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A CLINICAL AND SEROLOGIC COMPARISON OF AFRICAN-AMERICAN AND CAUCASIAN PATIENTS WITH SYSTEMIC SCLEROSIS

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Abstract

Objective—Epidemiology studies suggest that Systemic Sclerosis is more common, occurs at a younger age and is more severe in African-Americans than Caucasians. However, the scleroderma autoantibody profile is very different between these two ethnic subgroups. This study examines the demographic and disease features, frequency and severity of internal organ system involvement and survival in African-American and Caucasian SSc patients with particular attention to their serum autoantibody profiles.

Methods—Demographic, clinical, autoantibody, natural history of organ involvement and survival were studied in consecutive African-American and Caucasian patients seen between 1972 and 2007 as part of the Pittsburgh Scleroderma Database. The Medsger Disease Severity Scale was used to determine severe disease.

Results—African-American patients were more likely to have anti topoisomerase, anti U1RNP and U3 RNP auto-antibodies. Comparing African-American and Caucasians with these antibodies, African-American patients with anti topoisomerase antibody had more frequent and more severe pulmonary fibrosis than Caucasians and an associated decreased survival. Pulmonary fibrosis was also more severe in the U1 RNP patients but was not associated with a difference in survival between African Americans and Caucasians. Anti U3 RNP was associated with more severe gastrointestinal involvement in African-American's compared to Caucasians.

Conclusions—African Americans with systemic sclerosis have more severe disease complications than Caucasians both because of the type of autoantibody they have and because they have more severe interstitial lung disease even within the antibody subset. Early aggressive intervention in all African Americans with interstitial lung disease should be a priority.

Introduction

Several studies have suggested that African-Americans have an increased incidence of systemic sclerosis (SSc) and a worse prognosis than Caucasians with this disease (1;2). First, symptoms attributable to SSc occur at an earlier age in African-Americans, and interstitial

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lung disease (3) and pulmonary arterial hypertension (4) have both been shown to be more frequent and more severe in African-Americans.

Serum auto-antibodies in patients with SSc are strongly associated with clinical features, e.g. anti-centromere antibody (ACA) with pulmonary arterial hypertension, anti-topoisomerase I (topo I) antibody with interstitial lung disease and anti-RNA polymerase III (RNA pol III) antibody with “renal crisis” (5). Ethnicity is also strongly associated with the scleroderma autoantibodies and consistent with this, the frequency of serum autoantibodies differs between African-American and Caucasian SSc patients. Anti-topo I is somewhat more frequently detected in African-American SSc patients (6–8). Anti-U3RNP antibody is particularly common in African-American SSc patients (8–10). In contrast, ACA is uncommon in African-Americans (11).

There are genetic differences between African-Americans and Caucasians which probably contribute to why autoantibodies are different in the different patient populations (10). HLA DRB1*08 is more frequent in African-American SSc patients than in healthy African-Americans and Caucasian SSc patients. The frequency of HLA DRB1*1101 is increased in both African-American and Caucasian SSc patients with anti-topo I antibody. A recent study found a strong association of anti-fibrillarin (U3 RNP) with HLA DRB1*08:04(12). These genetic influences could be important factors contributing to differences in disease outcome. Some studies have suggested that, like systemic lupus erythematosus, socioeconomic differences between African-American and Caucasian patients influence survival (10), (8).

In our cumulative experience, the most frequent antibodies in Caucasian SSc patients are ACA, topo I and RNA pol III, while the most frequent in African-American SSc patients are topo I, U3RNP and U1RNP. Between 1984 and 1989, 462 consecutive SSc patients had all antibodies performed (13). The frequency of these auto-antibodies in African and Americans and Caucasians in these patients is as follows: anti-centromere 7% vs 25% (African-American vs Caucasian), anti-topoisomerase I 27% vs 21%, anti-RNA pol III 3% vs 31%, anti U1 RNP 16% vs 7%, anti U3-RNP 40% vs 2%, and anti Th/To 1% vs 4%. The former three antibodies account for over 75% of Caucasian SSc patients and the latter three for over 70% of African-American SSc patients. For these reasons, comparisons of cohorts of African-American and Caucasian SSc patients regarding clinical manifestations, organ system involvements and long-term outcomes need to consider autoantibody prevalence in the groups being studied.

This study examines the demographic and disease classification features, frequency and severity of internal organ system involvement and survival in African-American and Caucasian SSc patients with particular attention to their serum autoantibody profiles.

Methods

Patients

The Pittsburgh Scleroderma Databank is a prospective natural history study of consecutive systemic sclerosis (SSc) patients first evaluated beginning January 1, 1972. Patient outcomes, including organ system involvements and survival, were determined on all patients based on initial visit data, follow-up visits, managing physicians’ office records, annual/biannual patient completed questionnaires and telephone interviews (14). Deaths were confirmed through the Social Security Death Index as of December 31, 2009 and causes of death determined from hospital and physician records and death certificates (15). We have previously validated these methods of assessing severe internal organ involvement and causes of death in SSc patients (14). In this study, we included all African-American and Caucasian patients first evaluated during 1972–2007.

Organ System Involvement

Organ system involvements were defined as described previously (14).

Severe organ involvement was defined as being grade 3 (severe) or grade 4 (end stage) based on the revised Medsger SSc disease severity index (16), as follows:

Peripheral vascular: digital tip ulcers or gangrene.

Skin: modified Rodnan total skin thickness (mRSS) score >30.

Joints/tendons: fingertip to palm distance 4.0 + cm.

Skeletal muscles: severe proximal muscle weakness on physical examination or ambulation aids required.

Gastrointestinal (GI) tract: malabsorption syndrome, episodes of pseudo-obstruction, hyper alimentation required or death due to intestinal involvement.

Pulmonary fibrosis: pulmonary fibrosis on radiograph plus any one of the following: FVC <50% predicted, oxygen required for interstitial lung disease, lung transplantation performed or death due to SSc interstitial lung disease.

Pulmonary arterial hypertension or PAH (not secondary to pulmonary fibrosis): pulmonary artery systolic pressure 65+ mmHg estimated by echocardiogram or measured at right heart catheterization, oxygen required for PAH, or death due to SSc PAH.

Heart: left-sided congestive heart failure due to SSc (not secondary to renal crisis), arrhythmia requiring treatment, LVEF <40%, heart transplant performed, or death due to SSc heart disease.

Kidney: “renal crisis” with serum creatinine 3.0+ mg/dL at any time, dialysis required, renal transplant performed for SSc renal disease or death due to SSc renal disease.

Autoantibody Studies

All patients had an antinuclear antibody (ANA) test performed in the same laboratory using HEp-2 cells as substrate. SSc-specific antibodies, including (a) anti-centromere (ACA), (b) anti-topoisomerase I (topo I), (c) anti-U1RNP, (d) anti-RNA polymerase III (RNA pol III), (e) anti-U3RNP (U3RNP), (f) Ku and (g) anti-Th/To were performed according to previously described methods (6;9;17;18). SSc-specific autoantibody testing was not performed on all patients in the Databank since patient entry spanned over 3 decades. The few patients with more than one SSc-associated serum autoantibody were not included in this study.

Data Analysis

The Pittsburgh Scleroderma Databank uses the Medlog database management system. Baseline characteristics and organ system involvement between groups was compared using t-tests, Chi-square or Wilcoxon test when appropriate. Survival was assessed by Kaplan-Meier analysis and associations with mortality by Cox proportional hazards. Predictors of severe lung involvement were assessed by multivariable logistic regression.

Results

Baseline characteristics

There were 2945 Caucasian and 203 African-American SSc patients included in the study. Their baseline characteristics at first visit are presented in Table 1. African-American

patients were significantly younger at disease onset, first SSc diagnosis and first Pittsburgh visit. Although their disease duration was significantly shorter, they had worse functional scores at presentation (median HAQ disability index 1.33 vs. 0.86 p= 0.01). This finding may in part be attributable to African-American SSc patients more often having diffuse cutaneous (dc) involvement (51% vs. 44%, p=0.03). Autoantibody frequencies had a similar distribution in these patients as was seen with our smaller subset in whom all the Autoantibodies were tested. African-American patients had significantly higher frequencies of anti-U3-RNP (40% vs 2%), U1-RNP (16% vs. 7%) and anti-topo I (27% vs. 21%).

Organ involvement and survival

Table 2 depicts organ system involvements in African-American and Caucasian SSc patients. The overall frequency of such organ involvements, as well as severe organ system involvement is presented. Overall, skeletal muscle involvement was more common in African-American SSc patients (27% vs. 12%, p<0.001) Severe skeletal muscle involvement was also more often encountered in African-Americans (6% vs. 2%, p=0.001). The same was true of pulmonary fibrosis (54% vs 33%, p < 0.0001) and severe pulmonary fibrosis (32% vs. 13%, p=0.0001). Slightly more African-American patients developed GI involvement, although there was no difference in the frequency of severe GI disease. There were no differences in frequency of PH, cardiac, renal or joint/tendon involvement.

The overall survival curves are significantly different, with African-American patients having worse survival (66% vs. 75% at 5 years and 51% vs. 60% at 10 years, p=0.0063). After adjustment for age, gender and diffuse disease, African American patients were 1.68 times more likely (95% CI 1.30 – 2.16) to die at 5 years of follow-up than Caucasians (Table 3). Adjustment for tobacco use and interstitial lung disease did not change the overall results. The proportional hazards assumption was met for all models.

If we were to publish these data without qualifications, we would postulate that African-American patients had worse survival than Caucasian patients because they more often had diffuse scleroderma and severe pulmonary fibrosis, both recognized risk factors. In order to determine whether there were specific ethnic differences, we focused on the SSc-associated serum antibodies most frequently detected in African-Americans. We specifically compared African-American and Caucasian patients who had anti-topo I, anti-U3RNP and U1RNP antibodies, the antibodies most frequently detected in African-American SSc patients.

Autoantibody Characteristics

Anti-topoisomerase I antibody positive patients—We compared the demographic characteristics, HAQ scores and frequency of organ involvement between 48 African-American and 490 Caucasian SSc patients with anti-topo I antibody (Table 4). African-American topo I positive patients were younger than Caucasian patients at the onset of their disease (mean age 37 vs. 43 years; p = 0.005), but there was no difference in the frequency of diffuse cutaneous scleroderma in these patients (71% in African-American and 65% in Caucasians). The peak skin score was similar in both as well. Pulmonary fibrosis was more frequent in African-American SSc anti-topo I positive patients (72% vs. 52%, p=0.0135), with a significantly greater frequency of severe pulmonary fibrosis compared with Caucasian patients (44% vs. 18%, p=0.0001), despite no difference in disease duration at presentation. There were no other differences in the frequencies of severe organ system involvements between the two groups. After adjustment for age, gender and diffuse disease, African-American topo I positive patients were 75% more likely to die at five years than Caucasian topo I positive patients (hazard ratio 1.75, 95% CI 1.06 – 2.88, p=0.03), consistent with their more severe lung disease.

Anti-U3RNP antibody positive patients—24 African American and 61 Caucasian anti-U3RNP antibody positive SSc patients (Table 5) were compared. There were no age, sex or disease duration differences between the two groups. African-American anti-U3RNP antibody positive patients more frequently had dcSSc (71% vs. 44%, $p<0.05$) and thus a higher maximum skin score. Severe GI involvement was more common in African-American than Caucasians with anti U3-RNP antibody. This is in agreement with a prior Japanese study and is the only serum antibody marker associated with GI disease (19). Unlike anti topo patients, the frequency of any or of severe pulmonary fibrosis was not different between African-American and Caucasian patients. Compared to all patients, pulmonary arterial hypertension was increased in both African-American and Caucasian patients, 22% and 30%. (vs 11% in all patients) This is particularly important since most of the African-American patients had diffuse cutaneous scleroderma. Renal crisis was more frequent among African-Americans than Caucasians with anti-U3RNP (17% vs. 2%), but this is likely related to the higher frequency of dc SSc patients. After adjustment for age, gender and diffuse disease, there was no increased risk of death at five years of follow-up between African-American and Caucasian anti-U3RNP positive patients.

Anti-U1RNP antibody positive patients—In 30 African-American and 148 Caucasian SSc patients with anti-U1RNP antibody, there were no demographic differences between the groups (Table 6). Most patients had limited cutaneous disease (67% in African-Americans, 80% in Caucasians, po). Inflammatory muscle involvement was common (30%) in both African-American and Caucasians. Like in the anti-topo I antibody patients, any pulmonary fibrosis (74% vs. 31%, $p=0.0175$) and severe pulmonary fibrosis (40% vs. 9%, $p=0.0001$) were significantly more frequent in African-American anti-U1RNP positive patients (Table 6). Five-year survival was no different after adjustment for age, gender and diffuse disease.

Tobacco

To determine if there was any effect of cigarette smoking on the severity of pulmonary fibrosis, we examined smoking histories in African-Americans and Caucasians. African-Americans were more likely to be current smokers, (25% vs 16%, $p<0.0002$), but among smokers, thirty percent of African-Americans had severe pulmonary fibrosis compared with 13% of Caucasians ($p=0.0001$). Similarly, 29% of African-American lifelong non-smokers s vs. 10% of Caucasian lifelong non-smokers had severe pulmonary fibrosis ($p=0.0001$). In multivariable logistic analysis, after adjusting for age, gender and tobacco use, African-American patients were more likely to develop pulmonary fibrosis (OR 3.04, 95% CI 2.23 – 4.13, $p=0.008$) than Caucasians.

Discussion

Both incidence and prevalence of systemic sclerosis are greater in African-Americans than Caucasians (1;2). In a comprehensive epidemiologic study of women resident of the state of Michigan between 1980 and 1991, the annual incidence of SSc was 22.5 per million population at risk in African-Americans compared with 12.8 per million in Caucasians (2). Prior reports have shown that African-American SSc patients are younger at disease onset, diagnosed at an earlier age and more frequently have diffuse scleroderma (2;7;20) and interstitial lung disease (3;8).

Although all African-American patients combined were younger at onset than all Caucasians, the age difference was only significant for one of the 3 auto-antibody subsets, anti-topo I. In all the patients, African-Americans had slightly shorter disease duration, suggesting that delay in diagnosis is unlikely to be a cause for differences in outcomes. Also, the greatest education level was not different in our two patient groups. Thus,

socioeconomic status was not a factor in this cohort. However, the mean of 13 years of education in our African-American SSc patients was considerably higher than in some of the inner city systemic lupus erythematosus studies, where socioeconomic status seemed to play a greater role in outcome. Within the specific autoantibody analyses there were no differences in either of these features.

The proportion of patients with diffuse skin changes was greater in African-American than in Caucasian patients (56% vs. 43%, $p<0.03$), but now within the specific antibodies, there was only a marginally significant difference and only within the anti-U3RNP patients. The mean maximum RSS and frequency of severe skin involvement were similar in all 3 antibody groups. This suggests that the increased frequency of diffuse disease primarily reflects the difference in antibody profile between the races.

Among all SSc patients, the frequency of skeletal muscle involvement was significantly greater in African-American patients, but severe skeletal muscle was infrequent in all groups. The frequency of any gastrointestinal involvement was slightly higher overall in African American as well, but this is likely due to the differences in patients with anti U3RNP. Severe gastrointestinal involvement was strikingly more common in African-Americans than Caucasians with anti-U3RNP antibody (26% vs 9%, $p=0.04$). This subset of severe GI disease in anti-U3RNP positive SSc patients has been identified previously in Japanese SSc patients (19), in anti-fibrillarin African American scleroderma patients compared to African-American patients without anti fibrillarin antibodies (12) and in African-American males with severe small bowel involvement and ANAs showing nucleolar staining. with a nucleolar antibody (21). It is likely that the latter patients frequently had anti-U3-RNP antibody, but this testing was not available to the authors.

Multiple studies have consistently shown that African-American patients with scleroderma have more frequent and more severe pulmonary fibrosis than Caucasians. This study is the first on which documents that the frequency of severe pulmonary fibrosis was higher in African-Americans than Caucasians even within some autoantibody subsets, particularly anti topo and anti U1RNP which are intrinsically associated with pulmonary fibrosis. Interestingly this was not seen in patients with anti U3 RNP where severe pulmonary fibrosis is less common. The increase in pulmonary arterial hypertension in the U3 RNP was present in both African-Americans and Caucasians in these patients. Greidinger previously found more severe lung disease in African-Americans and anti-topo I positive patients (3). In our analysis, African-American race appears to be independently associated with the development of severe pulmonary fibrosis. Thus, African-Americans more frequently have antibodies associated with lung disease, but also are at greater risk for severe lung disease, possibly because of genetic or unrecognized environmental factors. Recent studies have shown that there are ethnic differences in anti-fibrotic hepatocyte growth factor expression in lung fibroblasts from Caucasian and African American subjects. Reduced levels of HGF as well as a deficiency in c-Met receptor function appear to be present in African American patients with SSc. These findings may explain in part the greater disease severity and worse prognosis observed in African-Americans with SSc. (22)

Several reports have suggested that African-Americans with SSc have a worse survival potentially related to ethnic disparities or quality of care (4;23). Age, SSc subtype, autoantibodies and socioeconomic status significantly influence these findings. Liang's study showed an increase in mortality in African-Americans which was significant when adjusted for age and disease subtype (2). Although we showed a significant decrease in survival when all African-Americans were compared to all Caucasians, this was present only in the anti topo patients where increased severity of pulmonary fibrosis was so prevalent. There was no survival difference between African-American and Caucasians patients with

anti U3RNP and anti U1-RNP antibodies. Thus, the overall prognosis seems to be most closely related to autoantibody type and the presence of pulmonary fibrosis rather than a more generalized racial effect. Survival differences in other studies are most likely because African-Americans have a higher frequency of these 3 antibodies than Caucasians (70% vs. 48%).

We have shown that there are major differences between African-Americans and Caucasians with respect to serologic and clinical phenotypes. Although this study was not specifically designed to carefully study socioeconomic status or delay of treatment differences, overall there were no differences in education (an often used surrogate for socioeconomic status) or in disease duration at time of first evaluation or first diagnosis in these different ethnic groups. We feel that most of the differences in organ system outcomes appear to be because different SSc-associated autoantibodies occur in African-Americans. However, there are also differences even within the antibody subsets. African-Americans with anti-topo I and U1-RNP clearly have more severe pulmonary fibrosis than Caucasians with the same antibodies and severe gastrointestinal disease was more frequent in African-Americans with anti U3RNP. Whether these are related to different environmental exposures or genetics remain to be seen. These findings have important implications for both clinical interventions and future pathogenic studies.

Reference List

1. Steen VD, Oddis CV, Conte CG, Janoski J, Casterline GZ, Medsger TA Jr. Incidence of systemic sclerosis in Allegheny County, Pennsylvania. A twenty-year study of hospital-diagnosed cases, 1963–1982. Arthritis Rheum. 1997; 40(3):441–5. [PubMed: 9082931]
2. Laing TJ, Gillespie BW, Toth MB, Mayes MD, Gallavan RH Jr, Burns CJ, et al. Racial differences in scleroderma among women in Michigan. Arthritis Rheum. 1997; 40(4):734–42. [PubMed: 9125258]
3. Greidinger EL, Flaherty KT, White B, Rosen A, Wigley FM, Wise RA. African-American race and antibodies to topoisomerase I are associated with increased severity of scleroderma lung disease. Chest. 1998; 114(3):801–7. [PubMed: 9743170]
4. Beall AD, Nietert PJ, Taylor MH, Mitchell HC, Shaftman SR, Silver RM, et al. Ethnic disparities among patients with pulmonary hypertension associated with systemic sclerosis. J Rheumatol. 2007; 34(6):1277–82. [PubMed: 17516621]
5. Steen VD. The many faces of scleroderma. Rheum Dis Clin North Am. 2008; 34(1):1–15. [PubMed: 18329529]
6. Steen VD, Powell DL, Medsger TA Jr. Clinical correlations and prognosis based on serum autoantibodies in patients with systemic sclerosis. Arthritis Rheum. 1988; 31(2):196–203. [PubMed: 3348823]
7. Reveille JD, Durban E, Goldstein R, Moreda R, Arnett FC. Racial differences in the frequencies of scleroderma-related autoantibodies [see comments]. Arthritis Rheum. 1992; 35(2):216–8. [PubMed: 1734910]
8. McNearney TA, Reveille JD, Fischbach M, Friedman AW, Lisse JR, Goel N, et al. Pulmonary involvement in systemic sclerosis: associations with genetic, serologic, sociodemographic, and behavioral factors. Arthritis Rheum. 2007; 57(2):318–26. [PubMed: 17330281]
9. Okano Y, Steen VD, Medsger TA Jr. Autoantibody to U3 nucleolar ribonucleoprotein (fibrillarin) in patients with systemic sclerosis. Arthritis Rheum. 1992; 35(1):95–100. [PubMed: 1731817]
10. Reveille JD, Fischbach M, McNearney T, Friedman AW, Aguilar MB, Lisse J, et al. Systemic sclerosis in 3 US ethnic groups: a comparison of clinical, sociodemographic, serologic, and immunogenetic determinants. Semin Arthritis Rheum. 2001; 30(5):332–46. [PubMed: 11303306]
11. Steen VD, Ziegler GL, Rodnan GP, Medsger TA Jr. Clinical and laboratory associations of anticentromere antibody in patients with progressive systemic sclerosis. Arthritis Rheum. 1984; 27(2):125–31. [PubMed: 6607734]

12. Sharif R, Fritzler MJ, Mayes MD, Gonzalez EB, McNearney TA, Draeger H, et al. Anti-Fibrillarin Antibody in African American Patients with Systemic Sclerosis: Immunogenetics, Clinical Features, and Survival Analysis. J Rheumatol. 2011; 38(8):1622–30. [PubMed: 21572159]
13. Steen VD. Autoantibodies in systemic sclerosis. Semin Arthritis Rheum. 2005; 35(1):35–42. [PubMed: 16084222]
14. Steen VD, Medsger TA Jr. Severe organ involvement in systemic sclerosis with diffuse scleroderma. Arthritis Rheum. 2000; 43(11):2437–44. [PubMed: 11083266]
15. Steen VD, Medsger TA. Changes in causes of death in systemic sclerosis, 1972–2002. Ann Rheum Dis. 2007; 66(7):940–4. [PubMed: 17329309]
16. Medsger TA Jr, Silman AJ, Steen VD, Black CM, Akesson A, Bacon PA, et al. A disease severity scale for systemic sclerosis: development and testing. J Rheumatol. 1999; 26(10):2159–67. [PubMed: 10529133]
17. Okano Y, Steen VD, Medsger TA Jr. Autoantibody reactive with RNA polymerase III in systemic sclerosis. Ann Intern Med. 1993; 119(10):1005–13. [PubMed: 8214977]
18. Okano Y, Medsger TA Jr. Autoantibody to Th ribonucleoprotein (nucleolar 7-2 RNA protein particle) in patients with systemic sclerosis. Arthritis Rheum. 1990; 33(12):1822–8. [PubMed: 1701994]
19. Nishimagi E, Tochimoto A, Kawaguchi Y, Satoh T, Kuwana M, Takagi K, et al. Characteristics of patients with early systemic sclerosis and severe gastrointestinal tract involvement. J Rheumatol. 2007; 34(10):2050–5. [PubMed: 17924608]
20. Nietert PJ, Mitchell HC, Bolster MB, Shaftman SR, Tilley BC, Silver RM. Racial variation in clinical and immunological manifestations of systemic sclerosis. J Rheumatol. 2006; 33(2):263–8. [PubMed: 16465656]
21. Azih, C. Small Bowel Involvement in Systemic Sclerosis. In: Peng, J.; Steen, V., editors. Arthritis Rheum. Vol. 58. 2008. p. S 377
22. Bogatkevich GS, Ludwicka-Bradley A, Highland KB, Hant F, Nietert PJ, Singleton CB, et al. Impairment of the antifibrotic effect of hepatocyte growth factor in lung fibroblasts from African Americans: possible role in systemic sclerosis. Arthritis Rheum. 2007; 56(7):2432–42. [PubMed: 17599773]
23. Mendoza F, Derk CT. Systemic sclerosis mortality in the United States: 1999–2002 implications for patient care. J Clin Rheumatol. 2007; 13(4):187–92. [PubMed: 17762451]

Table 1

Baseline characteristics at first visit of 3148 African-American and Caucasian systemic sclerosis patients seen between 1972–2007.

Features	African-American (n=203)	Caucasian (n=2945)	p-value
Sex (% female)	155 (76%)	2374 (81%)	NS
High school or higher education (%)	105 (52%)	1698 (58%)	NS
Residence within 100 miles of Pittsburgh	133 (66%)	1428 (48%)	<0.0001
Mean age at symptom onset (SD)	38.4 ± 14.3	42.9 ± 14.9	<0.001
Mean age at first visit (SD)	44.8 ± 12.3	50.6 ± 14.1	<0.001
Disease duration, defined as onset to first visit in years (IQR)	2.97 (1.27, 8.04)	3.46 (1.64, 10.84)	NS
Tobacco Use			0.002
Never	107	1618	
Prior	44	827	
Current	52	482	
Diffuse cutaneous involvement (%)	102(51%)	1264 (43%)	0.03
Overlap syndrome w with another connective tissue disease (%)	32 (16%)	237 (8%)	0.0002
Mean Body Mass Index (SD)	24.1 ± 4.9	24.1 ± 4.9	NS
Autoantibodies			
Anti-centromere	14 (7%)	45 (22%)	<0.0001
Anti-topoisomerase I	26 (25%)	530 (18%)	0.01
Anti-RNA polymerase III	20 (10%)	619 (21%)	0.001
Anti-U1-RNP	27 (13%)	12 (4%)	<0.0001
Anti-U3-RNP	33 (16%)	6 (2%)	<0.0001
Anti-Th/To	7 (3%)	18 (6%)	NS
HAQ disability index (median, IQR) *	1.33 (0.50, 1.81)	0.86 (0.30, 1.38)	0.01

* HAQ available in 23% of African-American and Caucasian patients

Table 2

Frequency of overall and severe organ involvement in African-American and Caucasian SSc patients.

Organ System	African-American (n=203)		Caucasian (n=2945)		p-value	
	Overall	Severe	Overall	Severe	Overall	Severe
Vascular	201 (99%)	97 (48%)	2880 (98%)	1296 (44%)	NS	NS
Skin		47 (23%)		618 (21%)		NS
Joint/tendons	172 (85%)	45 (22%)	2331 (79%)	589 (20%)	0.06	NS
Skeletal Muscle	54 (27%)	12 (6%)	367 (12%)	59 (2%)	< .0001	0.001
*GI Tract	70% 143/169	12% (20/169)	62% (1826/2312)	11% (254/2312)	0.02	NS
*Pulmonary Fibrosis	54% (100/186)	32% (60/186)	33% (973/2562)	13% (337/2562)	< .0001	0.0001
*PAH	11% (23/149)	11% (17/148)	11% (317/2005)	12% (243/2005)	NS	NS
*Heart	20% (43/173)	18% (31/173)	17% (529/2411)	16% (382/2411)	NS	NS
Kidney	25 (13%)	20 (10%)	282 (10%)	236 (8%)	NS	NS

* proportion of patients classified as severe with denominator being total number with objective data that permits severity assessment. All others used all patients as denominator.

Table 3

Risk factors for mortality within 5 years from the first Pittsburgh visit.

	Hazard Ratio	95% Confidence Interval	p-value
Age at first Pittsburgh visit	1.04	1.03 – 1.04	< .0001
Male	1.35	1.15 – 1.60	0.003
Diffuse cutaneous disease	1.34	1.16 – 1.54	< .0001
African-American	1.68	1.30 – 2.16	< .0001

Table 4

Demographic, disease classification features and frequency of severe organ system involvement of SSc patients with anti-topo I antibody first evaluated during 1972–2007.

Features	African-American (n= 48)	Caucasian (n= 490)	p-value
Sex (% female)	36 (75%)	366 (75%)	NS
Age at onset (mean ± SD)	36.6 ± 14.1	43.3 ± 15.9	0.005
Disease Duration: Onset to diagnosis (years ± SD)	3.0 ± 5.2	3.6 ± 6.0	NS
HAQ disability index: greatest	1.6 ± 1.0	1.3 ± 0.9	0.097
Diffuse disease (%)	34 (71 %)	317 (65%)	NS
Skin (mean maximum TSS mean ± SD)	20.8 ± 12.6	20.0 ± 13.2	NS
Vascular	25/48 (52%)	250/490 (51%)	NS
Skin	12/48 (25%)	127/490 (26%)	NS
Joint/tendon	19/48 (40%)	164/490 (33%)	NS.
Skeletal muscle	1/48 (2%)	8/490 (2%)	NS
*GI tract	5/38 (13%)	35/400 (9%)	NS
*Pulmonary fibrosis	19/43 (44%)	82/450 (18%)	0.0001
*PAH	2/39 (5%)	10/332 (3%)	NS
*Heart	10/38 (26%)	89/403 (22%)	NS
Kidney	4/48 (8%)	36/490 (7%)	NS

SD = standard deviation

HAQ = health assessment questionnaire

* proportion of patients classified as severe with denominator being total number with objective data that permits severity assessment

Table 5

Demographic, disease classification features and frequency of severe organ system involvement of SSc patients with anti-U3RNP antibody first evaluated during 1972–2007

Features	African-American (n= 24)	Caucasian (n=61)	p-value
Sex (% female)	17 (71%)	42 (69%)	NS
Age at onset (mean ± SD)	38.5 ± 14.6	39.9 ± 15.4	NS
Disease Durations: Onset to diagnosis (years ± SD)	2.8 ± 4.2	2.7 ± 4.3	NS
HAQ disability index: greatest	1.6 ± 0.7	1.2 ± 0.8	NS
Diffuse disease (%)	17 (71%)	27 (44%)	0.05
Skin (mean maximum TSS mean ± SD)	17.4 + 10.4	13.3 + 11.5	NS
Vascular	12/24 (50%)	26/61 (43%)	NS
Skin	5/24 (21%)	6/61 (10%)	NS
Joint/tendon	6/24 (25%)	8/61 (13%)	NS
Skeletal Muscle	2/24 (8%)	2/61 (3%)	NS
*GI tract	6/19 (26%)	4/46 (9%)	0.05
*Pulmonary fibrosis	3/21 (14%)	5/54 (9%)	NS
*PAH	4/18 (22%)	14/47 (30%)	NS
*Heart	4/22 (18%)	9/54 (17%)	NS
Kidney	4/24 (17%)	0/61 (0%)	0.001

SD = standard deviation

HAQ = health assessment questionnaire

* proportion of patients classified as severe with denominator being total number with objective data that permits severity assessment

Table 6

Demographic, disease classification features and frequency of severe organ system involvement of SSc patients with anti-U1RNP antibody first evaluated during 1972–2007.

Features	African-American (n= 30)	Caucasian (n= 148)	p-Value
Sex (% female)	23 (77%)	122 (82%)	NS
Age at onset (mean ± SD)	34.2 ± 12.3	36.7 ± 14.1	NS
Disease duration: Onset to diagnosis (years) ± SD	3.0 ± 6.9	3.9 ± 5.7	NS
HAQ disability index: greatest	1.1 ± 0.9	1.2 ± 0.8	NS
Diffuse disease (%)	10 (33%)	29 (20%)	NS
Skin (mean maximum TSS ± SD)	8.5 + 9.0	8.5 + 9.9	NS
Vascular	10/30 (33%)	60/148 (40%)	NS
Skin	1/30 (3%)	8/148 (5%)	NS
Joint/tendon	3/30 (10%)	21/148 (14%)	NS
Skeletal muscle	1/30 (3%)	4/148 (3%)	NS
*__GI__	1/24 (4%)	14/110 (13%)	NS
*__Pulmonary fibrosis__	12/23 (52%)	14/122 (11%)	0.0001
*__PAH__	1/21 (5%)	11/87 (13%)	NS
*__Heart__	4/24 (17%)	20/121 (16%)	NS
Kidney	0/30 (0%)	4/148 (3%)	NS

SD = standard deviation

HAQ = health assessment questionnaire

* proportion of patients classified as severe with denominator being total number with objective data that permits severity assessment