Arthritis Care & Research
Vol. 62, No. 5, May 2010, pp 624–631
DOI 10.1002/acr.20040
© 2010, American College of Rheumatology

ORIGINAL ARTICLE

Radiographic Severity of Rheumatoid Arthritis in African Americans: Results From a Multicenter Observational Study

S. LOUIS BRIDGES, JR.,[1] ZENORIA L. CAUSEY,[1] PAULA I. BURGOS,[2] B. QUYNH N. HUYNH,[1] LAURA B. HUGHES,[1] MARIA I. DANILA,[1] AMALIA VAN EVERDINGEN,[3] STEPHANIE LEDBETTER,[1] DOYT L. CONN,[4] ASHUTOSH TAMHANE,[1] ANDREW O. WESTFALL,[1] BETH L. JONAS,[5] LEIGH F. CALLAHAN,[5] EDWIN A. SMITH,[6] RICHARD BRASINGTON,[7] LARRY W. MORELAND,[1] GRACIELA S. ALARCÓN,[1] AND DÉSIRÉE M. VAN DER HEIJDE[8]

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

Methods. **Self-declared African American patients were enrolled in CLEAR I, a longitudinal cohort of early RA (disease duration of <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 were enrolled in CLEAR I and CLEAR II, respectively. 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% had JSN, and 54.4% had either. Among those patients without radiographic damage at baseline, 18.9% had progressed at the 36-month visit, compared with 57.1% of those with baseline damage ($P < 0.0001$). For the CLEAR II cohort, of 167 patients with RA of any duration, 65.3% exhibited joint erosions, 65.3% exhibited JSN, and 74.8% exhibited either. The mean radiographic score was 33.42.**

Conclusion. **To our knowledge, 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.**

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

Supported by the NIH (contract N01-AR-02247 and grant P60-AR48095 to the University of Alabama at Birmingham Multidisciplinary Clinical Research Center) and grants from the General Clinical Research Centers to the University of Alabama at Birmingham (M01-RR-00032), Emory University/Grady Hospital (M01-RR-00039), the University of North Carolina (M01-RR-00046), and the Medical University of South Carolina (M01-RR-01070). Dr. Burgos's work was supported by the Programa de Postgrado Beca Chile.

[1]S. Louis Bridges, Jr., MD, PhD, Zenoria L. Causey, MPH, B. Quynh N. Huynh, MD, Laura B. Hughes, MD, MSPH, Maria I. Danila, MD, MSc, Stephanie Ledbetter, MS, Ashutosh Tamhane, MD, MSPH, Andrew O. Westfall, MS, Larry W. Moreland, MD (current address: University of Pittsburgh, Pittsburgh, Pennsylvania), Graciela S. Alarcón, MD, MPH: University of Alabama, Birmingham; [2]Paula I. Burgos, MD: University of Alabama, Birmingham, and Pontifica Universidad Catolica de Chile, Santiago, Chile; [3]Amalia van Everdingen, MD, PhD: Medical Center Haaglanden, The Hague, The Netherlands; [4]Doyt L. Conn, MD: Emory University, Atlanta, Georgia; [5]Beth L. Jonas, MD, Leigh F. Callahan, PhD: The University of North Carolina, Chapel Hill; [6]Edwin A. Smith, MD: The Medical University of South Carolina, Charleston; [7]Richard Brasington, MD: Washington University, St. Louis, Missouri; [8]Désirée M. van der Heijde, MD, PhD: Leiden University Medical Center, Leiden, The Netherlands.

Dr. Brasington has received consultant fees, speaking fees,

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 underrepresented 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 (6–9). 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 with that of patients of European ancestry (white) (10).

Radiologic features of RA have been examined in African descendants in several studies (11–16). In a British study, participants of black African descent displayed less severe radiographic damage than white patients. These investigators suggested that longitudinal studies in larger populations were needed to confirm or refute their findings (17). Therefore, establishing a large registry of RA patients of African American ancestry is clearly required. To this end, we have established the Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis (CLEAR) Registry. We have previously reported some of the genetic and clinical features of the longitudinal arm of the CLEAR registry (18,19); 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 that enrolls patients with RA as defined by the revised American College of Rheumatology (ACR; formerly the American Rheumatism Association) criteria (20), age ≥19 years, and self-defined as African American. This registry was approved by the Institutional Review Boards of the participating institutions: the University of Alabama at Birmingham (Birmingham, Alabama), Emory University (Atlanta, Georgia), The Medical University of South Carolina (Charleston, South Carolina), The University of North Carolina at Chapel Hill (Chapel Hill, North Carolina), and Washington University (St. Louis, Missouri). 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 <2 years) from 2000 until 2005. Patients with RA were identified through the practices of the clinicians at each site. Comprehensive demographic, clinical, and radiographic data were obtained from these patients by interviews and examinations performed by trained study coordinators and investigators at each site during the baseline visit and at 36 and 60 months from disease onset; therefore, the interval from the baseline visit to the subsequent visits varies some depending on disease duration at enrollment. Also, information on current and previous drug treatments with disease-modifying antirheumatic drugs (DMARDs) and glucocorticoids was extracted from the medical records or during the patient's interview with the study physician (SLB, DLC, BLJ, EAS, or RB). For information on data and materials available for research on these subjects, please refer to: http://medicine.uab.edu/rheum/70918/.

CLEAR II. This cross-sectional registry began enrolling African Americans with RA (without limits of disease duration) in 2006 and is still enrolling patients. As in CLEAR I, comprehensive demographic, clinical, and radiographic data were obtained by interviews and examinations performed by trained study coordinators and investigators at each site during the enrollment study visits; no followup visits were performed. Current and previous drug treatments with DMARDs and glucocorticoids were noted, as in CLEAR I.

Subjects enrolled in CLEAR I were not eligible for enrollment in CLEAR II, so there is no overlap between the patients in CLEAR I and CLEAR II.

Variables ascertained. The ACR core set of variables (21), including the number of swollen joints, the number of painful joints (ascertained by study physicians or coordinators), 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 (22). The intensity of the patients' pain was assessed with a 10-cm visual analog scale (VAS), where 0 = no pain and 10 = the worst possible pain. The HAQ and VAS were self-administered during the patients' scheduled visits. The Joint Alignment and Motion (JAM) scale is scored on a 5-point scale, and it is based on an estimate of the percentage of joint range of motion and alignment lost

and/or honoraria (less than $10,000 each) from BMS, UCB, and Abbott, and (more than $10,000) from Centocor, and has served as a paid investment consultant for Guidepoint Global and Gerson Lehrman. Dr. van Everdingen has received a fee (less than $10,000) from the Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis Study for reading hand and foot radiographs.

Address correspondence to S. Louis Bridges, Jr., MD, PhD, The University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Shelby Biomedical Research Building, Room 178, 1825 University Boulevard, Birmingham, AL 35294-2182. E-mail: LBridges@uab.edu.

Submitted for publication June 2, 2009; accepted in revised form December 24, 2009.

(23). The examiner visually estimates whether a joint is normal in both motion and alignment or limited by quartiles. After each separate joint is assigned an individual JAM score, the total JAM score is calculated as the mean of all 44 joints examined. Shoulders, elbows, bilateral wrists, thumb interphalangeal (IP) joints, proximal interphalangeal joints 2–5, metacarpophalangeal joints 1–5, great toe IP joint and metatarsophalangeal joints 2–5, hips, knees, ankles, and subtalar joints were assessed at baseline. This instrument can be completed in approximately 5 minutes, providing a single numerical estimate of the degree of deformity of all or selected joints; it is strongly associated with disease severity, functional class, and radiographic progression (24). Rheumatoid factor (RF) and anti–cyclic citrullinated peptide (anti-CCP) autoantibodies were examined as previously reported and they were assayed at the coordinator center (25).

Radiographic scores. CLEAR I and CLEAR II patients underwent radiographic evaluations of their hands/wrists (posteroanterior views) and feet (anteroposterior views). Radiographic films for the CLEAR I patients were obtained at baseline (<2 years of disease duration) and at 36 and 60 months from disease onset, whereas they were obtained only at the intake visit in the CLEAR II patients. Study radiographs were submitted to the coordinating center, where all of the identifying information was removed and the radiographs were forwarded to be scored for erosions and JSN by an experienced reader (AvE) at the Medical Center Haaglanden, The Hague, The Netherlands, who was blinded to all clinical and demographic data; the Sharp method as modified by van der Heijde was used to score the radiographs (26,27). 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 (28).

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 followup or 3 units in 36 months (29,30).

Statistical analyses. Descriptive statistics were performed with the frequency (percentage), mean ± SD, and median (interquartile range [IQR]) being reported. A comparison between the baseline characteristics of CLEAR I and CLEAR II patients was performed; categorical measures were compared using Pearson's chi-square test, whereas continuous measures were compared by independent *t*-tests and the nonparametric Wilcoxon's rank-sum test, where appropriate. A 2-tailed *P* value less than 0.05 was chosen as statistically significant. To determine whether the progression of radiographic damage at the 36-month visit was significant in CLEAR I patients, the chi-square test for correlated proportions was used. A 2-tailed *P* value of less than 0.05 was selected as indicative of statistical significance. The risk rate was calculated as the incidence of progression in those with a total score of 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 CLEAR II, respectively; baseline radiographic were available in 294 patients for CLEAR I and 167 patients for CLEAR II and are included in these analyses. The baseline sociodemographic variables for the total cohort are shown in Tables 1 and 2.

Baseline sociodemographic and clinical features. The baseline sociodemographic variables for those patients with radiographic data in CLEAR I and CLEAR II are shown in Table 1. The majority of patients were women (82.7% and 84.4%, respectively), with a mean ± SD age at entry into the registry of 50.6 ± 13.5 and 56.2 ± 10.8 years, respectively ($P = 0.0016$), and a mean ± SD age at RA onset of 49.6 ± 13.5 and 42.8 ± 12.4 years, respectively. The distribution of education level (3.8% and 6.3%, respectively, for graduate and postgraduate) and poverty level (30.9% and 30.6%, respectively) were comparable in both CLEAR I and CLEAR II. Family history of RA was higher in the CLEAR II (43.1%; $P = 0.0043$) than in the CLEAR I patients (29.9%). 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 12.1 months [IQR 6.8–19.1 months] and 126.0 months [IQR 61.0–223.0 months], respectively; Wilcoxon's rank-sum test $P < 0.0001$).

The baseline clinical variables are depicted for patients with radiographic scores in Table 2. The median HAQ scores for CLEAR I and CLEAR II patients were 1.8 (IQR 0.9–2.4) and 2.0 (IQR 1.3–2.5), respectively ($P = 0.0509$). The median number of tender joints was higher in CLEAR I patients (7.0, IQR 2.0–18.0) than in CLEAR II patients (5.0, IQR 2.0–12.0; $P = 0.0786$), whereas the median number of swollen joints was similar in CLEAR I patients (4.0, IQR 1.0–8.0) and CLEAR II patients (5.0, IQR 0.0–13). The median scores for the JAM scale were 4.0 (IQR 0.0–14.0) in CLEAR I and 2.0 (IQR 0.0–13.0) in CLEAR II. The median pain scale score was 7.0 in both CLEAR I and CLEAR II.

RF positivity was ~80% in both groups, whereas anti-CCP antibody positivity was significantly higher in CLEAR II patients (80.0%) than in CLEAR I (61.3%) patients ($P < 0.0001$). Approximately 84% of the patients were taking at least 1 DMARD and ~2% were receiving biologic therapy (anakinra, etanercept, or infliximab), whereas ~65% were taking methotrexate; ~80% of the patients had taken glucocorticoids.

Radiographic assessment. The radiographic findings for patients in CLEAR I and CLEAR II are shown in Table 3. As noted, the CLEAR I analysis included 294 sets of

Table 1. Baseline sociodemographic 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*†	CLEAR I (n = 294)	CLEAR II (n = 167)	*P*†
Age at enrollment, mean ± SD years	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 years	50.0 ± 13.2	45.0 ± 13.0	0.7035	49.6 ± 13.5	42.8 ± 12.4	0.2290
Women, %	82.4	87.3	0.0533	82.7	84.4	0.6228
Disease duration at enrollment, median (IQR) months	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 Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis (CLEAR) Registry is still actively collecting radiographs at 36 months and 60 months of disease duration in CLEAR I and at study entry in CLEAR II. Thus, radiographic scores are not available for all of the subjects at the present time. IQR = interquartile range.
† Calculated by chi-square or Wilcoxon's rank-sum tests.
‡ 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).

baseline films, 147 sets of films at ~36 months of disease duration, and 39 sets of films at ~60 months of disease duration. At the baseline visit, the mean ± SD erosion score was 1.24 ± 3.68 and the median erosion score was 0.0 (IQR 0–1), with 25.9% of the patients showing erosions; the mean ± SD JSN score was 1.65 ± 4.73 and the median JSN score was 0.0 (IQR 0–0), with 19.4% displaying JSN; and the mean ± SD total score was 2.89 ± 7.65 and the median total score was 0.0 (IQR 0–2), with 32.0% of the patients showing either erosions or JSN. At 36 months, the mean ± SD erosion score was 2.22 ± 5.72 and the median erosion score was 0.0 (IQR 0–2), with 44.2% of

Table 2. Baseline clinical variables of African American patients with rheumatoid arthritis from the CLEAR Registry*

Variable	Total cohort			Subset with radiographic scores		
	CLEAR I (n = 357)	CLEAR II (n = 418)	*P*†	CLEAR I (n = 294)	CLEAR II (n = 167)	*P*†
HAQ score, median (IQR)	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 (IQR)	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
No. of tender joints, median (IQR)	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
No. of swollen joints, median (IQR)	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 (range 0–10 cm), median (IQR)	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 antibody positive‡	63.4	75.1	0.0007	61.3	80.0	< 0.0001
Medications, % ever used						
Glucocorticoids	77.8	79.9	0.4713	79.3	80.9	0.6833
DMARDs§	81.8	83.3	0.5930	84.4	83.8	0.8828
Methotrexate	62.5	61.6	0.8026	63.6	66.0	0.6057

* The Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis (CLEAR) Registry is still actively collecting radiographs at 36 months and 60 months of disease duration in CLEAR I and at study entry in CLEAR II. Thus, radiographic scores are not available for all of the subjects at the present time. HAQ = Health Assessment Questionnaire; IQR = interquartile range; JAM = Joint Alignment and Motion; anti-CCP = anti-cyclic citrullinated peptide; DMARDs = disease-modifying antirheumatic drugs.
† Calculated by chi-square or Wilcoxon's rank-sum tests.
‡ Second generation.
§ Shown in Appendix A.

Table 3. Radiographic findings for patients in CLEAR I (baseline, 36 months, and 60 months) and CLEAR II (baseline)*

	Patients, no. (%)	Sharp/van der Heijde score	
		Mean ± SD	Median (IQR)
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)

* CLEAR = Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis; IQR = interquartile range.
† Followup totals differ from baseline due to loss to followup and patients who had not yet reached their time planned visits.
‡ Study enrollment is ongoing.

the patients showing erosions; the mean ± SD JSN score was 3.44 ± 6.64 and the median JSN score was 0.00 (IQR 0–4), with 41.5% of the patients displaying JSN; and the mean ± SD total score was 5.65 ± 11.14 and the median total score was 0.0 (IQR 0–6), with 54.4% of the patients showing either erosions or JSN. At ~60 months of disease duration for 39 patients in CLEAR I, the mean ± SD erosion score was 4.74 ± 12.78 and the median erosion score was 0.0 (IQR 0–4), with 38.5% of the patients showing erosions; the mean ± SD JSN score was 7.87 ± 13.12 and the median JSN score was 0.0 (IQR 0–12), with 46.2% of the patients showing JSN; and the mean ± SD total score was 12.62 ± 24.95 and the median total score was 0.0 (IQR 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 erosion score was 14.68 ± 23.84 and the median erosion score was 4.0 (IQR 0–18), with 65.3% of the patients showing erosions; the mean ± SD JSN score was 18.74 ± 26.48 and the median JSN score was 7.0 (IQR 0–24), with 65.3% of the patients showing JSN; and finally, the mean ± SD total score was 33.42 ± 48.89 and the median total score was 11.0 (IQR 0–41), with 74.8% of the patients showing either erosions or JSN.

Of the 147 CLEAR I patients with radiographs at 36 months, 3 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, and of those with damage at baseline, 57.1% had progressed. The difference between these 2 groups was significant ($P < 0.0001$, $\chi^2 = 21.7$). These data are shown in Table 4. The median score differences between baseline and 36 months were 0.0 (IQR 0.0–2.0) and 3.0 (IQR 0.0–7.0) for those without damage at baseline and those with damage, respectively (Wilcoxon's rank-sum $P < 0.0001$). The risk ratio for baseline damage versus no baseline damage was 3.02 (95% confidence interval 1.86–4.88). There was no association between radiographic progression and methotrexate ($P = 0.4389$) or biologic therapy ($P = 0.7104$).

DISCUSSION

To our knowledge, 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 approximately 3. There-

Table 4. Radiographic progression at 36 months (n = 144) in patients from the CLEAR I Registry*

Baseline damage	Yes, no. (%)	No, no. (%)
Yes (total score >0)	28 (57.1)†	21 (42.9)
No (total score 0)	18 (18.9)†	77 (81.1)

* Progression was defined as an increase of 0.083 per month of total Sharp/van der Heijde score from the baseline visit. Three patients were excluded because they lacked baseline radiographs. CLEAR = Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis.
† $P < 0.0001$, $\chi^2 = 21.7$.

fore, RA in the African American population behaves similarly to other ethnic groups (3,31).

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 (32). 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 (31,33–35); 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 (28,32,36).

Other studies have reported different rates of erosive disease. For example, in one study of patients with early RA (<2 years of disease duration), erosive disease was found in 21.7% of subjects; 1-year radiographic progression (defined as an increase in Larsen score of ≥2) occurred in 36.6% of these patients (31). 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%, in 47% after 1 year, and in 63.6% at 3 years (37). 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. Therefore, although the prevalence of erosive disease at baseline in our study was comparable with that reported in studies of patients of different ethnicities (31,33,34,37), the rate of erosions and JSN reported in other studies is widely variable, between 21% and 67% (31,38–40). This variability probably reflects differences in inclusion criteria (e.g., the presence of RF), radiographic scoring method, disease duration, medication use, geographic region, and other potential confounders (13–15). 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 (10,15–17), limiting the conclusions to be drawn from these studies.

Although relatively few CLEAR subjects have had their 60-month followup 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 (35,37,41–43). Lindqvist et al described that among 181 patients with early RA, the most rapid radiologic progression occurred during the first 2 years of disease, 75% of all damage occurred during the first 5 years, and after 10 years, 90% of the patients had erosions (Larsen and Dale scoring method) (38). We will reexamine 5-year radiographic data when the majority of the CLEAR patients reach this time point; such analyses may provide more definitive conclusions.

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 in relation to methotrexate (44); in addition, only a relatively small number of patients were receiving biologic therapy so definitive conclusions can not be reached. Finally, some patients may have received these therapies for a relatively short time for their effect to be noted. 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 differences between CLEAR I and CLEAR II patients such as age at enrollment and family history can be explained by differences in the entry criteria for CLEAR I and CLEAR II. CLEAR II includes an older population because patients with longstanding disease constituted this registry; therefore, the median disease duration was 9 years. In contrast, CLEAR I includes patients with less than 2 years of disease duration for a median of 1 year. As described above, it should be noted that the study design was quite different for CLEAR I and CLEAR II. The differences in demographic and clinical features may be due to a variety of factors, but most likely reflect the difference in disease duration required for inclusion. Many of the subjects enrolled in CLEAR II had years of disease activity with obvious RA deformities due to joint destruction; those in CLEAR I had much less radiographic damage. Subjects with milder disease who are seen early in the course of disease and are therefore relatively young would be enrolled in CLEAR I, whereas those with mild longstanding disease may no longer be followed at an academic medical center and therefore not be eligible for enrollment in CLEAR II.

Some limitations of this study are worth noting. First, not all of the 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. Second, by design, longitudinal data are not available in the CLEAR II participants, so we cannot compare their rates of radiographic progression with those with early RA in CLEAR I and preclude performing analyses of the combined registries. Third, this is an interim analysis of the initial 167 patients (of a total of approximately 600 to be enrolled) in CLEAR II; however, we do not think the data for those patients will be substantially different since most of the recruited patients tend to have established disease (mean of approximately 12 years of disease duration) and the proportion of patients with erosions (65.3%) is consistent with the proportions reported in other studies after more than 5 years of disease (38,45,46). Fourth, 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 the 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.

ACKNOWLEDGMENTS

We thank these additional investigators of the CLEAR Registry: George Howard, DrPH, and Gary S. Gilkeson, MD. We also thank all of the patients participating in the CLEAR Registry, and the physicians at the 5 academic centers for referring patients. We gratefully acknowledge the following physicians, who have also enrolled patients: Adahli Estrada Massey, MD, Auburn, Alabama; Runas Powers, MD, Alexander City, Alabama; Ben Wang, MD, Memphis, Tennessee; Jacob Aelion, MD, Jackson, Tennessee; Sohrab Fallahi, MD, Montgomery, Alabama; Richard Jones, PhD, MD, Tuscaloosa, Alabama; Donna Paul, MD, Montgomery, Alabama; William Shergy, MD, Huntsville, Alabama; and the staff and coordinators at the following sites: Selena Luckett-Smith, RN, CRNC, Laticia Woodruff, RN, MSN, Stephanie McLean, BS, Candace Miller, MS, Jin Yi Wang, MS, Yuanqing Edberg: University of Alabama at Birmingham, Birmingham, Alabama; Joyce Carlone, RN, RNP, Karla Caylor, BSN, RN, Sharon Henderson, BSN, RN: Emory University, Atlanta, Georgia; Pat Cummins, RN, Diane Bresch, RN: University of North Carolina, Chapel Hill, North Carolina; Trisha Sturgill, Donna Jordon, Kelley Gibson: Medical University of South Carolina, Charleston, South Carolina; Teresa Arb, RN, BSN, CCRC: Washington University, St. Louis, Missouri.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Bridges had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Bridges, Causey, Jonas, Smith, Moreland, Alarcón.

Acquisition of data. Bridges, Causey, van Everdingen, Ledbetter, Conn, Tamhane, Westfall, Jonas, Callahan, Smith, Brasington, Moreland.

Analysis and interpretation of data. Bridges, Causey, Burgos, Huynh, Hughes, Danila, Tamhane, Westfall, Smith, Brasington, Moreland, Alarcón, van der Heijde.

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;41:778–99.
2. Pincus T, Sokka T, Wolfe F. Premature mortality in patients with rheumatoid arthritis: evolving concepts [editorial]. Arthritis Rheum 2001;44:1234–6.
3. Scott DL. Prognostic factors in early rheumatoid arthritis. Rheumatology (Oxford) 2000;39 Suppl 1:24–9.
4. Aletaha D, Smolen J, Ward MM. Measuring function in rheumatoid arthritis: identifying reversible and irreversible components. Arthritis Rheum 2006;54:2784–92.
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;28:1326–35.
6. Austin JS, Ambrose RF, Young PK, Moreland LW, Saway PA, Alarcon GS. Rheumatoid arthritis patients and clinical drug trials: a case–control study. Arthritis Care Res 1991;4:22–6.
7. Alarcon GS, Barger BO, Acton RT, Koopman WJ. HLA antigens and gold toxicity in American blacks with rheumatoid arthritis. Rheumatol Int 1986;6:13–7.
8. Alarcon GS, Koopman WJ, Acton RT, Barger BO. DR antigen distribution in blacks with rheumatoid arthritis. J Rheumatol 1983;10:579–83.
9. McDaniel DO, Alarcon GS, Pratt PW, Reveille JD. Most African-American patients with rheumatoid arthritis do not have the rheumatoid antigenic determinant (epitope). Ann Intern Med 1995;123:181–7.
10. Lopez-Mendez A, Paul WA, Alarcon GS. Rheumatoid arthritis in American blacks: a clinical and radiological study. J Rheumatol 1989;16:1197–200.
11. Mody GM, Meyers OL. Rheumatoid arthritis in blacks in South Africa. Ann Rheum Dis 1989;48:69–72.
12. Beighton P, Solomon L, Valkenburg HA. Rheumatoid arthritis in a rural South African Negro population. Ann Rheum Dis 1975;34:136–41.
13. Solomon L, Robin G, Valkenburg HA. Rheumatoid arthritis in an urban South African Negro population. Ann Rheum Dis 1975;34:128–35.
14. Anaya JM, Correa PA, Mantilla RD, Jimenez F, Kuffner T, McNicholl JM. Rheumatoid arthritis in African Colombians from Quibdo. Semin Arthritis Rheum 2001;31:191–8.
15. Maritz NG, Gerber AJ, Greyling SJ, Sandra BB. A radiological study of the rheumatoid hand in black South Africans. S Afr Med J 2005;95:795–7.
16. 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;21:2011–5.
17. 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;27:97–100.
18. 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;58:349–58.
19. Mikuls TR, Hughes LB, Westfall AO, Holers VM, Parrish L, van der Heijde D, et al. Cigarette smoking, disease severity and autoantibody expression in African Americans with recent-onset rheumatoid arthritis. Ann Rheum Dis 2008;67:1529–34.
20. 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;31:315–24.
21. Felson DT, Anderson JJ, Boers M, Bombardier C, Chernoff M, Fried B, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. Arthritis Rheum 1993;36:729–40.
22. Fries JF, Spitz P, Kraines G, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137–45.
23. 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;14:887–92.
24. Parker JW, Harrell PB, Alarcon GS. The value of the joint alignment and motion scale in rheumatoid arthritis. J Rheumatol 1988;15:1212–5.
25. 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;54:3057–9.
26. Van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. J Rheumatol 2000;27:261–3.
27. Van der Heijde DM, van Riel PL, Nuver-Zwart IH, Gribnau FW, van de Putte LB. Effects of hydroxychloroquine and sulphasalazine on progression of joint damage in rheumatoid arthritis. Lancet 1989;1:1036–8.
28. 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 2009;68:1535–40.
29. Syversen SW, Goll GL, van der Heijde D, Landewe R, Gaarder PI, Odegard S, et al. Cartilage and bone biomarkers in rheu-

matoid arthritis: prediction of 10-year radiographic progression. J Rheumatol 2009;36:266–72.
30. 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;46:913–20.
31. 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. Rheumatology (Oxford) 2003;42:1044–9.
32. Van der Heijde D, Boonen A, Boers M, Kostense P, van der Linden S. 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;38:1213–20.
33. Mottonen TT. Prediction of erosiveness and rate of development of new erosions in early rheumatoid arthritis. Ann Rheum Dis 1988;47:648–53.
34. 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;34:815–21.
35. 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;35:1106–15.
36. Redlich K, Hayer S, Maier A, Dunstan CR, Tohidast-Akrad M, Lang S, et al. Tumor necrosis factor α–mediated joint destruction is inhibited by targeting osteoclasts with osteoprotegerin. Arthritis Rheum 2002;46:785–92.
37. 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;46:342–9.
38. 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;62:611–6.
39. Higami K, Hakoda M, Matsuda Y, Ueda H, Kashiwazaki S. Lack of association of HLA–DRB1 genotype with radiologic progression in Japanese patients with early rheumatoid arthritis. Arthritis Rheum 1997;40:2241–7.
40. Richi P, Balsa A, Munoz-Fernandez S, Villaverde V, Fernandez-Prada M, Vicario JL, et al. Factors related to radiological damage in 61 Spaniards with early rheumatoid arthritis. Ann Rheum Dis 2002;61:270–2.
41. Van der Heijde DM, van Leeuwen MA, van Riel PL, Koster AM, van '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;35:26–34.
42. 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;44:2009–17.
43. Bruynesteyn K, van der Heijde, Boers M, Verhoeven A, Boonen A, van der Linden S. Contribution of progression of erosive damage in previously eroded joints in early rheumatoid arthritis trials: COBRA trial as an example. Arthritis Rheum 2002;47:532–6.
44. 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;27:883–9.
45. Sharp JT, Wolfe F, Mitchell DM, Bloch DA. The progression of erosion and joint space narrowing scores in rheumatoid arthritis during the first twenty-five years of disease. Arthritis Rheum 1991;34:660–8.
46. Plant MJ, Jones PW, Saklatvala J, Ollier WE, Dawes PT. Patterns of radiological progression in early rheumatoid arthritis: results of an 8 year prospective study. J Rheumatol 1998;25:417–26.

APPENDIX A: 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 injections or tablets	Gold salts, either injections or tablets
Penicillamine	Penicillamine
Sulfasalazine	Sulfasalazine
Infliximab	Minocycline
Etanercept	Infliximab
Anakinra	Etanercept
	Anakinra
	Adalimumab
	Rituximab

* CLEAR = Consortium for the Longitudinal Evaluations of African Americans with Early Rheumatoid Arthritis.