EJR European Journal of Rheumatology

DOI: 10.5152/eurjrheum.2025.24124

Original Article

The Frequency and Importance of Subchondral Radius Cysts (Geodes) in Rheumatoid Arthritis Patients

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Abstract

Background: Geodes are subchondral cysts that appear as radiolucent lesions on conventional radiography. The aim was to identify the characteristics of radius geodes in rheumatoid arthritis (RA) patients from a biologic disease-modifying anti-rheumatic drug (bDMARD) cohort.

Methods: The most recent anterior-posterior standard hand radiographs from the first 500 of 2355 patients in the HUR-BIO (Hacettepe University Rheumatology Biologic Registry) database were evaluated to analyze the details of geodes. Demographic and clinical characteristics were analyzed and compared between patients with geodes and those without.

Results: From 500 patients, 448 had radiograph qualified enough to be interpreted and resulted in 63/448 (14.1%) having geodes. When comparing patients with and without geodes, differences were observed in male gender, anti–cyclic citrullinated peptide (CCP) positivity, and disease duration. Patients with subchondral cysts had higher Larsen scores in the carpal bones. Among 26 patients with multiple cysts, anti-CCP antibody positivity was more common ($P = .04$), and a Larsen score of grade 2 or higher was more frequent ($P = .02$). Additionally, patients with subchondral cysts larger than 50 mm^2 were more likely to be male ($P < .01$) and had a higher prevalence of smoking ($P < .02$).

Conclusion: In a cohort of RA patients receiving bDMARDs, geodes in the radius were observed in 14% of cases. The association between the size and number of geodes with anti-CCP positivity and gender may indicate a link to a more erosive disease progression.

Keywords: Conventional radiography, geodes, radius cysts, rheumatoid arthritis

Introduction

The presence of subchondral cysts in rheumatoid arthritis (RA) patients has been acknowledged for a long time. On conventional radiographs, subchondral cysts appear as radiolucent lesions. These lesions have been named in different ways: synovial cyst, subchondral cyst, subarticular pseudocyst, necrobiotic pseudocyst, geodes.[1] The pathological definition of a cyst is a cavitary lesion surrounded by epithelial cells. However, subchondral cysts do not have such a cell array and do not contain a uniform cavity.[1] Therefore, the concept of geodes used in geology is used here. Geodes are used to describe gas-filled cavities between rocks.[1] Moore et al[2] described magnetic resonance images of these cystic lesions in a case report. Accordingly, the cysts were described as "joint sinu." Indeed, pathologically this region is filled with joint debris and synovial fluid.[1] The term geodes will be used in this study. Geodes can be seen in different joint diseases. A pathological/radiological examination of the hip joint revealed that subchondral cysts are frequently seen in patients with osteoarthritis, RA, osteonecrosis, and calcium pyrophosphate crystal deposition disease.[1]

In 1978, Mannerfelt et al[3] studied the etiology and clinical significance of cystic formations found in the wrist of RA patients.[3] Conventional radiographs are used for radiological scoring in RA. For RA, 9 different scoring systems were developed between 1971 and 1999.[4] In these scores, erosion, joint space narrowing, osteoporosis, soft tissue swelling, alignment/subluxation, ankylosis, and cysts were evaluated. The cyst was included in the Sharp score defined in 1971,[5] but it was also included in the Kaye score defined in 1987.[6] Sharp modified the first scoring system in 1971 in 1985 and excluded the presence of a cyst from the score.[7] Cysts are not included in the Van der Heijde/Sharp scoring system, which is the most widely used scoring system today.[8]

While some radiographic scoring systems include cystic changes, since their initial description by Mannerfelt, detailed characterization of geodes remains scarce. With advancements in RA management, understanding their prevalence and clinical implications is essential. For this reason, this study aimed to

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Cite this article as: Kalyoncu U, Ayan G. The frequency and importance of subchondral radius cysts (geodes) in rheumatoid arthritis patients. *Eur J Rheumatol.* 2025, 12(3), 0124, doi:10.5152/eurjrheum.2025.24124.

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Received: November 26, 2024
Revision Requested: March 30, 2025
Last Revision Received: April 30, 2025
Accepted: May 20, 2025
Publication Date: October 30, 2025

assess the frequency, distribution, and characteristics of geodes in the radius of RA patients within a biologic disease-modifying anti-rheumatic drug (bDMARD) cohort.

Material and Methods

Patient Selection and Demographic/Clinical Data

The HUR-BIO database was established in 2005, with 2355 RA patients registered as of January 2023. Rheumatoid arthritis was diagnosed by a clinician. Patients using at least 1 bDMARD (adalimumab, infliximab, etanercept, golimumab, certalizumab, tocilizumab, rituximab, abatacept) or targeted synthetic DMARD (tofacitinib, baricitinib) are registered in the database. Date of birth, gender, dates of onset of complaints, time of diagnosis, education level, smoking, body mass index (BMI) at the time of bDMARD initiation, comorbidities (such as, Diabetes Mellitus, Hypertension, Coronary Artery Disease etc.), rheumatoid factor (RF) and anti–cyclic citrullinated peptide (anti-CCP), conventional DMARD (methotrexate, sulfasalazine, leflunomide, hydroxychloroquine) and steroid use were recorded in the database. In HUR-BIO, disease activity and functional scales were recorded at the time of bDMARD initiation and at the last follow-up visit. For this purpose, Disease Activity Score in 28 Joints (DAS-28), pain-visual analogue scale (VAS), patient global assessment-VAS, fatigue-VAS, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and Health Assessment Questionnaire Disability Index (HAQ-DI) scores were recorded.

Conventional Hand Radiograph and Radius Cysts

The anterior-posterior standard hand radiographs (bilaterally per procedure) of the first 500 patients in HUR-BIO who had at least 1 hand radiograph were reviewed. To estimate the required sample size, 100 initial patient radiographs were reviewed and a geode frequency of ~10% was observed. Based on this, a minimum sample size of 316 for 80% power and 437 for 90% power with 95% CIs was calculated, assuming a geode frequency of 15%. To ensure robustness, 500 patients were included for the final analysis. The most recent radiograph for each patient was analyzed. For patients with multiple hand radiographs, earlier images showing geodes in the radius were also examined, focusing on cyst size and location. Radiographs with insufficient image quality, whether due to scanning issues (such as technique or radiation dose) or patient-related factors (such as compromised bone integrity preventing accurate measurements) were excluded from the analysis. Patients' radiographs were evaluated by 1 rheumatologist with more than 20 years of experience. The location and size of the geodes, as well as the distances from the distal radius, from the geodes to the radius, and from the radius to the carpal bones, were measured. For the localisation of the geodes, the distal part of the radius was divided into 3 equal parts. The part close to the ulna is the first section, the centre is the second section and the lateral part is the third section. Horizontal and vertical distances of the cyst were recorded. Cyst area was calculated accordingly. The presence of sclerosis around the cyst was graded (absent, mild, moderate, severe) according to the evaluator's decision. The distances between the radius and the scaphoid, as well as between the radius and the lunate, were measured at their narrowest points. (Figure 1). Progression was defined as a 20% or more increase in the size of the cyst and regression was defined as a 20% or less decrease in the size of the cyst in patients with hand radiographs at follow-up.

Carpal bone involvement was assessed using the modified Larsen score.[9] Accordingly, normal was classified as grade 1 (osteoporosis, periarticular soft tissue swelling, with or without narrowing of the joint space), grade 2 (erosion and at least 50% narrowing of the joint space), grade 3 (moderate destruction, obliteration of the joint space), grade 4 (severe destruction, joint borders still discernible), grade 5 (mutilance, joint borders not discernible).

Ethics

Our study was conducted in accordance with the 2013 amendment of the Declaration of Helsinki, and ethical approval was obtained from Hacettepe University Institutional Review Board (KA-22005Date: 23.08.2022), and written informed consent was obtained from each participant.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics for Windows, version 23.0 (IBM SPSS Corp.; Armonk, NY, USA). The normality of numerical variables was tested by visual (histogram and probability plots) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Descriptive analyses were presented as mean ± SD for continuous variables and as frequencies and percentages for categorical variables. In independent groups, categorical data and rates were compared among groups using the eligibility criteria, Chi-square, or Fisher tests. The independent samples t-test compared the means of 2 independent groups for normally distributed parameters. $P < .05$ was accepted as statistically significant. Intra-reader reliability was evaluated using the intraclass correlation coefficient (ICC). Intraclass correlation coefficient estimates and their 95% CIs were calculated based on absolute agreement using a two-way mixed-effects model. A subset of 20 patients was selected from the 63 patients with cysts, ensuring that at least 10% of the patients with cysts on both the right and left sides were re-evaluated. All continuous measurements for these patients were re-assessed after 6 months. Multivariate analysis was performed to find variables predicting geodes presence using the backward

Main Points

- Subchondral cysts have been recognized in rheumatoid arthritis and included in several radiographic scoring systems.
- Around 14% of patients have subchondral cysts in a bDMARD cohort.
- The characteristics of patients signal the relation of more erosive course in patients with cysts.

Figure 1. Radius geodes in the second region. Measurement of the size of the geodes, the relationship with the carpal bones is shown.

elimination method with variables with a *P*-value of .2 or less in univariate analysis.

Results

Characteristics of Patients with and Without Subchondral Cysts at the Radius

Radiographs of 500 patients diagnosed with RA were analyzed. The presence or absence of subchondral cysts on radiographs could not be determined in 28 (5.6%) patients. Cystic-erosive changes in the radius were observed in 24 (4.8%) patients; however, these patients were excluded from the analysis due to compromised bone integrity in the radius cortex. Overall, subchondral cysts were found in 63/448 (14.1%) of these patients. In 5 of the 63 patients, the radiography was done before bDMARD initiation (range 10-30 months). In 4% of cases, the disease duration was 10 years or less, while in 10%, it exceeded 10 years.

When comparing patients with and without subchondral cysts, differences were observed in male gender and anti-CCP positivity, but no differences were found regarding comorbidities, smoking, BMI, bDMARD treatments, or disease activity scales (VAS pain, VAS global, DAS-28, CRP, ESR) at baseline or at last visit after mean (SD) 59.5 (51) months. When gender and anti-CCP positivity were analyzed in multivariate analysis adjusting for disease duration, only male gender stayed significant (*P* = .006). Patients with subchondral cysts had a more severe Larsen score in the carpal bones (Table 1). The mean (SD) age of patients with/out geodes at the time of the most current radiograph was 54.4 (12.4) and 51.1 (12.9) years, respectively. The time from both symptom and diagnosis to the the most current radiograph was longer in patients with geodes. Intraclass correlation coefficient values for all measurements ranged from 0.98 to 0.99, with corresponding 95% CI ranging from 0.96 to 0.99.

Table 1. Characteristics of Patients with and Without Geodes in the Radius

	Radius Subcondral Cyst (+) n = 63	Radius Subcondral Cyst (-) n = 385	*P*
Age at the time of the most recent radiograph, year, mean (SD)	54.4 (12.4)	51.1 (12.9)	.07
Gender (Male), n (%)	21 (33)	82 (21)	.04
Disease duration from diagnosis, to the most recent radiograph years, mean (SD)	16.1 (8.3)	9.5 (8)	**<.001**
Disease duration from symptom onset to the most recent radiograph, year, mean (SD)	16.7 (7.2)	11.4 (8.7)	**<.001**
Time between symptom onset-bDMARD start, year, mean (SD)	12.0 (7.0)	8.3 (7.6)	**<.001**
Time between diagnosis bDMARD start, year, mean (SD)	11.5 (8.4)	6.4 (6.9)	**<.001**
Anti-CCP positivity, n (%)	36 (75)	186 (60)	.04
RF positivity, n (%)	44 (71)	247 (65)	.37
Smoking*, (Ever), n(%)	32/61(52)	167 (44)	.23
BMI*, mean (SD)	29.2 (6.1)	29.4 (5.9)	.84
DAS-28*, mean (SD)	3.30 (1.48)	3.57 (2.05)	.33
HAQ-DI*, mean (SD)	0.73 (0.65)	0.87 (1.21)	.41
Carpal bone involvement n(%)			
Grade 0	2 (3)	119 (31)	**<.001**
Grade 1	12 (19)	157 (41)	
Grade 2	23 (37)	59 (15)	
Grade 3	22 (35)	41 (11)	
Grade 4	4 (6)	9 (2)	

Percentages presented are valid percents. Bold values indicate significant differences. Anti-CCP, anti- cyclic citrullinated peptide; bDMARD, biologic disease-modifying anti-rheumatic drug; BMI, body mass index; DAS 28, Disease Activity Score in 28 Joints; IQR, inter-quartile range; RF, rheumatoid factor. *The assessments are done at baseline visits.

Features of Subchondral Cysts in the Radius

The Relationship Between Radius and Carpal Bones

The distribution of patients with geodes in the radius according to the Larsen score of the carpal bones was as follows: grade 0: 2 (3.2%), stage 1: 12 (19.0%), grade 2: 23 (36.5%), grade 3: 22 (34.9%), and grade 4: 4 (6.3%). The width of the distal end of the radius was median (min-max) 30.7 (24.6-38.6) mm. The radioscaphoid distance in the right wrist was mean (SD) 1.14 (0.72) mm, the radioscaphoid distance in the left wrist was mean (SD) 1.16 (0.75) mm. Radio-lunate distance in the right wrist was mean (SD) 1.09 (0.73) mm, radio-lunate distance in the left wrist was was mean (SD) 1.11 (0.77) mm.

Number and Distribution of Subchondral Cysts in the Radius

A total of 98 cysts were identified in 63 patients: 8 patients (12.6%) had a unilateral single cyst, 37 patients (58.7%) had a unilateral double cyst, and 14 patients (22.2%) had bilateral cysts. The dominant cyst on the right was observed in 40 patients, with the second cyst found in 14 patients. The dominant cyst on the left was present in 35 patients, and the second cyst was found in 9 patients. The distribution of the 98 cysts on the radius was as follows: 18 (18.4%) in the first zone, 3 (3.1%) between the first and second zones, 50 (51.0%) in the second zone, 16 (16.3%) between the second and third zones, and 11 (11.2%) in the third zone. The distribution of sclerosis surrounding these cysts was as follows: 4 (4.1%) had no sclerosis, 59 (60.2%) had mild sclerosis, 33 (33.7%) had moderate sclerosis, and 2 (2.0%) had marked sclerosis. The mean (SD) distance from the upper end of the cyst to the radius was 1.7 (0.67) mm.

In 26 patients with multiple cysts, anti-CCP antibody positivity was more common (90.0% vs 64.3%, *P* = .043), and a Larsen score of grade 2 or higher was more frequently observed (92.3% vs 67.6%, *P* = .020) (Table 2).

Structure of Subchondral Cysts

The structure of the cysts were as follows; round 42 (42.8%), top-flattened ellipse 29 (29.6%), side-flattened ellipse 27 (27.6%). Horizontal length was mean (SD) 6.3 (2.7) mm, vertical length was mean (SD) 6.2 (2.3) mm. Horizontal/vertical length ratio was mean (SD) 1.06 (0.37). The mean (SD) area of the right dominant (n = 40) cyst was 38.7 (23.6) mm^2, the mean (SD) area of the right 2nd cyst (n = 14) was 27.8 (26.9) mm^2, the mean (SD) area of the left dominant (n = 35) cyst was 34.4 (27.2) mm^2, the mean (SD) area of the left 2nd cyst (n = 9) was 31 (24.3) mm^2. Patients with subchondral cysts larger than 50 mm^2 were more likely to

Table 2. Patient Features Regarding to Cyst Number and Cyst Area

	Number of Subchondral Cysts			Subchondral Cyst Area		
	One Cyst n = 37	More Than One Cyst n = 26	*P*	≥50 mm² n = 17	<50 mm² n = 46	*P*
Gender (male), n (%)	12 (32)	9 (35)	.85	11 (65)	10 (22)	.001
Age at the time of the most recent radiograph years year, mean (SD)	54.0 (12.2)	54.9 (12.8)	.85	57.5 (13.0)	53.2 (12.0)	.21
Anti-CCP positivity, n (%)	18 (64)	18/20 (69)	.04	11 (92)	25 (69)	.12
RF positivity, n (%)	23 (64)	21 (81)	.14	11 (69)	33 (72)	.82
Smoking*, (Ever), n(%)	21 (60)	11 (42)	.17	13 (76)	19 (43)	.02
BMI*, mean (SD)	29.8 (6.6)	28.4 (5.4)	.45	32.1 (7.2)	28.0 (5.3)	.04
DAS-28*, mean (SD)	3.42 (1.59)	3.11 (1.30)	.45	3.02 (1.46)	3.40 (1.49)	.50
HAQ-DI*, mean (SD)	0.78 (0.68)	0.67 (0.62)	.54	0.73 (0.73)	0.73 (0.63)	.99
Carpal bone involvement (≥ grade2), n(%)	25 (68)	24 (92)	.02	11 (65)	38 (83)	.13
Right RS distance (mm), mean (SD)	13.0 (7.7)	9.1 (5.7)	.03	1.17 (0.53)	1.12 (0.77)	.83
Right RL distance (mm), mean (SD)	12.1 (7.2)	9.3 (7.2)	.14	1.19 (0.62)	1.06 (0.72)	.54
Left RS distance (mm), mean (SD)	12.6 (7.2)	10.2 (7.9)	.22	1.19 (0.55)	1.15 (0.82)	.87
Left RL distance (mm), mean (SD)	12.4 (7.5)	9.3 (7.9)	.11	1.08 (0.72)	1.12 (0.80)	.84

Percentages presented are valid percents.
Anti-CCP, anti-cyclic citrullinated peptide; BMI, body mass index; DAS 28, Disease Activity Score in 28 Joints; RF, rheumatoid factor; RL, radio-lunate; RS, radioscaphoid.
*The assessments are done at baseline visits.

be male (64.7% vs 21.7%, *P* = .001) and had a higher prevalence of smoking (76.5% vs 43.2%, *P* = .020) (Table 2).

Change of Subchondral Cysts at Follow-Up

About 34/63 (53.9%) patients had more than 1 hand radiograph. The interval between the first and last radiographs of these 34 patients was mean (SD) 6.2 (3.2) years. Subchondral cysts progressed in 14 (41.2%), regressed in 11 (32.4%), remained the same in 7 (20.6%), regressed/progressed in 2 (5.8%).

Discussion

The frequency of subchondral cysts in the radius on conventional radiographs in RA patients using biological DMARDs is 14.1%. Subchondral radius cysts are more common in RA patients with advanced age, males, anti-CCP positive patients, patients with a long duration of time until bDMARD initiation and RA patients with more prominent carpal bone involvement. Although subchondral cysts are usually unilateral and single, they can be bilateral in one-fifth of patients. Cysts are more frequently seen in the middle (median) region of the radius. The area of the cyst is larger in males, anti-CCP positive patients and smokers.

Subchondral cysts may occur in different joint regions in RA patients. Geodes have been reported most frequently in large joints such as the knee and hip.[1] The presence of these cysts in the radius has been known for a long time.[3] It may be difficult to differentiate small sized geodes with conventional radiographs. As a matter of fact, in the study, approximately 5% of the patients could not be clearly differentiated. There are not many studies involving computed tomography (CT)/magnetic resonance imaging (MRI), one of the more advanced imaging modalities, in this patient group; there are only case reports. Although there are not many comprehensive studies on these geodes, it is almost a rule that they cause significant remodelling and destruction in the joint. The main pathogenetic event in RA and geodes patients is thought to be the growth of pannus tissue like a tumoral tissue.[1,10] With pannus tissue, the cartilage is completely destructed and a hole is formed in the subchondral and epiphyseal area.[1] This was also demonstrated by MRI in 1 case.[2] This hole is filled with debris and causes radiolucent appearance radiographically and pseudocyst formation in pathological examination. According to the generally accepted opinion, geodes occur in areas subjected to significant pressure.[1] In this study, it was observed that geodes formed most prominently in the central part of the radius. On the other hand, since these cysts can also occur in the medial and lateral part of the radius, it can be considered that other factors other than mechanical pressure effect may also play a role.

There are some known risk factors for the development of erosive disease in RA patients. Age, gender, seropositivity, disease duration, smoking, BMI, presence of symmetrical polyarthritis, disease activity, functional status, extra-articular involvement and some genetic factors (such as shared epitope) have been defined.[11,12]In this study, there are some factors related to cyst development in the radius. Age and disease duration are the prominent factors in this respect. Anti-CCP positivity in RA patients are known risk factors for severe erosive joint involvement.[11] In this study, the development of geodes was more common in anti-CCP positive patients. The presence of more than 1 geodes and the detection of cysts with larger areas are seen especially in anti-CCP positive RA patients. Although there are reports that the development of erosive changes is more common in female patients, in this study, both the frequency and severity were more prominent in males.[12] There is a correlation between smoking, which is a well-known risk factor, and the larger area of the cysts.[12] There is a significant correlation between the prolongation of the time until the start of bDMARD and the development of geodes. In addition, radius geodes occur more frequently in patients with more severe carpal bone destruction. All these findings suggest that geodes develop in association with severe pannus tissue in accordance with previous data.[1,11] On the other hand, no cross-sectional difference was found between patients with and without geodes in terms of disease activity and function.

The detected geodes are usually single, bilateral in approximately one-fifth of the patients, usually in the middle region of the radius, both in the right and left hand, may be round or elliptical from the top or side, around 6 mm in diameter, with a radiographically prominent sclerosis area around it. These descriptions are

important because there is no previous systematic study on the structure and distribution of radius geodes. The fact that the radius geodes regressed in approximately one-third of the patients is also a very important finding. It is not known how to modify the treatment when these cysts are detected. At least in a certain group of patients, the fact that the diameter of the cysts regressed with advanced treatments suggests that they should be taken into consideration when making treatment decisions.

This study represents the first systematic evaluation of radius geodes in an RA cohort. However, several limitations should be acknowledged. A key limitation is the absence of a control group, which prevents direct comparisons with healthy individuals or patients with other types of inflammatory arthritis. Additionally, the potential impact of occupational or work-related factors on these changes was not assessed. Hand radiographs were obtained based on clinical necessity rather than a standardized study protocol, and treatment decisions were not influenced by radiographic findings. While disease activity and general function were evaluated using HAQ-DI, specific hand function assessments were not included. Furthermore, the relationship between these cysts and overall joint health, including their association with fractures and joint damage, was not explored in depth. Finally, the study did not utilize a gold-standard imaging method, such as MRI or CT, to confirm the nature of these cysts. Future research addressing these gaps would provide valuable insights.

In conclusion, among a cohort of RA patients receiving bDMARD treatment, geodes were present in the radius in 14.1% of cases. These cysts were predominantly located in the central region of the radius, typically single but bilateral in approximately one-fifth of patients, with a mean diameter of 6 mm. The correlation between the size and number of geodes, anti-CCP positivity, and gender suggests that these patients may represent a subgroup with a more erosive disease course.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by Ethics Committee of Hacettepe University (Approval No.: KA-22005; Date: 23.08.2022).

Informed Consent: Written informed consent was obtained from the participants who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – U.K., G.A.; Design – U.K., G.A.; Supervision – U.K.; Resources – U.K., G.A.; Materials – U.K., G.A.; Data Collection and/or Processing – U.K., G.A.; Analysis and/or Interpretation – U.K., G.A.; Literature Search – U.K., G.A.; Writing – U.K., G.A.; Critical Review – U.K.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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