Impact of Age on Clinical Manifestations and Outcome in Puerto Ricans with Rheumatoid Arthritis

Yesenia Santiago-Casas, MD; Tania C. González-Rivera, MD; Lesliane E. Castro-Santana, MD; Grissel Ríos, MD; David Martínez, MD; Vanessa E. Rodríguez, MD; Rafael González-Alcover, MD; Angel M. Mayor, MD, MS; Luis M. Vilá, MD

Introduction: Disease expression and outcomes in rheumatoid arthritis (RA) vary among different ethnic groups. There are limited data on the impact of age on disease severity and outcomes among Hispanics. Thus, we determined the demographic characteristics, clinical manifestations, comorbidities, pharmacologic profile, and functional status among Puerto Ricans with RA of different age groups.

Methods: A cross-sectional study was conducted in 214 Puerto Rican patients with RA (per American College of Rheumatology classification criteria). Demographic features, health-related behaviors, cumulative RA manifestations, treatment profiles, disease activity (Disease Activity Score 28), comorbid conditions, and functional status (Health Assessment Questionnaire) were determined at study visit. Three age groups were studied: <40, 40–59, and ≥60 years. Data were examined using univariable and multivariable (logistic regression) analyses.

Results: The mean (SD) age of the study population was 56.5 (13.6) years with a mean disease duration (SD) of 10.8 (9.7) years; 180 patients (84.1%) were women. In the multivariable analyses, patients aged ≥60 years were more likely to have joint deformities, extra-articular manifestations, and comorbidities such as dyslipidemia, arterial hypertension, diabetes mellitus, vascular events, osteoarthritis, low back pain, and osteoporosis. In addition, older patients used corticosteroids more frequently. No differences were found for the use of disease-modifying anti-rheumatic drugs or biologic agents.

Conclusions: Puerto Rican RA patients aged ≥60 years present a severe type of disease having more joint damage, extra-articular manifestations, and comorbidities than younger patients. These disparities must be considered when establishing effective therapy for older RA patients. (*Ethn Dis*. 2010;20[Suppl 1]:S1-191–S1-195)

Key Words: Rheumatoid Arthritis, Outcome, Hispanics, Puerto Ricans

From Division of Rheumatology, Department of Medicine, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico (YSC, LECS, GR, DM, VER, RGA, AMM, LMV); and Division of Rheumatology, Department of Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan (TCGR).

Address correspondence and reprint requests to Luis M. Vilá, MD; Chief and Program Director, Division of Rheumatology; University of Puerto Rico Medical Sciences Campus; PO Box 365067; San Juan, PR 00936-5067; 787-758-2525, ext. 1825; 787-764-6839 (fax); luis.vila2@upr.edu

Introduction

Rheumatoid arthritis (RA) is the most common type of inflammatory arthritis, occurring in approximately 1% of the population worldwide.[1] The incidence and prevalence increase with age up to a peak of approximately 70 years.[1] The prevalence in the geriatric population is reported to be around 2%.[2] Rheumatoid arthritis in elderly patients can be categorized in two clinical presentations: elderly-onset RA (EORA), defined as disease onset at ≥60 years, and elderly patients with younger-onset RA (<60 years) having long-standing disease.[3] In contrast to younger-onset RA, EORA patients exhibit a more uniform sex distribution, tend to present an acute onset of disease with prominent pain and morning stiffness, and those with positive rheumatoid factor usually have a worse clinical outcome.[3]

The prevalence of RA varies among different ethnic populations. For instance, higher prevalence rates have been described among Native Americans and Alaska natives.[4] Moreover, differences in clinical features and outcomes have been described among different ethnic groups.[5] There are limited data on the clinical characteristics of RA among Hispanic populations.[5–7] Furthermore, the impact of age on the manifestations and outcomes of RA in this population has not been examined. Our study was aimed at determining the clinical manifestations and outcome of RA in Hispanics from Puerto Rico of different age groups; this could lead to a better understanding of this debilitating disease.

Patients and Methods

Patient Population

A cross-sectional study was performed in 214 patients with RA. All patients were aged ≥21 years, had Puerto Rican ethnicity (self and four grandparents) and fulfilled the American College of Rheumatology (ACR) revised classification for RA.[8] The patients were evaluated between February 2007 and April 2008 at the rheumatology clinics of the University of Puerto Rico Medical Sciences Campus in San Juan, Puerto Rico, and at three private rheumatology practices located in San Juan, Puerto Rico. The study was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus.

The patients had their routine visits at 2–3 month intervals. Additional visits were scheduled as needed by disease activity or complications. At each visit, laboratory testing such as complete blood cell count, serum chemistries, urine analysis, erythrocyte sedimentation rate (ESR), and lipid panel were routinely ordered. Rheumatoid factor was done at RA diagnosis. At study visit a structured questionnaire was completed for each patient to gather data about demographic parameters, life-style behaviors, clinical manifestations, labora-

tory tests, pharmacologic treatment, disease activity and disease damage.

Variables

The following demographic features were examined: age, sex, and disease duration. Age at onset was defined as age at which patient had the first symptom attributable to RA and age at diagnosis as the age at which patient met the ACR criteria for RA. For analyses, patients were allocated to three age groups: <40, 40–59 and ≥60 years. Disease duration was defined as the time interval between RA diagnosis and study visit. Health-related behaviors including cigarette smoking, alcohol consumption and exercise were also evaluated. The latter was defined as regular participation in physical activity as part of a personal fitness plan.

The cumulative RA manifestations and comorbid diseases were determined at study visit. Rheumatoid arthritis manifestations included joint deformities/contractures (defined as loss of more than 20% of range of motion, lax collaterals, malalignment or subluxation), radiographic evidence of joint damage, joint replacement surgeries and extra-articular manifestations. Among extra-articular manifestations we determined the presence of subcutaneous nodules and ocular (keratoconjuctivitis sicca, episcleritis, scleritis, scleromacia or uveitis), pulmonary (pleuritis, pleural effusion, pulmonary nodules, interstitial lung disease or pulmonary fibrosis), cardiac (pericarditis, myocarditis, valvular nodules or coronary vasculitis) and neurologic (neuropathies, peripheral neuropathy or mononeuritis multiplex) manifestations. The following comorbid conditions were determined: dyslipidemia, arterial hypertension, type 2 diabetes mellitus, metabolic syndrome (per the American Heart Association and National Heart, Lung and Blood Institute classification),[9] arterial vascular events, peripheral venous disease, obstructive pulmonary disease, malignancy, depression, osteoarthritis, fibromyalgia syndrome, chronic low back pain and osteoporosis.

Disease activity was assessed using the European League Against Rheumatism (EULAR) Disease Activity Score 28 (DAS-28).[10] The DAS-28 score uses the 28-joint count, the ESR, and the patient's visual analogue scale for overall health to assess disease activity. The number of RA exacerbations (onset of new joint, organ or system involvement, worsening of previous coexistent condition, or disease that requires modification of therapy) and hospitalizations attributed to RA were also evaluated. Functional status was assessed with the Health Assessment Questionnaire (HAQ).[11] This validated instrument assesses the degree of difficulty in accomplishing eight functional tasks.

The cumulative exposure and duration of therapy of the following therapeutic agents was recorded: corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), antimalarials, azathioprine, cyclosporine, methotrexate, sulfasalazine, leflunomide, gold salts, infliximab, etanercept, adalimumab, anakinra, rituximab and abatacept.

Statistical Analysis

The Statistical Package of Social Sciences (SPSS: Chicago III, 12.0 version) program was used to perform univariable and multivariable analyses. Differences between study groups were analyzed with chi-square, Fisher's exact and Student's *t*-tests. Variables that were significant in the univariable analyses were entered in logistic and linear regression analyses controlling for age groups, disease duration, sex and corticosteroid use. A *P*-value of ≤.05 was considered to represent statistical significance.

Table 1. Demographic features and health related behaviors by age groups

Features	<40 years (*n*=22)	40–59 years (*n*=91)	>60 years (*n*=101)	*P* value
Age, mean (SD) years	31.0 (4.6)	50.0 (5.9)	68.1 (6.2)	<.001
Sex, % female	90.0	82.4	84.2	.620
Disease duration, mean (SD) years	3.4 (2.9)	9.5 (8.2)	13.6 (10.7)	<.001
Alcohol use, %	4.5	3.3	4.0	.950
Smoking, %	4.5	11.0	7.9	.569
Exercise, %	31.8	15.4	17.8	.015

SD: Standard deviation

RESULTS

A total of 214 patients with RA were examined; 180 were females (84.1%). The mean age (standard deviation [SD]) was 56.5 (13.6) years and the mean (SD) disease duration was 10.8 (9.7) years. Table 1 shows the demographic features and health-related behaviors of the study patients by age group. Elderly patients had significantly longer disease duration than middle age and young adults. Elderly and middle age patients were less likely to exercise. There were no significant differences for sex, cigarette smoking or alcohol use.

Table 2 shows the clinical manifestations, disease activity and outcome measures. Elderly patients were more likely to have joint contractures/deformities and extra-articular manifestations (particularly neurological conditions) than younger patients. Rheumatoid arthritis exacerbations were more common in middle age and elderly patients. There were no differences for radiographic findings of joint damage, joint replacement surgeries, ESR, disease activity (by DAS-28), rheumatoid factor, hospitalizations, and functional status.

The following comorbid conditions were more common in elderly patients: dyslipidemia, arterial hypertension, type 2 diabetes mellitus, arterial vascular events (particularly cerebrovascular ac-

Table 2. Clinical manifestations, disease activity and outcome measures by age groups

Features	<40 years (*n*=22)	40–59 years (*n*=91)	>60 years (*n*=101)	*P*-value
Joint deformities/contractures, %	22.7	49.5	70.3	<.001
Radiographic evidence of joint damage, %	36.4	47.3	57.4	.131
Joint replacement surgeries, %	13.6	14.3	22.0	.328
Overall extra-articular manifestations, %	31.8	62.6	73.3	.001
Ocular	9.1	31.9	35.6	.051
Pulmonary	4.5	6.6	8.9	.713
Cardiac	4.5	1.1	1.0	.415
Neurologic	4.5	12.1	24.8	.017
Subcutaneous nodules	13.6	34.1	32.7	.165
Elevated ESR, %	81.0	92.2	91.0	.276
Disease activity (DAS-28), mean (SD)	2.9 (1.8)	3.7 (1.7)	3.7 (1.6)	.102
Rheumatoid factor, % positive	52.4	52.9	57.1	.752
Exacerbations, mean (SD)	1.23 (1.34)	3.11 (3.26)	3.00 (3.51)	.045
Hospitalizations, mean (SD)	.05 (.21)	.07 (.29)	.09 (.40)	.812
Functional status (HAQ), mean (SD)	.81 (.78)	1.12 (.78)	1.13 (.88)	.261

ESR: Erythrocyte sedimentation rate, SD: Standard deviation, DAS: Disease Activity Score, HAQ: Health Assessment Questionnaire

cidents), malignancy, low back pain, osteoarthritis and osteoporosis (Table 3). Conversely, depression was more frequent in middle age patients.

The use of corticosteroids was more frequent among older patients, when compared to patients aged 40–59 and <40 years (82.2%, 78.0% and 54.5% respectively, $P=.019$). No significant differences were noted for the use of NSAIDs, classic disease modifying antirheumatic drugs (DMARDs), biologic agents, or combination therapy consisting of at least one classic DMARD and a biologic agent (data not shown).

In the logistic regression analyses (Table 4), the effect of age on the following variables remained significant: joint deformities/contractures, extra-articular manifestations (including neurological conditions), dyslipidemia, arterial hypertension, type 2 diabetes mellitus, arterial vascular events, osteoarthritis, chronic low back pain, and osteoporosis. In the lineal regression analyses, the effect of age on RA exacerbations did not retain significance (data not shown).

Table 3. Comorbid conditions among different age groups

Conditions	<40 years (*n*=22) %	40–59 years (*n*=91) %	>60 years (*n*=101) %	*P*-value
Dyslipidemia	9.1	52.7	58.4	<.001
Arterial hypertension	13.6	40.7	76.2	<.001
Type 2 diabetes mellitus	4.5	4.4	19.8	.002
Metabolic syndrome	18.2	39.6	43.4	.089
Arterial vascular events	0	4.4	22.8	<.001
Angina pectoris	0	1.1	4.0	.311
Myocardial infarction	0	2.2	9.1	.052
Peripheral artery disease	0	1.1	5.0	.186
Cerebrovascular accident	0	1.1	8.0	.035
Heart failure	0	1.1	5.0	.191
Coronary artery bypass graft	0	0	4.0	.102
Peripheral venous disease	0	5.5	9.0	.262
Obstructive pulmonary disease	0	1.1	4.0	.316
Malignancy	0	1.1	7.9	.037
Depression	0	15.4	3.0	.002
Osteoarthritis	27.3	48.4	68.3	.002
Fibromyalgia syndrome	0	2.2	4.0	.534
Chronic low back pain	0	8.8	17.8	.029
Osteoporosis	4.5	8.8	25.7	.002

DISCUSSION

Elderly people represent the fastest growing population in the United States; thus, there is an emerging interest to study the disease expression, pharmacologic profile and health outcomes in this population. Rheumatoid arthritis is the most common inflammatory arthritis affecting older adults.[1] However, there is limited data on the clinical manifestations and outcomes of older RA patients, especially in Hispanic populations. Here, we report that Puerto Ricans with RA aged ≥60 years have a severe type of disease manifested by a higher frequency of joint deformities/contractures, extra-articular manifestations and comorbid conditions when compared to younger patients.

The limited number of studies evaluating the outcome of elderly patients with RA is conflictive, even with the data presented here. In agreement with our work, a longitudinal study showed a worse clinical outcome in elderly patients.[12] Conversely, other studies have reported better outcomes in patients with EORA when compared to younger patients.[13] With regards to biomarkers, the presence of positive rheumatoid factor and elevated ESR increase with age.[14] Seropositive EORA patients have been noted to exhibit a worse prognosis than younger seropositive RA patients; having more swollen joints, radiographic changes, and higher mortality.[3] In contrast, our study did not reveal significant differences in the frequency of rheumatoid factor positivity or elevation of ESR among different age

Table 4. Factors associated with age by logistic regression analysis*

Variable	OR	95% CI
Exercise	.91	.53–1.56
Joint deformities/contractures	1.80	1.09–2.97
Extra-articular manifestations	1.84	1.16–2.91
Neurologic manifestations	2.69	1.38–5.26
Dyslipidemia	1.93	1.22–3.03
Arterial hypertension	4.15	2.45–7.01
Type 2 diabetes mellitus	3.95	1.57–9.94
Arterial vascular events	7.70	2.60–22.75
Cerebrovascular accidents	8.06	1.04–62.81
Depression	.49	.22–2.17
Osteoarthritis	2.66	1.66–4.27
Chronic low back pain	2.51	1.11–5.70
Osteoporosis	2.90	1.37–6.12

* Controlled by age, sex, disease duration and corticosteroid use; OR: Odds ratio, CI: Confidence interval

groups. We emphasize, however, that our study evaluated elderly patients according to age at study visit, whereas in the above mentioned studies patients were evaluated according to age at onset of RA.

Other factors that may affect the outcome in older RA patients include the presence of comorbidities, which together with long standing RA contributes to a decline in functional status. As expected, our study showed a higher frequency of comorbid conditions among elderly patients, particularly chronic illnesses such as arterial hypertension, diabetes, arterial vascular events, osteoarthritis, and osteoporosis. Each of these disorders can lead to further damage to an already compromised musculoskeletal system. The presence of these comorbidities is also accompanied by a higher exposure to medications which could interfere or further limit the use of therapeutic options for RA.

The difference between the results presented here and previous studies may be attributed to variations in RA treatment modalities. In contrast to our report, a previous study revealed that EORA patients receive multiple DMARDs and biological agents less frequently than patients with younger-onset disease.[15] Certainly, the indications for initiating RA therapy in the elderly population should not differ considerably from those for younger patients. Nevertheless, before establishing a particular therapy for elderly patients several aspects must be considered, including alterations in the pharmacokinetics, as well as hepatic and renal function. Careful attention must be given to the presence of coexistent medical conditions and the concomitant use of multiple medications. Although some studies have shown certain adverse events occurring more frequently among elderly patients (eg, cytopenias, gastrointestinal symptoms, retinopathy and liver disease) other studies have not disclosed any significant differences on the effectiveness and tolerance of DMARDs between older and younger patients.[16,17]

Another explanation for the differences observed could be related to variations among ethnic populations.[5] For example, a more severe type of disease, a younger age at onset, and a positive family history have been observed in American Indians and Alaska native populations.[4] In addition, the frequency of erosive disease, rheumatoid nodules and presence of rheumatoid factor are more prominent in these populations. African Americans seem to have reduced physical activity and increased disease activity than Caucasians.[18] A study in Japanese patients with EORA revealed differences from younger onset RA in terms of the presence of HLA-DRB1 alleles; thus disparities in the immunogenetic background might explain some of the different clinical expressions of RA among age groups.[19]

Our study is not without limitations, including those inherent to a retrospective analysis. In addition, joint imaging studies were not available for all the patients and thus precluded a complete assessment of articular damage. Another consideration is that older patients had longer disease duration which could lead to progressive joint damage and higher risk of disability. However, the association of joint damage, extra-articular manifestations and several comorbid conditions with older age remained significant after controlling for disease duration. Finally, it might appear contradictory that although older patients had more joint deformities/contractures, extra-articular manifestations and comorbid conditions, they did not exhibit a worse functional status or disease activity compared to younger patients. A plausible explanation is that current measures of disease activity and functional status may not be applicable to older patients or may not be consistently comparable among different age groups.

In summary, Puerto Rican RA patients aged $\geq$60 years present a severe type of disease having more joint damage, extra-articular manifestations and comorbidities than younger patients. These findings may represent a different biologic behavior of RA in older patients that could partially be related to a distinct biology (eg, T-cell immunosenescence) that makes them more vulnerable to selected complications (eg, vascular events). Further studies are needed to assess the outcomes of RA in elderly patients to further improve the management of this potentially disabling disease for this vulnerable population.

IMPLICATIONS FOR IMPROVING HEALTH DISPARITIES

Studies in elderly patients with RA are limited, particularly for Hispanic populations. Our study shows that elderly Puerto Rican RA patients have a more severe type of disease when compared to younger patients. Data from this study may help clinicians who care for elderly patients to recognize these disparities and deliver better medical care. Future research should assess the effectiveness and tolerability of classic DMARDs and biologic agents among these patients.

ACKNOWLEDGMENTS

Supported by the National Center for Research Resources (NCRR/NIH) RCMI Clinical Research Infrastructure Initiative (RCRII) award #1P20 RR11126 (UPR-MSC) and by an unrestricted educational grant from Abbott Laboratories (Puerto Rico), Inc.

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