Differences in Clinical Status Measures in Different Ethnic/Racial Groups with Early Rheumatoid Arthritis: Implications for Interpretation of Clinical Trial Data

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ABSTRACT. ***Objective.*** Studies have documented differences in health status, disease prevalence, treatment outcomes, and healthcare utilization among different ethnic groups. We compared patients with early rheumatoid arthritis (RA) of different ethnic/racial groups according to disease activity measures, to identify possible differences in patterns of severity of clinical status.

Methods. An early RA treatment evaluation registry (ERATER) with more than 500 patients with less than 3 years of RA was established; 118 ERATER patients are followed in Brooklyn, NY, USA. At each visit, all patients complete a multidimensional Health Assessment Questionnaire (MDHAQ), including functional status, pain, fatigue, global assessment on a 10 cm visual analog scale, psychological distress, and duration of morning stiffness. Clinical evaluation includes tender and swollen joint counts and erythrocyte sedimentation rate (ESR). Baseline measures were collected before patients started any treatments. Clinical status measures in 3 ethnic/racial groups were compared.

Results. Hispanic patients with RA scored worst in all self-report measures compared to Caucasians and African Americans, with statistically significant differences in MHAQ functional score, psychological distress, and morning stiffness. The groups were not statistically significantly different in joint counts, ESR, or physician global assessment.

Conclusion. Our findings indicate differences between ethnic/racial groups in patient derived measures in patients with early RA at presentation. Cultural differences and possible ethnic influences on disease activity measures in clinical trials and clinical care may be important in interpreting differences in prognosis and outcomes of patients with RA. (J Rheumatol 2007;34:311–5)

Key Indexing Terms:
ETHNIC/RACIAL DIFFERENCES RHEUMATOID ARTHRITIS OUTCOME MEASURES

Studies have documented differences in health status, disease prevalence, treatment outcomes, and healthcare utilization among different ethnic/racial groups[1,2]. Even after adjustment for health insurance status, age, sex, income or education, stage and severity of disease, and hospital type or resources, racial and ethnic minority patients consistently receive lower quality diagnostic assessment and treatment choices than Caucasian patients[3,4].

Most of these studies have included cardiac, diabetic, and cancer patients[5,6]. Few studies that examined the influence of ethnicity/race on rheumatic diseases found differences between ethnic/racial groups[7-11].

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Most of the clinical trials of rheumatoid arthritis (RA) in the 1990s and the recent anti-tumor necrosis factor studies included over 90% Caucasian patients[12-16]. This number is higher in Europe, which has a more homogenous Caucasian population[17]. The majority of studies do not even report the ethnic/racial composition of the cohort under study[18]. In addition, studies have demonstrated that most patients seen in routine clinical care do not fulfill the inclusion criteria for most of the RA trials[19-22]. These factors likely make the results and conclusions of these very important studies less relevant and applicable to patients from minority groups.

We examined and compared patients with early RA of different ethnic/racial groups according to disease activity measures, to determine possible differences in patterns of severity of clinical status according to physician global assessment, joint count, erythrocyte sedimentation rate (ESR), and patient self-report measures.

MATERIALS AND METHODS

An early RA treatment evaluation registry (ERATER) has been established that includes more than 500 patients (from Brooklyn, New York, Nashville, Tennessee, and Boston, Massachusetts, USA) with RA whose onset of disease occurred after 1998[23]. A total of 118 of the ERATER patients from an academic private practice in Brooklyn, NY, were analyzed. This is the only site where there is a good mixture of patients with different ethnic/racial back-

grounds. The remainder of the ERATER cohort is predominantly Caucasian. These patients are also part of the Brooklyn Outcomes of Arthritis Registry database, in existence since 2001[24].

At each visit, all patients complete a multidimensional Health Assessment Questionnaire (MDHAQ), available in English and Spanish, which includes an 8-item modified Health Assessment Questionnaire, MHAQ, as well as 2 complex activities that together with MHAQ form a 10-item scale called FNHAQ to assess functional capacity. The self-report questionnaire also includes pain, fatigue, and global assessment on a 10 cm visual analog scale (VAS), psychological distress (PSHAQ), and duration of morning stiffness (AM). Ethnicity/race of all patients is self-declared.

All patients with RA were evaluated for tender (TJC) and swollen joint count (SJC) by one author (YY). The 28-joint count includes 10 proximal interphalangeal joints of the hands, 10 metacarpophalangeal joints, 2 wrists, 2 elbows, 2 shoulders, and 2 knees, and the 42-joint count includes these joints plus 2 hips and 2 ankles and 10 metatarsophalangeal joints. Most RA patients have assessment of ESR at most visits. Hand and foot radiographs are done yearly. All patients fulfilled the diagnostic criteria for RA of the American College of Rheumatology (ACR)[25].

Baseline measures were collected before patients started any treatment. Median values with interquartile ranges were computed for the clinical status variables, and tested for statistical significance using the Kruskal-Wallis test. Clinical status measures in 3 ethnic/racial groups (Asians excluded) were also compared using a quantile regression model with bootstrapped standard error (5000 replications), adjusted for age and duration of disease. Hommel's adjustments were applied to correct levels of significance for multiple testing when appropriate. Differences between categorical values were compared for statistical significance using the chi-square test. Swollen joint count and MHAQ were plotted, and Spearman correlations of these variables were calculated in each ethnic/racial group.

RESULTS

There were 31 Caucasian, 43 African American, 37 Hispanic, and 7 Asian patients in our cohort, with 91 women (77%). Demographic details are given in Table 1. The groups (Caucasians, African Americans, and Hispanics) were similar to each other for sex, age, years of education, disease duration, and rheumatoid factor (RF) positivity. Even though the ERATER database includes all patients with less than 3 years of disease, mean disease duration for this cohort was less than 12 months. Asians, not included in the assessment because of low numbers, had a mean age of 62 years and disease duration of 6 months, and 68% were RF-positive.

Baseline assessment data according to clinical status measures are given by ethnic/racial group in Table 2. All patients were disease modifying antirheumatic drug (DMARD)-naive (no history of any DMARD use) at the time of presentation. Thirty-six percent of Caucasians, 47% of African Americans, 62% of Hispanics, and 43% of Asians were taking nonsteroidal antiinflammatory drugs.

Hispanic patients with RA scored worst in all self-report measures, i.e., functional disability, pain, patient global assessment of disease activity, fatigue, and morning stiffness. There was a statistically significant difference among the different ethnic/racial groups in MHAQ functional score, psychological distress score, and morning stiffness score. The groups were not statistically significantly different in joint counts, ESR, or physician global assessment.

There was a significant correlation between swollen joint counts and MHAQ score in Caucasians [r = 0.53 (95% CI 0.22 to 0.75)]. For African Americans and Hispanics, no correlation was seen [r = 0.17 (95% CI –0.13 to 0.45) and r = 0.23 (95% CI –0.10 to 0.52), respectively; Figure 1].

DISCUSSION

Our findings indicate differences in some of the clinical status measures in patients with early RA in different ethnic/racial groups. Functional status, morning stiffness, and psychological distress scores appeared to be statistically significantly higher in Hispanics compared to African Americans and Caucasians. Significant differences according to ethnic/racial group were seen in 3 patient self-report measures, but not in joint count or ESR measures. This is also important for another reason. Measures of functional status are more significant predictors of severe outcomes of RA like work disability, joint replacement surgery, and premature death than laboratory tests, joint counts, or radiographic scores[26,27]. Recently, it has also been shown that patient-reported outcomes discriminate active treatment from placebo in randomized clinical trials (RCT) of RA as well as if not better than indices that include physician-reported and laboratory variables like the ACR20 or the Disease Activity Score 28-joint count (DAS28)[28,29]. This would suggest that differences between ethnic/racial groups in patient-reported measures may have an important influence on analysis of the data and conclusions of RCT.

Del Rincon, *et al* have found Hispanic patients to have more tender and swollen joints, higher ESR, and more RF

Table 1. Demographic information and disease characteristics of patients with early RA, according to ethnic/racial group.

	Ethnic/Racial Group			
	Caucasian	African American	Hispanic	p
Patients, n	31	43	37	
Female, n (%)	22 (71)	34 (79)	29 (78)	0.68
Age, median yrs (IQR)	53 (48–62)	53 (48–61)	49 (41–63)	0.15
Education, yrs (IQR)	12 (12–13)	12 (12–16)	12 (11–13)	0.24
Disease duration, mo (IQR)	7 (3–23)	6 (3–17)	11 (4–24)	0.52
RF+, n (%)	18 (60)	29 (69)	27 (73)	0.52

IQR: interquartile range.

Table 2. Clinical status measures in patients with early RA according to ethnic/racial group. Data are median (IQR).

	Ethnic/Racial Group			
	Caucasian	African American	Hispanic	p Value Between Groups (multiple comparison)*
Self-report measures				
Physical function				
MHAQ (0 to 3)	0.38 (0.13, 0.75)	0.38 (0.00, 0.75)	1.00 (0.25, 1.56)	0.040 (Ca/Hi, AA/Hi)
FNHAQ (0 to 3)	0.80 (0.40, 1.30)	0.70 (0.1, 1.3)	1.4 (0.4, 2.2)	0.087
PSHAQ (0 to 3)	0.33 (0.33, 1.00)	0.33 (0.00, 1.00)	1.00 (0.33, 1.67)	0.017 (Ca/Hi, AA/Hi)
Pain (VAS)	5.2 (2.2, 7.6)	5.5 (2.0, 8.0)	7.1 (5.2, 8.8)	0.16
Patient's global assessment (VAS)	4.8 (2.8, 6.5)	4.2 (1.5, 5.7)	6.2 (3.4, 8.4)	0.087
Fatigue (VAS)	3.4 (1.4, 7.4)	4.5 (0.8, 6.5)	5.0 (1.9, 7.0)	0.48
Morning stiffness	30 (10, 60)	15 (0, 60)	60 (15, 120)	0.016 (Ca/Hi, AA/Hi)
Clinical measures				
No. of swollen joints (0 to 42)	1.0 (0, 8.0)	2.0 (0, 5.0)	2.0 (0, 6.8)	0.70
No. of tender joints (0 to 42)	10.0 (5.0, 16.0)	8.0 (4.0, 11.0)	10.0 (4.3, 17.8)	0.38
Erythrocyte sedimentation rate (mm/h)	18 (7, 30)	20 (10, 55)	24 (8, 53)	0.66
Physician's global assessment (VAS)	2.8 (1.9, 4.5)	3.0 (1.8, 4.1)	2.9 (2.1, 4.2)	0.98

* p values from a quantile regression model with bootstrapped standard error (5000 replications); adjusted to age and disease duration. Hommel's adjustments to correct significance levels ($p < 0.05$) for multiple testing. IQR: interquartile range, MHAQ: modified Health Assessment Questionnaire, FNHAQ: Functional HAQ, PSHAQ: Psychological HAQ, VAS: visual analog scale, all 0–10. Ca: Caucasian, Hi: Hispanic, AA: African American.

positivity[30]. Bruce, *et al*[31] recently reported ethnic disparities in health status among over 5000 patients with RA from the ARAMIS database. They also found that Hispanic patients reported worse functional, pain, and global assessment scores compared to Caucasians and African Americans. Iren, *et al*[32] reported worse HAQ and DAS28 scores among African Americans compared to Caucasians in a university clinic setting, but did not find ethnicity to be independently associated with outcomes when socioeconomic status and psychological factors were controlled for.

The majority of RA clinical trials and observational cohorts have included patients mostly of Caucasian origin. Our patient base in Brooklyn is an ethnically and racially diverse population, who live in the same geographic area, providing us with the opportunity to examine the outcomes of inflammatory arthritis, responses to treatment, work disability, and radiographic progression in this group and compare the different groups in our registry.

Most patients in RA clinical trials are selected for certain disease characteristics. It has been shown that most patients seen in routine RA care do not fulfill criteria to be included in these trials, and these trials hence do not provide information that is applicable to most of the patients with RA[33]. This cohort gives us the opportunity to examine the effects of treatment with classic DMARD therapies and also the new biologic therapies in RA, in an unselected, multiethnic, and multiracial cohort.

In 1993, the US National Institutes of Health developed a policy on inclusion of women and minorities in clinical research in response to a lack of diversity among research participants and concern about the generalizability of research results from homogeneous samples[34]. Implicit in that concern was that if members of these social groups were systematically excluded from clinical research, there was potential for resultant harm to the group as a whole[35].

Currently, one US early RA register focuses on African Americans[23]. The Consortium for the Longitudinal Evaluations of African-Americans with Early Rheumatoid Arthritis (CLEAR) study collects data about the genetics of RA in African Americans. In addition, the registry plans to provide clinical and radiographic data to monitor disease course and outcomes. However, they do not have a control arm of groups of patients from other racial/ethnic groups. This is the only RA study to our knowledge to focus on African Americans alone.

Our study is the first, to our knowledge, to study Caucasian, African American, Hispanic, and Asian patients with early RA from the same geographic area, treated by the same physician, with outcomes data collected as a standard of care for any and all patients seen. This is helpful in eliminating, at least partially, certain biases related to geography and patient selection[36,37]. We are aware that these are mostly referred patients, but observed no trend in referring one race more frequently over another just because of racial and/or ethnic reasons. The low number of patients in our study is a limitation; however, our results are in line with larger databases[30], and also report on more aspects of clinical status. A type II error could also account for this showing of a significant difference in only 3 of our patient-derived measures.

Our findings indicate differences in patient-derived measures in patients with early RA among different ethnic/racial groups. Cultural differences and possible ethnic influences on disease activity measures in clinical trials and clinical care may be important in interpreting differences in prognosis and outcomes of patients with RA.

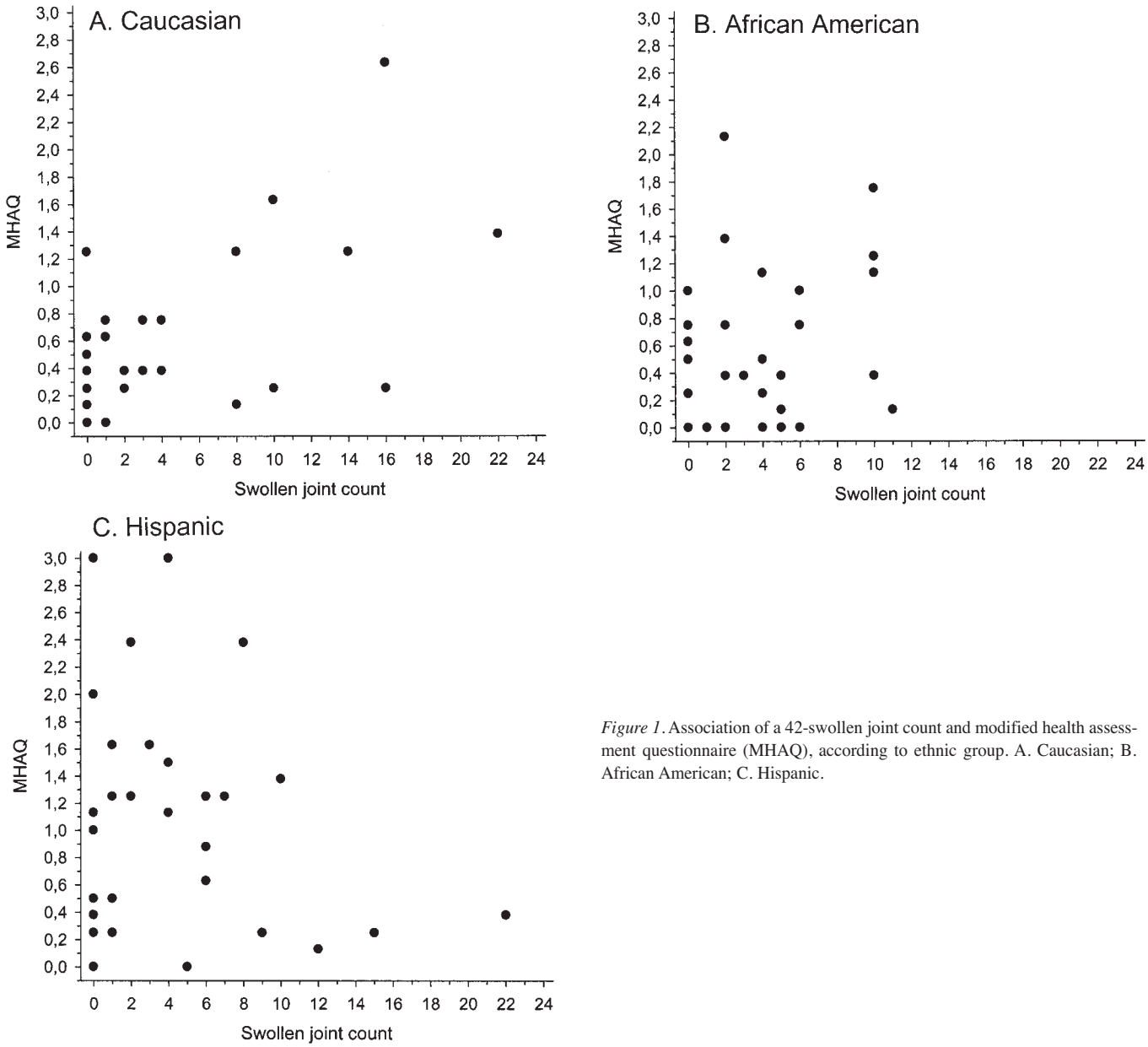

Figure 1. Association of a 42-swollen joint count and modified health assessment questionnaire (MHAQ), according to ethnic group. A. Caucasian; B. African American; C. Hispanic.

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