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Radiographic Severity of Rheumatoid Arthritis in African-Americans: Results from the CLEAR Registry

S. Louis Bridges Jr., MD, PhD[1], **Zenoria L. Causey, MPH**[1], **Paula I. Burgos, MD**[1], **B. Quynh N. Huynh, MD**[1], **Laura B. Hughes, MD, MSPH**[1], **Maria I. Danila, MD, MSc**[1], **Amalia van Everdingen, MD, PhD**[2], **Stephanie Ledbetter, MS**[1], **Doyt L. Conn, MD**[3], **Ashutosh Tamhane, MD, MSPH**[1], **Andrew O. Westfall, MS**[1], **Beth L. Jonas, MD**[4], **Leigh F. Callahan, PhD**[4], **Edwin A. Smith, MD**[5], **Richard Brasington, MD**[6], **Larry W. Moreland, MD**[1,7], **Graciela S. Alarcón, MD, MPH**[1], and **Désirée M. van der Heijde, MD, PhD**[2]

[1]The University of Alabama at Birmingham, Birmingham, Alabama [2]Medical Center Haaglanden, The Hague, The Netherlands [3]Emory University, Atlanta, Georgia [4]The University of North Carolina, Chapel Hill, North Carolina [5]The Medical University of South Carolina, Charleston, South Carolina [6]Washington University at St. Louis, Missouri

Abstract

Objective—To describe radiographic changes in African-Americans with rheumatoid arthritis (RA) from the CLEAR (Consortium for the Longitudinal Evaluation of African-Americans with Early Rheumatoid Arthritis) Registry, a multicenter observational study.

Methods—Self-declared African-American patients, were enrolled in CLEAR I, a longitudinal cohort of early RA (disease duration <2 years) from 2000 to 2005; or in CLEAR II, a cross-sectional cohort (any disease duration), from 2006 to the present. Demographic and clinical data were obtained, and sets of hand/wrist and foot radiographs were scored using the modified Sharp/van der Heijde scoring system.

Results—A total of 357 and 418 patients, respectively, have been enrolled into CLEAR I and CLEAR II. We report here an interim analysis of radiographic severity in these patients. For the CLEAR I cohort, 294 patients had a mean radiographic score of 2.89 at the baseline visit; 32.0% showed either erosions (25.9%) or joint space narrowing (JSN) (19.4%). At the 36-month visit the mean score was 5.65; 44.2% had erosions, 41.5% JSN and 55.4% had either. Among those patients without radiographic damage at baseline, 18.9% had progressed at the 36-month visit, compared to 57.1% of those with baseline damage ($p<0.0001$). For the CLEAR II cohort, 167 patients with RA of any duration, 65.3% exhibited joint erosions, 65.3% JSN and 74.8% exhibited either. The mean radiographic score was 33.42.

Conclusion—This is the largest radiographic study of African American RA patients. Damage occurs early in the disease and is associated with radiographic progression at 3 years of disease duration. The CLEAR Registry will provide a valuable resource for future analyses of genetic, clinical, and environmental factors associated with radiographic severity of RA in African-Americans.

Address for Correspondence and Reprint Requests:, S. Louis Bridges, Jr., MD, PhD, The University of Alabama at Birmingham, 1530 3rd Avenue South, 210 SHEL, Birmingham, Alabama 35294-2182, Telephone: 205-934-7995, Fax: 205-996-6734, LBridges@uab.edu.
[7]Current Address: The University of Pittsburgh, Pittsburgh, Pennsylvania

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects 1.3 million Americans (1). It is characterized by inflammation of the synovial membrane and has a variable course ranging from self-limited to progressive destructive disease with a higher mortality rate than the general population (2). Patients with RA who develop erosions early in the course of their disease are more likely to rapidly progress to joint destruction and functional limitations (3;4). Radiographs of the hands and feet are typically scored for the presence of erosions and joint space narrowing (JSN) and when examined over time allow the assessment of disease progression (5).

RA progression has been extensively examined in many ethnic groups with the exception of the African American population. This population, often under represented in both observational studies and randomized clinical trials, needs to be evaluated in order to understand the disease course and the potential presence of ethnic-specific risk factors (6–8). To date, there have been few descriptions of the clinical features of RA in this racial/ethnic group. For example, data from a cross-sectional study of a convenience sample of 100 patients with established RA followed at a single institution suggested that the course of disease in African Americans was comparable to that of patients of European ancestry (Caucasian) (9).

Radiological features of RA have been examined in African descendants in several studies (10–15). In a British study, participants of black African descent displayed less severe radiographic damage than Caucasian patients. These investigators suggested that longitudinal studies in larger populations were needed to confirm or refute their findings (16). Thus, establishing a large registry of RA patients of African American ancestry is clearly required. To this end we have established the CLEAR registry. We have previously reported some of the genetic and clinical features of the longitudinal arm of the CLEAR registry (17;18); we now report the radiographic features of participants enrolled in both longitudinal and cross-sectional arms of the registry.

PATIENTS AND METHODS

Study population

The CLEAR Registry is a National Institute of Arthritis and Musculoskeletal and Skin Diseases-funded program which enrolls self-defined African Americans with RA as defined by the revised American Rheumatism Association (now the American College of Rheumatology [ACR]) criteria (19). This registry was approved by the Institutional Review Boards of the participating institutions: The University of Alabama at Birmingham (Birmingham, AL), Emory University (Atlanta, GA); The Medical University of South Carolina (Charleston, SC), The University of North Carolina at Chapel Hill (Chapel Hill, NC), and Washington University (St. Louis, MO). The University of Alabama at Birmingham is the Coordinating Center for the CLEAR Registry. These studies were conducted in accordance with the Declaration of Helsinki for the protection of human subjects in research and were carefully monitored by regulatory agencies.

CLEAR I. This longitudinal registry enrolled African Americans with early RA (disease duration less than 2 years) from 2000 until 2005. Patients with RA were identified through the practices of clinicians at each site. Comprehensive demographic, clinical and radiographic data were obtained from these patients at the baseline visit and at 36 and 60 months from disease onset, so the interval from the baseline visit to the subsequent visits vary some depending on disease duration at enrollment. Also current and previous drug treatments with disease-modifying anti-rheumatic drugs (DMARDs) and glucocorticoids

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were annotated. For information on data and materials available for research on these subjects, please refer to: http://www.dom.uab.edu/rheum/CLEAR%20home.htm

CLEAR II. This cross-sectional registry began enrolling African Americans with RA (without limits of disease duration) in 2006 and is still enrolling patients. Comprehensive demographic, clinical and radiographic data are collected from these patients at enrollment, with no follow-up visits. Current and previous drug treatments with DMARDs and glucocorticoids were noted as in CLEAR I.

Variables ascertained

The ACR core of set of variables (20) including the number of swollen joints, the number of painful joints and a pain scale were recorded at each visit. Functional status was assessed with the Health Assessment Questionnaire (HAQ); the HAQ is scored on a scale of 0–3, with higher scores indicating higher levels of disability (21). The intensity of their pain was assessed by scale between 0 and 10 (0: no pain; and 10: the worst possible pain). The Joint Alignment and Motion (JAM) scale is scored on a 5-point scale and it is based on an estimate of the percent of joint range of motion and alignment lost (22); thirty-two joints were assessed: bilateral wrists, thumb interphalangeal (IP) joints, proximal interphalangeal (PIP) joints 2–5, metacarpophalangeal (MCP) joints 1–5, great toe IP joint and metatarsophalangeal (MTP) joints 2–5. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) autoantibodies were examined as previously reported (23).

Radiographic Scores

CLEAR I and CLEAR II patients underwent radiographic evaluations of their hands/wrists (postero-anterior views) and feet (antero-posterior views). Radiographic films for the CLEAR I patients were obtained at baseline (< 2 years' disease duration) and at 36 and 60 months from disease onset, while they were obtained only at the intake visit in the CLEAR II patients. Study radiographs were submitted to the Coordinating Center where all identifying information was removed and the radiographs forwarded to be scored for erosions and joint space narrowing (JSN) by an experienced reader (AVE) blinded to all clinical and demographic data; Sharp's method as modified by van der Heijde was used to score the radiographs (24;25). This method assigns an erosion score (range 0–280) and JSN score (range 0–168) to each set of radiographs. The total score (range 0–448) is the sum of the erosion and JSN scores. The presence of erosions and JSN for each patient was defined by scores greater than zero (26).

Radiographs were categorized as not having damage (total score = 0) or having damage (total score > 0). Overall progression of radiographic damage in CLEAR I was defined by an increase in the Total Score of 0.083 units per month between the baseline visit and the 36-month visit or approximately 1 unit per year of follow up or 3 units in 36 months (27;28).

Statistical Analyses

Descriptive statistics were performed with frequencies (percentages), means (standard deviations), and medians (inter-quartile range) being reported. A comparison between the baseline characteristics of CLEAR I and CLEAR II patients was performed; categorical measures were compared using the Pearson Chi-square test whereas continuous measures were compared by independent t-tests and the non-parametric Wilcoxon Rank-sum test where appropriate. A two-tailed p value < 0.05 was chosen as statistically significant. To determine whether the progression of radiographic damage at 36-month visit was significant in CLEAR I patients, the Chi-square test for correlated proportions was used. A two-tailed p value of <0.05 was selected as indicative of statistical significance. The risk rate was

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calculated as the incidence of progression in those with a total score more than zero divided by incidence of progression in those with a total score equal to zero.

RESULTS

At the time of this interim analysis, a total of 357 and 418 patients had been enrolled in CLEAR I and II, respectively; baseline radiographic were available in 294 for CLEAR I and 167 for CLEAR II and are included in these analyses. The baseline socio-demographic variables for the total cohort are depicted in Table 1 and 2.

Baseline socio-demographic and clinical features

The baseline socio-demographic variables for those patients with radiographic data are shown in Table 1. The majority of patients were women (82.7% and 84.4%), with a mean [standard deviation (SD)] age at entry into the registry of 50.6 (13.5) and 56.2 (10.8) (p =0.0016) years, and mean (SD) age at RA onset of 49.6 (13.5) and 42.8 (12.4) years (CLEAR I and CLEAR II, respectively). The distribution of education level (3.8% and 6.3% for graduate and post-graduate) and poverty level (30.9% and 30.6%) were comparable in both groups. Family history of RA (29.9% and 43.1%) was higher in the CLEAR II (p=0.0043) than in the CLEAR I patients. Smoking, both current and ever, was comparable in both groups; current alcohol use was higher in CLEAR II (p = 0.0791). As expected, disease duration was significantly different for CLEAR I and CLEAR II patients [median (25%–75% Interquantiles (IQ): 12.1 months (6.8–19.1) and 126.0 months (61.0–223.0) (Wilcoxon Rank-sum, $p \leq 0.0001$), respectively].

The baseline clinical variables are depicted for patients with radiographic scores in Table 2. The median (25%–75%) for the HAQ for CLEAR I and II patients were 1.8 (0.9–2.4) and 2.0 (1.3–2.5) with a p value 0.0509. The median (25%–75%) number of tender joints was higher in CLEAR I [7.0 (2.0–18.0)] than CLEAR II [5.0 (2.0–12.0)] with a p= 0.0786, while the number of swollen joints was similar in CLEAR I [4.0 (1.0–8.0)] and CLEAR II [5.0 (0.0–13)]. The median (25%–75% IQ) scores for the JAM scale were 4.0 (0.0–14.0) in CLEAR I and 2.0 (0.0–13.0) in CLEAR II. The Pain scale was a median of 7.0 in both CLEAR I and II.

Rheumatoid factor-positivity (RF) was about 80% in both groups whereas anti-CCP antibody-positivity was significantly higher in CLEAR II (80.0%) than CLEAR I (61.3%) patients (p <0.0001). Approximately 84% of the patients were taking at least one DMARD; approximately 65% were taking methotrexate, while approximately 80% of patients had taken glucocorticoids.

Radiographic Assessment

The radiographic findings for patients in CLEAR I and II are depicted in Table 3. As noted, the CLEAR I analysis included 294 sets of baseline films; 147 sets of films at approximately 36 months of disease duration; and 39 sets of films at approximately 60 months of disease duration. At the baseline visit the mean (SD) and median (25%–75% IQ) erosion scores were 1.24 (3.68) and 0.0 (0–1) with 25.9% of the patients showing erosions; at the baseline visit the mean (SD) and median (25%–75% IQ) JSN scores were 1.65 (4.73) and 0.0 (0–0) with 19.4% displaying JSN; at this visit the mean (SD) and median (25%–75% IQ) total scores were 2.89 (7.65) and 0.0 (0–2) with 32.0% of the patients showing either erosions or JSN. At 36 months the mean (SD) and median (25%–75% IQ) erosion scores were 2.22 (5.72) and 0.0 (0–2) with 44.2% of the patients showing erosions, whereas the mean (SD) and median (25%–75% IQ) JNS scores were 3.44 (6.64) and 0.00 (0–4) with 41.5% of the patients displaying JSN; the mean (SD) and median (25%–75% IQ) total scores were 5.65

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(11.14) and 0.0 (0–6) with 54.4% of the patients showing either erosions or JSN. At approximately 60 months of disease duration for 39 patients in CLEAR I the mean (SD) and median (25%–75% IQ) erosion scores were 4.74 (12.78) and 0.0 (0–4) with 38.5% of the patients showing erosions, whereas the mean (SD) and median (25%–75% IQ) JSN scores were 7.87 (13.12) and 0.0 (0–12) with 46.2% of the patients showing JSN; the mean (SD) and median (25%–75% IQ) total scores were 12.62 (24.95) and 0.0 (0–16) with 53.8% of the patients showing either erosions or JSN.

The radiographic findings for 167 CLEAR II patients are also shown in Table 3. The mean (SD) and median (25%–75% IQ) erosion scores were 14.68 (23.84) and 4.0 (0–18) with 65.3% of the patients showing erosions; the mean (SD) and median (25%–75% IQ) JSN scores were 18.74 (26.48) and 7.0 (0–24) with 65.3% of the patients showing JSN; finally, the mean (SD) and median (25%–75% IQ) total scores were 33.42 (48.89) and 11.0 (0–41) with 74.8% of the patients showing either erosions or JSN.

Of the 147 CLEAR I patients with radiographs at 36 months, three could not be included in the assessment of progression because they lacked baseline films. Overall, 31.9% of the patients had progressed; of those patients without damage at baseline, 18.9 % had progressed; of those with damage at baseline 57.1% had progressed. The difference between these two groups was significant with a Wilcoxon Rank-sum p value <0.0001. These data are depicted in Table 4. The scores differences [median (25%–75% IQ)] between the baseline and 36 months were 0.0 (0.0–2.0) and 3.0 (0.0–7.0) for those without damage at baseline and those with damage, respectively, (Wilcoxon rank-sum p<0.0001). The risk ratio for baseline damage versus no baseline damage was 3.02 (95% CI: 1.86 –4.88).

DISCUSSION

This is the largest radiographic study of RA patients of African American ancestry conducted to date; we have had the unique ability to study structural joint damage longitudinally in patients with early RA, as well as cross-sectionally in those with longstanding disease. Not surprisingly, damage occurs early in the course of the disease, and it is the harbinger of further damage in these patients with a risk ratio of about 3. Thus, RA in the African American population behaves similarly to other ethnic groups (3;29).

In this study, we have examined two important variables: when joints show erosions or JSN for the first time; and whether or not joint damage increases over the time (30). The majority of patients from CLEAR I, the longitudinal cohort, did not exhibit radiographic damage at baseline (68%) as has been shown in other studies (29;31–33); patients who manifest damage have more frequent erosions than JSN. These findings are consistent with observations described by other investigators suggesting that bone degradation occurs earlier than cartilage degradation or can be seen earlier on radiographs (26;30;34).

Other studies have reported different rates of erosive disease. For example, in one study of patients with early RA (< 2 years disease duration), erosive disease was found in 21.7% of subjects; one-year radiographic progression (defined as an increase in Larsen score of ≥ 2) occurred in 36.6% of these patients (29). Patients of black African descent who did not declare themselves as African-American were not included in this study. In another study involving 55 patients with less than 3 months of symptoms, erosive disease was present at baseline in 7.2%, after one year in 47%, and at 3 years in 63.6% (35). It should be noted that the scoring method used was different from that used in our analysis, and most of the patients were of European ancestry. Thus, although the prevalence of erosive disease at baseline in our study was comparable to that reported in studies of patients of different ethnicities (29;31;32;35), the rate of erosions and JSN reported in other studies is widely

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variable, between 21% and 67% (29;36–38). This variability probably reflects differences in inclusion criteria (e.g. presence of rheumatoid factor); radiographic scoring method; disease duration; medication use; geographic region; and other potential confounders (12–14). Sample size is likely a major determinant of the large variation in radiographic damage among African-Americans with RA; many of the radiographic studies had 100 patients or fewer, (9;14–16) limiting conclusions to be drawn from these studies.

Even though relatively few CLEAR subjects have had their 60 month follow up visit to date, our long-term data are consistent with those from other studies, in that radiographic progression occurs early in the course of disease (33;35;39–41). Lindqvist *et al.* described that among 181 patients with early RA, the most rapid radiological progression occurred during the first two years of disease; 75% of all damage occurred during the first five years; and after 10 years 90% of the patients had erosions (Larsen and Dale scoring method) (36). We will re-examine five year radiographic data when the majority of the CLEAR patients reach this time point.

Of interest, a considerable proportion of CLEAR patients developed damage or progressed despite the use of drug therapy that appears to be appropriate for RA, predominantly methotrexate. Problems with treatment adherence could explain these observations (42). This study reinforces the notion that aggressive treatment is needed for patients with RA from disease onset and the African American patient population is not an exception.

Some limitations of this study are worth noting. Firstly, not all patients have had their 36 and 60-month visits, which limits the conclusions that can be drawn about progression during the first 5 years of RA in this population, and 63 patients' baseline radiographic data were not available due to operational issues. Secondly, by design, longitudinal data are not available in CLEAR II participants, so we cannot compare their rates of radiographic progression to those with early RA in CLEAR I. Thirdly, this is an interim analysis of the initial 167 patients (of a total of ~600 to be enrolled) in CLEAR II; however, we do not think the data for those patients will be substantially different since most recruited patients tend to have established disease (mean ~12 years disease duration). Fourthly, we have not considered other factors (genetic, autoantibody presence, disease duration, use of specific medications, etc.) that can account for the rate of radiographic progression in African American patients with early RA; we plan to conduct such studies in near future.

In summary, we present detailed, cross sectional and longitudinal, radiographic data in the largest cohort of African American RA patients reported to date. We have shown that African Americans with early and established RA have rates of joint damage comparable with those of patients from other ethnic groups, and that early damage heralds disease progression, suggesting that African-American patients with early disease (as is the case with other races/ethnicities) should be treated aggressively to attempt to halt radiographic progression.

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References

1. Lawrence RC, Helmick CG, Arnett FC, Deyo RA, Felson DT, Giannini EH, et al. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. Arthritis Rheum 1998;41:778–799. [PubMed: 9588729]
2. Pincus T, Sokka T, Wolfe F. Premature mortality in patients with rheumatoid arthritis: evolving concepts. Arthritis Rheum 2001;44(6):1234–1236. [PubMed: 11407680]
3. Scott DL. Prognostic factors in early rheumatoid arthritis. Rheumatology (Oxford) 2000;39 Suppl 1:24–29. [PubMed: 11001376]
4. Aletaha D, Smolen J, Ward MM. Measuring function in rheumatoid arthritis: Identifying reversible and irreversible components. Arthritis Rheum 2006;54(9):2784–2792. [PubMed: 16947781]
5. Sharp JT, Young DY, Bluhm GB, Brook A, Brower AC, Corbett M, et al. How many joints in the hands and wrists should be included in a score of radiologic abnormalities used to assess rheumatoid arthritis? Arthritis Rheum 1985;28:1326–1335. [PubMed: 4084327]
6. Austin JS, Ambrose RF, Young PK, Moreland LW, Alarcón GS. Rheumatoid arthritis patients and clinical drugs trials: A case-control study. Arthritis Care Res 1991;4(1):22–26. [PubMed: 11188582]
7. Alarcón GS, Barger BO, Acton RT, Koopman WJ. HLA antigens and gold toxicity in American blacks with rheumatoid arthritis. Rheumatol Int 1986;6:13–17. [PubMed: 3466334]
8. Alarcón GS, Koopman WJ, Acton RT, Barger BO. DR antigen distribution in blacks with rheumatoid arthritis. J Rheumatol 1983;10:579–583. [PubMed: 6604813]
9. Lopez-Mendez A, Paul WA, Alarcon GS. Rheumatoid arthritis in American blacks: a clinical and radiological study. J Rheumatol 1989;16(9):1197–1200. [PubMed: 2810275]
10. Mody GM, Meyers OL. Rheumatoid arthritis in blacks in South Africa. Ann Rheum Dis 1989;48(1):69–72. [PubMed: 2923506]
11. Beighton P, Solomon L, Valkenburg HA. Rheumatoid arthritis in a rural South African Negro population. Ann Rheum Dis 1975;34(2):136–141. [PubMed: 1137440]
12. Solomon L, Robin G, Valkenburg HA. Rheumatoid arthritis in an urban South African Negro population. Ann Rheum Dis 1975;34(2):128–135. [PubMed: 1137439]
13. Anaya JM, Correa PA, Mantilla RD, Jimenez F, Kuffner T, McNicholl JM. Rheumatoid arthritis in African Colombians from Quibdo. Sem Arthritis Rheum 2001;31(3):191–198.
14. Maritz NG, Gerber AJ, Greyling SJ, Sandra BB. A radiological study of the rheumatoid hand in black South Africans. S Afr Med J 2005;95(10):795–797. [PubMed: 16341335]
15. Chikanza IC, Stein M, Lutalo S, Gibson T. The clinical, serologic and radiologic features of rheumatoid arthritis in ethnic black Zimbabwean and British Caucasian patients. J Rheumatol 1994;21(11):2011–2015. [PubMed: 7869302]
16. Ravindran V, Seah MA, Elias DA, Choy EH, Scott DL, Gordon PA. Clinical and radiological features of rheumatoid arthritis in British black Africans. Clin Rheumatol 2008;27(1):97–100. [PubMed: 17932617]

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17. Hughes LB, Morrison D, Kelley JM, Padilla MA, Vaughan LK, Westfall AO, et al. The HLA-DRB1 shared epitope is associated with susceptibility to rheumatoid arthritis in African Americans through European genetic admixture. Arthritis Rheum 2008;58(2):349–358. [PubMed: 18240241]
18. Mikuls TR, Hughes LB, Westfall AO, Holers VM, Parrish L, van der HD, et al. Cigarette smoking, disease severity and autoantibody expression in African Americans with recent-onset rheumatoid arthritis. Ann Rheum Dis 2008;67(11):1529–1534. [PubMed: 18198196]
19. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315–324. [PubMed: 3358796]
20. Felson DT, Anderson JJ, Boers M, Bombardier C, Chernoff M, Fried B. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum 1993;36:729–740. [PubMed: 8507213]
21. Fries JF, Spitz P, Kraines G, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137–145. [PubMed: 7362664]
22. Spiegel TM, Spiegel JS, Paulus HE. The joint alignment and motion scale: a simple measure of joint deformity in patients with rheumatoid arthritis. J Rheumatol 1987;14(5):887–892. [PubMed: 3430519]
23. Mikuls TR, Holers VM, Parrish L, Kuhn KA, Conn DL, Gilkeson G, et al. Anti-cyclic citrullinated peptide antibody and rheumatoid factor isotypes in African Americans with early rheumatoid arthritis. Arthritis Rheum 2006;54(9):3057–3059. [PubMed: 16948136]
24. van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. J Rheumatol 2000;27:261–263. [PubMed: 10648051]
25. van der Heijde DM, van Riel PL, Nuver-Zwart IH, Gribnau FW, vad de Putte LB. Effects of hydroxychloroquine and sulphasalazine on progression of joint damage in rheumatoid arthritis. Lancet 1989;1(8646):1036–1038. [PubMed: 2565997]
26. Smolen JS, van der Heijde DM, Aletaha D, Xu S, Han J, Baker D, et al. Progression of radiographic joint damage in rheumatoid arthritis: Independence of erosions and joint space narrowing. Ann Rheum Dis. 2008
27. Syversen SW, Goll GL, van der HD, Landewe R, Gaarder PI, Odegard S, et al. Cartilage and bone biomarkers in rheumatoid arthritis: prediction of 10-year radiographic progression. J Rheumatol 2009;36(2):266–272. [PubMed: 19132792]
28. Bruynesteyn K, van der Heijde D, Boers M, Saudan A, Peloso P, Paulus H, et al. Determination of the minimal clinically important difference in rheumatoid arthritis joint damage of the Sharp/van der Heijde and Larsen/Scott scoring methods by clinical experts and comparison with the smallest detectable difference. Arthritis Rheum 2002;46(4):913–920. [PubMed: 11953967]
29. Sanmarti R, Gomez A, Ercilla G, Gratacos J, Larrosa M, Suris X, et al. Radiological progression in early rheumatoid arthritis after DMARDS: a one-year follow-up study in a clinical setting. Rheumatol 2003;42(9):1044–1049.
30. van der HD, Boonen A, Boers M, Kostense P, van der LS. Reading radiographs in chronological order, in pairs or as single films has important implications for the discriminative power of rheumatoid arthritis clinical trials. Rheumatology (Oxford) 1999;38(12):1213–1220. [PubMed: 10587548]
31. Mottonen TT. Prediction of erosiveness and rate of development of new erosions in early rheumatoid arthritis. Ann Rheum Dis 1988;47:648–653. [PubMed: 3137902]
32. Paimela L, Heiskanen A, Kurki P, Helve T, Leirisalo-repo M. Serum hyaluronate level as a predictor of radiologic progression in early rheumatoid arthritis. Arthritis Rheum 1991;34(7):815–821. [PubMed: 2059229]
33. Fex E, Jonsson K, Johnson U, Eberhardt K. Development of radiographic damage during the first 5–6 yr of rheumatoid arthritis. A prospective follow-up study of a Swedish cohort. Br J Rheumatol 1996;35(11):1106–1115. [PubMed: 8948297]
34. Redlich K, Hayer S, Maier A, Dunstan CR, Tohidast-Akrad M, Lang S, et al. Tumor necrosis factor alpha-mediated joint destruction is inhibited by targeting osteoclasts with osteoprotegerin. Arthritis Rheum 2002;46(3):785–792. [PubMed: 11920416]

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35. Machold KP, Stamm TA, Nell VP, Pflugbeil S, Aletaha D, Steiner G, et al. Very recent onset rheumatoid arthritis: clinical and serological patient characteristics associated with radiographic progression over the first years of disease. Rheumatology (Oxford) 2007;46(2):342–349. [PubMed: 16899498]

36. Lindqvist E, Jonsson K, Saxne T, Eberhardt K. Course of radiographic damage over 10 years in a cohort with early rheumatoid arthritis. Ann Rheum Dis 2003;62(7):611–616. [PubMed: 12810421]

37. Higami K, Hakoda M, Matsuda Y, Ueda H, Kashiwazaki S. Lack of association of HLA-DRB1 genotype with radiologic progession in Japanese patients with early rheumatoid arthritis. Arthritis Rheum 1997;40:2241–2247. [PubMed: 9416863]

38. Richi P, Balsa A, Muñoz-Fernández S, Villaverde V, Fernández-Prada M, Vicario JL, et al. Factors related to radiological damage in 61 Spaniards with early rheumatoid arthritis. Ann Rheum Dis 2002;61:270–272. [PubMed: 11830438]

39. van der Heijde DM, van Leeuwen MA, van Riel PL, Koster AM, 't Hof MA, van Rijswijk MH, et al. Biannual radiographic assessments of hands and feet in a three-year prospective followup of patients with early rheumatoid arthritis. Arthritis Rheum 1992;35(1):26–34. [PubMed: 1731813]

40. Welsing PM, van Gestel AM, Swinkels HL, Kiemeney LA, van Riel PL. The relationship between disease activity, joint destruction, and functional capacity over the course of rheumatoid arthritis. Arthritis Rheum 2001;44(9):2009–2017. [PubMed: 11592361]

41. Bruynesteyn K, van der HD, Boers M, Verhoeven A, Boonen A, van der LS. Contribution of progression of erosive damage in previously eroded joints in early rheumatoid arthritis trials: COBRA trial as an example. Arthritis Rheum 2002;47(5):532–536. [PubMed: 12382303]

42. Garcia-Gonzalez A, Richardson M, Garcia Popa-Lisseanu M, Cox V, Kallen MA, Janssen N, et al. Treatment adherence in patients with rheumatoid arthritis and systemic lupus erythematosus. Clin Rheumatol 2008;27(7):883–889. [PubMed: 18185905]

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Table 1

Baseline Socio-Demographic Variables of African American Patients with Rheumatoid Arthritis (RA) from the CLEAR Registry*

Variable	Total Cohort			Subset with Radiographic Scores		
	CLEAR I n=357	CLEAR II n=418	*p* value†	CLEAR I n=294	CLEAR II n=167	*p* value†
Age at enrollment, years, mean (SD)	51.0 (13.2)	56.9 (11.6)	0.0103	50.6 (13.5)	56.2 (10.8)	0.0016
Age at RA onset, mean (SD)	50.0 (13.2)	45.0 (13.0)	0.7035	49.6 (13.5)	42.8 (12.4)	0.2290
Gender (female), %	82.4	87.3	0.0533	82.7	84.4	0.6228
Disease duration at enrollment, months, median (IQ 25–75)	11.5 (6.3–17.9)	108.0 (40.0–213.0)	<0.0001	12.1 (6.8–19.1)	126.0 (61.0–223.0)	<0.0001
Education, %			0.5613			0.4284
Elementary	7.8	5.7		8.0	5.0	
High school	51.2	49.4		50.2	52.2	
College	36.7	40.0		38.0	36.5	
Graduate and postgraduate	4.3	4.9		3.8	6.3	
Poverty‡, %	31.0	33.7	0.4409	30.9	30.6	0.9426
Family history of RA§ %	31.4	38.8	0.0321	29.9	43.1	0.0043
Smoking¶						
current %	29.1	24.2	0.1180	28.9	23.4	0.1958
ever %	52.7	55.0	0.5107	52.7	56.3	0.4602
Alcohol¶						
current %	16.8	22.5	0.0482	16.7	23.4	0.0791
ever %	65.8	73.2	0.0257	66.7	73.7	0.1184

*The CLEAR Registry is still actively collecting radiographs at 36 months and 60 months disease duration in CLEAR I and at study entry in CLEAR II. Thus, radiographic scores are not available for all subjects at the present time;

†*p*-value calculated by Chi-square or Wilcoxon Rank-sum;

‡Poverty as per the US Federal government guidelines adjusted for the number of persons in the household;

§First degree (including mother, father, or sibling);

¶Any time (Yes or No).

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Table 2

Baseline Clinical Variables of African American Patients with RA from the CLEAR Registry*

Variable	Total Cohort			Subset with Radiographic Scores		
	CLEAR I n=357	CLEAR II n=418	*p* value†	CLEAR I n=294	CLEAR II n=167	*p* value†
HAQ‡ Score, median (IQ 25–75)	1.8 (0.0–2.4)	2.0 (0.0–3.0)	0.0037	1.8 (0.9–2.4)	2.0 (1.3–2.5)	0.0509
JAM § Score, median (IQ 25–75)	4.0 (0.0–14.0)	2.0 (0.0–14.0)	0.0313	4.0 (0.0–14.0)	2.0 (0.0–13.0)	0.1381
Number of tender joints, median (IQ 25–75)	8.0 (2.0–19.0)	6.0 (2.0–14.0)	0.0286	7.0 (2.0–18.0)	5.0 (2.0–12.0)	0.0786
Number of swollen joints, median (IQ 25–75)	4.0 (1.0–10.0)	5.0 (1.0–12)	0.1642	4.0 (1.0–8.0)	5.0 (0.0–13.0)	0.2681
Pain scale¶ (0–10 cm), median (IQ 25–75)	7.0 (4.0–8.0)	7.0 (5.0–8.0)	0.3062	7.0 (4.0–8.0)	7.0 (4.0–9.0)	0.5795
Laboratory						
Rheumatoid factor, % positive	80.1	79.7	0.8953	77.3	84.1	0.1080
Anti-CCP** antibodies, % positive	63.4	75.1	0.0007	61.3	80.0	<0.0001
Medications						
Glucocorticoids, ever used%	77.8	79.9	0.4713	79.3	80.9	0.6833
DMARDs††, current use%	81.8	83.3	0.5930	84.4	83.8	0.8828
Methotrexate, current use%	62.5	61.6	0.8026	63.6	66.0	0.6057

*The CLEAR Registry is still actively collecting radiographs at 36 months and 60 months in CLEAR I and at study entry in CLEAR II. Thus, radiographic scores are not available for all subjects at the present time;

†*p*-value calculated by Chi-square or Wilcoxon Rank-sum;

‡Health Assessment Questionnaire;

§Joint Alignment and Motion;

¶Pain scale (0–10);

**Anti-cyclic citrullinated peptide second generation;

††Disease- modifying anti-rheumatic drugs (DMARDs) (shown in Appendix 1).

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Table 3

Radiographic* Findings for Patients in the CLEAR I (Baseline, 36 month and 60 months) and CLEAR II (Baseline).

	Number of patients (%)	Sharp van der Heijde Score Mean (SD)	Sharp van der Heijde Score Median (IQ 25–75))
CLEAR I †			
Baseline (n=294)			
Joint Erosions	76 (25.9)	1.24 (3.68)	0.0 (0–1)
Joint Space Narrowing	57 (19.4)	1.65 (4.73)	0.0 (0–0)
Total Score	94 (32.0)	2.89 (7.65)	0.0 (0–2)
36 months (n=147)			
Joint Erosions	65 (44.2)	2.22 (5.72)	0.0 (0–2)
Joint Space Narrowing	61 (41.5)	3.44 (6.64)	0.0 (0–4)
Total Score	80 (54.4)	5.65 (11.14)	0.0 (0–6)
60 months (n=39)			
Joint Erosions	15 (38.5)	4.74 (12.78)	0.0 (0–4)
Joint Space Narrowing	18 (46.2)	7.87 (13.12)	0.0 (0–12)
Total Score	21 (53.8)	12.62 (24.95)	0.0 (0–16)
CLEAR II (n=167)‡			
Joint Erosions	109 (65.3)	14.68 (23.84)	4.0 (0–18)
Joint Space Narrowing	109 (65.3)	18.74 (26.48)	7.0 (0–24)
Total Score	125 (74.8)	33.42 (48.89)	11.0 (0–41)

*Sharp van der Heijde;

†Follow up totals differs from baseline due to loss to follow up and patients who had not yet reached their time planned visits,

‡Study enrolment ongoing.

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Table 4

Radiographic Progression* at 36 Months (n=144†) in Patients from the CLEAR I Registry.

	Progression*	
Baseline Damage	**Yes (%)**	**No (%)**
Yes (total score >0)	28 (57.1)‡	21 (42.9)
No (total score = 0)	18 (18.9)‡	77 (81.1)

*Defined as an increase of 0.083 per month of Total Sharp van der Heijde Score from the baseline visit;

†Three patients were excluded as they lacked baseline radiographs;

‡*p*-value <0.0001 (*Chi* square = 21.7)

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Appendix 1

Medications Used by Any Patient in CLEAR I or CLEAR II

CLEAR I	CLEAR II
Hydroxychloroquine	Hydroxychloroquine
Leflunomide	Leflunomide
Methotrexate	Methotrexate
Azathioprine	Azathioprine
Cyclophosphamide	Cyclophosphamide
Cyclosporin	Cyclosporin
Gold salts either Shot or tablets	Gold salts either Shot or tablets
Penicillamine	Penicillamine
Sulfasalazine	Sulfasalazine
Infliximab	Minocycline
Etanercept	Infliximab
Anakinra	Etanercept
	Anakinra
	Adalimumab
	Rituximab