMJ pain prevalence occurred in the first year (from 10.6% at baseline to 3.6% at 1 year after diagnosis). A comparable decrease in joint complaints in the same EAC cohort was found for the forefoot joints.¹⁸ These results could be explained by the effect of early medical treatment of these patients, which was provided as part of their usual care. In future studies, a longer follow-up might clarify more on the course of TMJ pain in patients with RA.

The disease activity at baseline as measured with the DAS28 was found to be the most significant associated factor for TMJ pain. This confirms earlier findings of Moen et al.⁹ The DAS28 is a commonly used instrument; however, the DAS28 does not include examination of the TMJ. Patients with RA should also have a TMJ examination so that possible TMJ involvement in the disease is not missed. The present study investigated which of the variables of the DAS28 (ESR, tender joint count, swollen joint count, and global health) were responsible for the positive association with TMJ pain at baseline, and tender joint count and global health showed equal associations. Bessa-Noqueira et al also found the tender joint count to be significantly associated with pain on TMJ palpation.¹⁰ The results of the present study demonstrate that patients with pain in other joints and worse global health have a greater chance of experiencing TMJ pain. The remaining variables included in the analysis (gender, age, symptom duration, RF, anti-CCP, CRP, HAQ, and anxiety/depression) were not significantly associated with TMJ pain at baseline. It is remarkable that no association of anxiety and depression with TMJ pain was found, which is in contrast with the findings of Kindler et al.¹⁷ It could be that the disease severity in patients with RA weighs more than the psychological state of the patients. Alternatively, since TMJ pain in the present study was based on palpation, patients might have been unaware of their pain, thus making an association between TMJ pain and anxiety/depression less likely.

A strength of the present study was the use of a large sample of patients with newly diagnosed RA; however, a limitation was the dropout of patients during follow-up. To check for selection bias, the demographics and clinical features of patients with a full follow-up were compared to those without a full follow-up. In this comparison, no statistical differences were found, suggesting that selection bias was minimal, if at all present.

Another limitation of the present study was that TMJ pain was assessed only by nonstandardized palpation by several noncalibrated (albeit thoroughly trained) examiners. The number of false positives with palpation is relatively high,¹⁹ and the results could thus be an overestimation of the true number of early RA patients with TMJ pain. It is difficult to compare the prevalence found in the present study with available literature because of the different disease stages. The addition of a control group would give more insight into the prevalence of TMJ pain in RA patients in comparison with the normal population. On the other hand, the use of palpation is also an advantage, because the majority of other studies also used palpation to assess tender joints. Still, caution with the interpretation of the study results is needed.

For future studies, it is advised to add dynamic/static tests to diagnose pain in the TMJ and/or masticatory muscles.¹⁹ Dynamic tests mimic the function of the TMJ (opening, closing, and protrusion movement of the lower jaw), and when the familiar pain in the TMJ is provoked,²⁰ TMJ pain is considered present. With static tests, manual pressure is used to load the jaw muscles to diagnose a myogenous pain complaint. The study of Visscher et al concluded that these tests have less false positives in comparison with palpation.¹⁹ Alternatively, the widely applied (Research) Diagnostic Criteria for TMD ([R]DC/TMD)^{21,22} could be used in future studies as well, which has the advantage of more possibilities for comparison with other studies rather than use of the less frequently adopted dynamic/static tests. Use of the (R)DC/TMD in future studies would yield the additional advantage of being able to also assess the dysfunction of the masticatory system (eg, TMJ sounds, mandibular movement limitations). Further, the (R)DC/TMD protocol has the advantage of using standardized palpation sites and forces, which will further improve insights into the prevalence and associated factors of TMJ pain in early RA.

Conclusions

The prevalence of TMJ pain in patients with newly diagnosed RA in the EAC was approximately 10% and decreased especially in the first year after the start of medical treatment. This study indicated that disease activity at baseline is a significant associated factor for TMJ pain in patients with newly diagnosed RA, while gender, age, symptom duration, RF, anti-CCP, CRP, HAQ, and EQ5D–anxiety/depression were not.

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