Characterizing systemic sclerosis in Northern California: focus on Asian and Hispanic patients

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ABSTRACT

Objective. *Previous studies suggest that Asian and Hispanic patients with systemic sclerosis (SSc) may have more severe disease than their Caucasian counterparts. The purpose of this study is to compare the clinical features of a group of Asian, Hispanic, and Caucasian patients with SSc in Northern California.*

Methods. *We performed a cross-sectional study of patients receiving care at Stanford University Medical Center, Palo Alto Veterans Affairs Hospital, Santa Clara Valley Medical Center and San Francisco General Hospital between 1996 and 2006. Patients included in the analyses fulfilled the American College of Rheumatology criteria for SSc and could be classified as Caucasian, Asian, or Hispanic. Analyses using Caucasians as the reference group were performed.*

Results. *One hundred and ninety-nine patients met the criteria for SSc, and 165 of these patients were classified as Caucasian (47%), Asian (26%), or Hispanic (27%). Disease subtype did not differ significantly among the three groups. Asian patients were less likely to have digital ulcers (26% vs. 47%, p=0.02) or anemia (26% vs. 45%, p=0.04) than Caucasians, and Hispanic patients had a lower frequency of lung disease than Caucasians (48% vs. 67%, p=0.04), but there were no other significant differences in disease manifestations.*

Conclusions. *In our cohort of SSc patients living in Northern California, clinical manifestations in Asian and Hispanic patients did not differ substantially from Caucasians. Further research is necessary to confirm these results and to investigate gene-environment interactions which may affect the clinical expression of disease in different racial groups.*

Introduction

Systemic sclerosis (SSc) is a complex autoimmune disease characterized by excessive collagen deposition, vascular damage, and inflammation (1). Most studies evaluating racial differences in the clinical manifestations of SSc have focused on Caucasians and African Americans (2-6).

The few studies examining Hispanic and Asian patients with SSc indicate that these racial groups may have more severe disease than Caucasians. Two studies have shown that Hispanic patients in the U.S. are more likely to have diffuse skin disease, digital ulcers, and advanced pulmonary disease at initial presentation compared with Caucasians (2, 7). Thai patients have been shown to have higher frequencies of diffuse skin disease and musculoskeletal, gastrointestinal, and pulmonary involvement than Caucasians (8, 9). Patients from Japan have been found to have a higher prevalence of severe pulmonary fibrosis compared to Caucasians (10). To our knowledge, studies evaluating clinical features of Asian patients living in the U.S. have not been published.

This study examines the clinical features of a racially heterogeneous population of SSc patients from Northern California. In particular, we focus on a large number of Hispanic and Asian patients to assess for differences in disease manifestations.

Materials and methods

Study population and data sources

We performed a cross-sectional analysis of patients seen at least once at one of four hospitals in Northern California: Stanford University Medical Center, a tertiary care center, Palo Alto Veterans Affairs Hospital (VAH), and two county hospitals, Santa Clara Valley Medical Center and San Francisco General Hospital. Outpatient medical

records of all patients who received an International Classification of Diseases, Ninth Revision (ICD-9) code of 710.1 between 1996 and 2006 were reviewed. Prevalent and incident cases were included. Patients who could be classified into one of three racial groups (Caucasian, Asian, or Hispanic) and fulfilled the American College of Rheumatology (ACR) criteria for SSc were included in the analyses. Patients with at least 3 of 5 manifestations of the CREST (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, telangiectasias) syndrome were also included. Approval from the Institutional Review Board at each center was obtained prior to initiation of the study.

A data abstraction form was developed to collect the following information: race, gender, age, disease subtype, disease duration (from onset of the first non-Raynaud's symptom to last follow-up), tobacco and alcohol use, comorbid diseases, studies and procedures performed, and medications ever taken. A rheumatologist from each center reviewed each medical record for the presence of the following characteristics: calcinosis, telangiectasias, Raynaud's phenomenon, joint pain, joint contractures, digital gangrene, digital pits or ulcerations, myositis, sicca symptoms, dyspnea, gastroesophageal reflux disease, congestive heart failure, arrhythmia, and renal crisis. Clinical features such as anemia and pericardial effusion were considered present if they were reported by the physician in the medical record or if there was evidence for them based on results of laboratory studies or procedures. Pulmonary hypertension was considered present if patients had a mean pulmonary artery pressure of ≥25 mmHg at rest or ≥30 mmHg with exercise on right heart catheterization or an echocardiogram with a right ventricular systolic pressure of ≥40 mmHg. Pulmonary fibrosis was considered present if chest radiograph or computed tomography showed evidence of honeycombing.

Statistical analysis

Bivariate analyses using Caucasian patients as the reference group were performed using Student's *t*-test for continuous variables, and chi-square or Fisher's exact tests for categorical variables, with $p<0.05$ considered statistically significant.

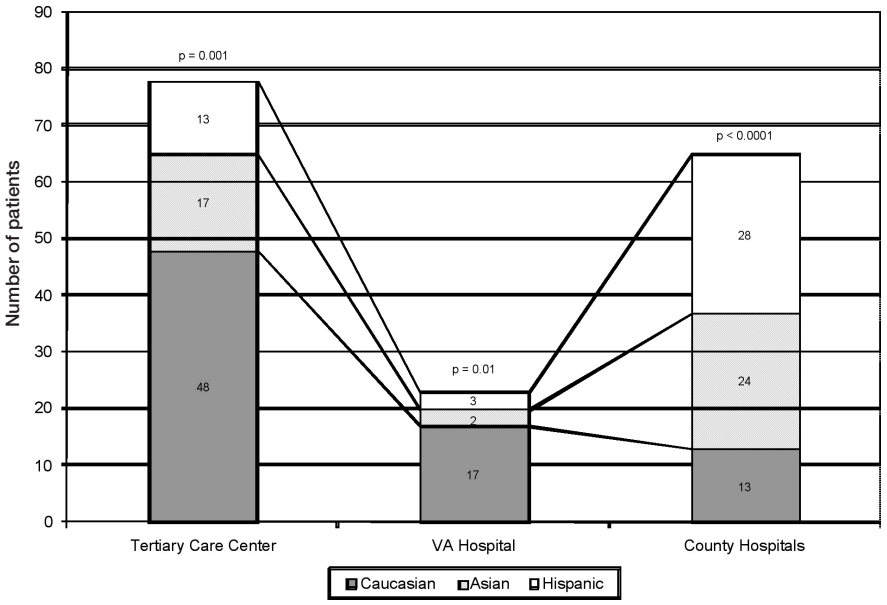

Fig. 1. Distribution of patients, by race, according to hospital. African American patients have been excluded. P-values are from chi-squared or Fisher's exact test, showing that the racial distribution at each hospital is significantly skewed.

Table I. Socio-demographic and comorbid conditions by racial group.

	Caucasian (n=78)	Asian (n=43)	*p*-value†	Hispanic (n=44)	*p*-value‡
Female:male ratio	2.7:1	7.6:1	0.06	6.3:1	0.11
Diffuse cutaneous SSc, %	26	27	0.88	43	0.06
Age at onset, mean ± SD (years)	46± 14	46 ± 14	0.97	43 ± 13	0.26
Disease duration, mean ± SD (months)	144± 121	109 ± 107	0.13	98 ± 80	0.03
Follow-up time, mean ± SD (months)	38± 39	50 ± 69	0.25	47 ± 64	0.32
Ever smokers, %	51	5	<0.0001	29	0.03
Ever alcohol use, %	50	13	<0.0001	23	0.005
Comorbid diseases					
Hypertension, %	59	49	0.34	47	0.25
Diabetes mellitus, %	7	7	1.00	12	0.49
Osteoporosis, %	8	12	0.52	7	1.00
Malignancy, %	18	9	0.30	7	0.10
Thyroid disease, %	28	12	0.06	16	0.18

†Comparing Asians with Caucasians; ‡Comparing Hispanics with Caucasians.
Notes: Disease duration defined from onset of the first non-Raynaud's symptom to last follow-up.
Months of follow-up defined as months between first and last clinic visit documented.
Clinical features considered present if they were reported by the physicians in the medical record or if there was evidence for them based on results of laboratory studies or procedures.

Results

A total of 199 patients with an ICD-9 code of 710.1 from the four hospitals met ACR criteria for the diagnosis of SSc. Twenty three (12%) patients were either missing race information or were unable to be classified into one of four racial groups and were excluded from the analysis. African American patients (n=11, 6.3%) were also excluded. Of the remaining 165 patients, 78 (47%) were Caucasian, 43 (26%) were Asian, and 44 (27%) were Hispanic. Almost half of the patients were evaluated at Stanford Hospital (47%); 65 patients (40%) were evaluated at one of the county hospitals, and 22 (13%) at the VA hospital (Fig. 1). The majority of the non-Caucasian patients were seen at the county hospitals.

Eighty percent of the patients in the study were female with slightly higher female to male ratios in non-Cauca-

Table II. Clinical characteristics and organ system involvement by racial group*.

Clinical characteristic, n (%)	Caucasian (n=78)	Asian (n=43)	*p*-value†	Hispanic (n=44)	*p*-value‡
Calcinosis	15 (20)	4 (10)	0.14	10 (24)	0.63
Telangiectasias	47 (64)	24 (57)	0.50	23 (56)	0.43
Raynaud's phenomenon	71 (93)	39 (93)	1.00	37 (88)	0.32
Joint pain	56 (74)	33 (77)	0.71	34 (81)	0.37
Joint contractures	19 (26)	11 (26)	1.00	11 (27)	0.89
Digital gangrene	7 (9)	2 (5)	0.48	7 (18)	0.24
Digital ulcers/pits	35 (47)	11 (26)	0.02	17 (43)	0.67
Myositis	3 (4)	0 (0)	0.30	6 (15)	0.06
Sicca symptoms	16 (23)	10 (23)	1.00	7 (17)	0.45
Dyspnea	43 (60)	22 (51)	0.37	17 (40)	0.05
Pulmonary hypertension**	21 (30)	7 (16)	0.10	8 (20)	0.25
Pulmonary fibrosis**	23 (32)	15 (35)	0.78	13 (32)	1.00
Any lung involvement◊	52 (67)	24 (56)	0.24	21 (48)	0.04
Anemia	35 (45)	11 (26)	0.04	15 (35)	0.29
Gastroesophageal reflux	56 (73)	33 (79)	0.48	35 (83)	0.19
Congestive heart failure	9 (12)	1 (2)	0.09	6 (14)	0.72
Arrhythmia	3 (4)	1 (2)	1.00	3 (7)	0.67
Pericardial effusion	9 (12)	3 (7)	0.53	5 (12)	1.00
Renal crisis	4 (5)	2 (5)	1.00	0 (0)	0.30

*Parameters may have a lower n. than listed for total in each racial group; †Comparing Asians with Caucasians; ‡Comparing Hispanics with Caucasians; **Pulmonary hypertension was considered present if patients had a mean pulmonary artery pressure of ≥ 25 mmHg at rest or ≥ 30 mmHg with exercise on right heart catheterization or an echocardiogram with a right ventricular systolic pressure of ≥ 40mmHg. Pulmonary fibrosis was considered present if chest radiograph or computed tomography-showed evidence of honeycombing; ◊Includes pulmonary hypertension, pulmonary fibrosis, alveolitis, dyspnea, and home oxygen.

Table III. Studies and procedures performed by racial group.

Study ever performed, %	Caucasian (n=78)	Asian (n=43)	*p*-value†	Hispanic (n=44)	*p*-value‡
Pulmonary function tests	79	60	0.02	70	0.30
Forced vital capacity*	42 (82)	21 (70)	0.70	23 (86)	1.00
Diffusing capacity of carbon monoxide*	41 (57)	19 (52)	0.45	24 (61)	0.85
High resolution chest CT	53	40	0.21	50	0.78
Transthoracic echocardiogram	71	69	0.82	75	0.64
Right ventricular systolic pressure**	38 (41)	22 (39)	0.85	24 (37)	0.57
Right heart catheterization	13	10	0.77	9	0.50
Barium swallow	16	21	0.46	23	0.36
Upper GI endoscopy	29	14	0.07	25	0.61
Hand radiographs	16	31	0.06	30	0.08
Bone density scan	12	14	0.72	2	0.09
Tuberculin skin test	28	53	0.01	59	0.002

†Comparing Asians with Caucasians. ‡Comparing Hispanics with Caucasians. *Values are n (mean % predicted). **Values are n (mean mmHg).

sian patients (Table I). If the VA patients were excluded, the female:male ratio was similar in all racial groups (approximately 9:1). Overall, approximately one third of patients had diffuse skin disease; the remainder had limited skin involvement. Hispanic patients had a higher frequency of diffuse skin disease compared with Caucasians, but this did not reach statistical significance (43% versus 26%, p=0.06). In addition, Hispanic patients had a shorter disease duration compared with Caucasian patients (98±80 vs. 141±121 months, p=0.03). Both Asian and Hispanic patients were less likely to smoke or drink alcohol than Caucasian patients.

Table II shows the clinical characteristics and organ system involvement by racial group. Overall, the groups were similar to each other. However, Asian patients were significantly less likely to have digital ulcers or digital pits (26% *vs*. 47%, *p*=0.02) and anemia (26% *vs*. 45%, *p*=0.04) compared with Caucasian patients. Hispanic patients had less lung disease compared with Caucasians (48% *vs*. 67%, *p*=0.04).

Studies, procedures and medications were utilized with similar rates among the racial groups (see Tables III and IV). However, compared with Caucasians, Asians were less likely to have had pulmonary function testing (PFT's) (60% *vs*. 79%, p=0.02), to have used home oxygen (2% *vs*. 14%, *p*=0.05), or to have taken a medication approved for pulmonary arterial hypertension (PAH) (5% *vs*. 18%, *p*=0.04). Both Asian and Hispanic patients were more likely to have ever had a tuberculin skin test (TST).

Discussion

Prior studies addressing racial disparities in the clinical manifestations of SSc have principally focused on African American patients. To our knowledge, this study is the first to describe the clinical features of both Asian and Hispanic SSc patients and to compare them with Caucasians living in the same geographic area. Overall, we found few differences among with racial groups. The frequency of diffuse cutaneous disease, mean age of disease onset, prevalence of comorbid conditions, clinical manifestations, and organ system involvement were similar. Studies and procedures were performed uniformly, except TSTs were more commonly done in Asian and Hispanic patients, likely because these populations are at higher risk for exposure to tuberculosis. Asians were less likely to undergo PFT's or to take medications approved for PAH despite having a similar prevalence of this complication compared with Caucasian patients. Since the majority of non-Caucasian patients were seen at the county hospitals, it is possible that differences in procedures performed and medications prescribed were related to the practice setting or access to care.

As opposed to studies of patients in Asia (8-10), our study indicates that Asian patients with SSc in the U.S. have similar clinical manifestations as their Caucasian counterparts. Interestingly,

Table IV. Medications ever taken by racial group.

Medication ever taken, %	Caucasian (n=78)	Asian (n=43)	*p*-value†	Hispanic (n=44)	*p*-value‡
ACE-inhibitor§	34	21	0.14	23	0.23
Aspirin	26	12	0.06	26	1.00
Calcium channel blocker	64	58	0.52	63	0.89
Cyclophosphamide	13	7	0.38	9	0.53
Methotrexate	12	7	0.54	7	0.54
D-penicillamine	9	16	0.24	12	0.75
Hydroxychloroquine	17	23	0.38	12	0.46
Prednisone	40	35	0.60	33	0.43
Proton pump inhibitor	71	63	0.38	74	0.65
SSRI§	14	12	0.68	26	0.13
Warfarin	5	0	0.30	2	0.65
Home oxygen	14	2	0.05	10	0.49
PAH medication*	18	5	0.04	7	0.09
Calcium and vitamin D	29	44	0.10	27	0.80
Bisphosphonate	14	9	0.43	5	0.13

†Comparing Asians with Caucasians; ‡Comparing Hispanics with Caucasians; §ACE: angiotensin converting enzyme; SSRI: selective serotonin reuptake inhibitor; *Includes epoprostenol, treprostinil, iloprost, bosentan, and sildenafil.

Asian patients had a very low frequency of smoking and drinking, which may be related to cultural or socioeconomic factors. Asians also had a lower frequency of digital ulcers and anemia. Prior reports suggest Hispanic patients have more severe disease than Caucasians (2, 7). Reveille *et al*. found that Hispanic patients in Texas were more likely to have diffuse skin disease and digital ulcers compared with Caucasians (7). While our results suggest a trend toward an increased prevalence of the diffuse subtype in Hispanic patients, they were not more likely to have digital ulcers. McNearney *et al*. found that Hispanics had a lower percent predicted forced vital capacity, forced expiratory volume in one second, and diffusing capacity for carbon monoxide at their initial clinic visits compared with Caucasians (2). We found no difference between Hispanics and Caucasians in any individual lung-related manifestation. Moreover, a composite measure of lung disease suggests that pulmonary involvement may be *less* likely to occur among Hispanic patients. This may in part be explained by a lower likelihood of smoking in the Hispanic patients in our cohort.

Given the design of our study, we were unable to obtain information on treatments rendered outside of the 4 hospitals studied. We had insufficient information on socioeconomic status, autoantibody profiles, or physical examination findings, such as skin scores and tendon friction rubs, which have been shown to correlate with disease severity (11-15). Although medical record racial classifications have been shown to correlate with self-reported race 92% of the time, misclassification may have occurred in a small percentage of our cohort (16). Lastly, the cross-sectional study design prohibited us from making any conclusions regarding differences in survival among these racial groups.

In conclusion, clinical manifestations in Asian and Hispanic patients with SSc in Northern California do not differ substantially from Caucasians. More research is needed in a larger cohort of patients to confirm our findings and to investigate gene-environment interactions which likely impact the clinical expression of disease in various racial groups. In particular, the differences in clinical manifestations of SSc between Asian patients living in Asia compared with Asian patients living in the U.S. warrant further study.

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