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RACIAL DIFFERENCES IN SCLERODERMA AMONG WOMEN IN MICHIGAN

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Objective. **To examine racial differences in disease onset, extent, manifestations, and survival among women with scleroderma.**

Methods. **A retrospective cohort study of women with scleroderma, diagnosed in Michigan between 1980 and 1991, was conducted. Clinical, laboratory, and demographic data were abstracted from the patients' medical records.**

Results. **A total of 514 women with scleroderma were identified: 117 (23%) were black and 397 (77%) were white. Among black women, the mean age at diagnosis was lower (44.5 years versus 51.5 years; $P < 0.001$) and diffuse disease was more common (49.6% versus 24.9%; $P < 0.001$) than among white women. The overall incidence of scleroderma was 14.1 per million per year: 22.5 per million per year in black women versus 12.8 per million per year in white women ($P < 0.001$). Pericarditis ($P = 0.009$), pulmonary hypertension ($P < 0.001$), pleural effusions ($P = 0.01$), myositis ($P = 0.02$), and an erythrocyte sedimentation rate >40 mm/hour ($P < 0.001$) were more frequent among black women, while white women were more likely to have digital infarctions ($P < 0.001$). Survival at 7 years from diagnosis was 72.5% among black women and 77.6% among white women. Age-adjusted survival was significantly reduced among black women ($P = 0.033$), most likely because of increased diffuse involvement. Survival among those with renal or pulmonary involvement was also significantly reduced.**

Conclusion. **Black women with scleroderma were significantly more likely than white women to develop diffuse disease, be diagnosed at a younger age, have a higher incidence of inflammatory features, and have a worse age-adjusted survival rate.**

Scleroderma is an uncommon connective tissue disease that is characterized by variable degrees of fibrosis within the skin and internal organs. Previous epidemiologic studies have provided estimates of incidence, prevalence, and mortality, and have identified the various clinical and laboratory manifestations that distinguish the diffuse and limited scleroderma subtypes (1,2). In addition, some investigators have suggested important differences between black and white women with regard to incidence, mortality, case fatality, and extent of disease manifestations (3–5). However, few studies have contained sufficient numbers of both black and white women to completely identify and confirm these observations.

As part of a population-based case–control study to identify potential risk factors among women with scleroderma, we recruited a large, racially diverse cohort of women with scleroderma in Michigan (6). During review of their medical records, 74 clinical and laboratory parameters were recorded, as well as demographic information, date of diagnosis, and date of death or last followup examination. These data enabled us to examine racial differences in age at diagnosis, extent of disease, clinical manifestations, incidence of disease, and survival.

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Table 1. Sources of eligible patients with scleroderma in Michigan

Source	No. of patients identified by each source
University of Michigan	106
Wayne State University	196
Physician referral	104
United Scleroderma Foundation	147
Health Care Investment Analysts	282
Other	15
Total	514*

* 141 women were identified by 2 sources, 72 by 3 sources, and 17 by 4 sources.

PATIENTS AND METHODS

Patients. We attempted to identify all women 18 years or older who were diagnosed with scleroderma in Michigan between January 1, 1980 and December 31, 1991. Patients were recruited from 5 different sources: 1) a comprehensive hospital discharge diagnosis database (Health Care Investment Analysts, Inc. [HCIA], Ann Arbor, Michigan), 2) the University of Michigan Hospitals database, 3) Wayne State University Hospitals database, 4) inquiries to all Michigan rheumatologists, and 5) solicitation by mail of the members of the Southeast Michigan chapter of the United Scleroderma Foundation.

HCIA initially contacted 201 hospitals and requested that consent forms be sent to all potentially eligible women. Among these hospitals, 128 (64%) agreed to participate (representing 78% of potential subjects), 49 (24%) declined due to staffing shortages, and 24 (12%) had closed or were operating under another hospital system. The University of Michigan and Wayne State hospital databases allowed chart reviews of all potentially eligible women. Of 109 Michigan rheumatologists, 76 (70%) agreed to mail consent forms to their potentially eligible patients. Finally, the United Scleroderma Foundation of Michigan mailed consent forms to all of their members. The contributions of each source to the final patient pool are shown in Table 1.

A precise estimate of the response rate cannot be calculated because of the constraints on patient anonymity required by most patient sources. However, the response rate to patient mailings was estimated to be between 75% and 80% after adjusting for duplicate names, ineligible patients, and incorrect mailing addresses. Of those who returned forms, 93% agreed to participate. A capture-recapture analysis (7), which estimates a population size based on the overlap of cases identified from different sources, yielded an estimated capture proportion of 81% when stratified by geographic region (Detroit metropolitan area versus the rest of the state).

Data collection. Patient charts were abstracted by study personnel using a coding form containing 74 clinical and laboratory variables (6). Each of these variables was recorded as normal, abnormal, or not performed. A given disease manifestation was coded as present if it appeared at any time in the charts. All abstractors were trained by study rheumatologists and were given several practice charts to review while in the presence of the rheumatologist. Interrater reliability was evaluated by requiring all abstractors to review the same 5 charts. Any discrepancies or omissions were discussed with the abstractors. The final diagnosis and eligibility were determined by 1 of the study rheumatologists after reviewing the information on the abstraction form. If the diagnosis, eligibility, or other elements of the clinical data were unclear, additional chart sources were sought and/or the patient's physician was contacted by telephone. The date of diagnosis was defined as the date scleroderma was first mentioned by the attending physician.

Eligible women either met the American College of Rheumatology (ACR; formerly, the American Rheumatism Association) criteria for definite scleroderma (8), or were judged to have had probable scleroderma (sclerodactyly and 1 or more of the following: calcinosis, Raynaud's phenomenon, esophageal dysmotility, and telangiectasias [CREST]). Eligible patients were then further classified as having diffuse scleroderma (labeled as such in the chart, or if sclerodermatous skin changes in the trunk, thighs, or upper arms were described), limited scleroderma (labeled in the chart as limited or CREST, or found to have Raynaud's phenomenon, sclerodactyly, and telangiectasias), or unspecified scleroderma (labeled as scleroderma in the chart, but with insufficient information regarding skin involvement to distinguish between diffuse and limited involvement).

The data abstracted from the charts were also used to identify internal organ system involvement. Renal involvement was defined as a serum creatinine level of $\geq$1.8 mg/dl or a history of hypertensive crisis. Pulmonary involvement consisted of pulmonary fibrosis (defined as fibrosis on a chest radiograph) or pulmonary hypertension. Gastrointestinal involvement was considered to be present if either esophageal dysmotility or malabsorption was documented. Myositis was considered to be present if labeled as such in the chart and accompanied by an elevated serum creatine phosphokinase (CPK) level. Cardiac involvement was not assessed.

To ensure accuracy in the chart abstraction process, approximately two-thirds of the eligible cases were reabstracted by a different member of the study team. Most of the reabstracted charts were from the University of Michigan and Wayne State University Hospitals. As a result of this effort, 2 patients were reclassified as ineligible because a diagnosis date was found prior to 1980, 46 cases of probable scleroderma were reclassified as definite scleroderma, pulmonary hypertension was identified in 4 additional patients, and pulmonary fibrosis was identified in 11 others. Many additional minor laboratory and physical features were found on reabstraction.

Statistical analysis. Statistical tests for equality of proportions were performed using standard chi-square analyses. Since many hospitals did not have computerized patient records prior to 1985, patients diagnosed during that period were usually identified only if they were alive in the later 1980s. Therefore, because of more complete ascertainment of cases, and to avoid selection of patients with longer durations of clinical disease, incidence and survival estimates were based only on those cases diagnosed between 1985 and 1991.

Incidence (technically, incidence density), expressed per million women per year, was calculated as

$$\frac{\text{No. of cases diagnosed between 1985 and 1991}}{(7 \text{ years} \times \text{no. of women age 18 or older in Michigan})/10^6}.$$

The denominator was obtained from 1990 census figures. Age- and race-specific incidence estimates were calculated using the respective subsets of the 1990 census. Confidence intervals (CI) for the true incidences were obtained by assuming that the number of incident cases follows a binomial distribution. Given that case ascertainment in the state was not complete, the incidence estimates represent lower bound estimates.

Survival time was defined as the time from diagnosis until death, with the date of death obtained from the medical record and/or death certificate. For patients still alive, the censoring time was the date of the telephone interview for those patients who participated in the interview required for the case–control study, and the last date of followup recorded in the current medical record for those who did not. For patients with incomplete vital status information, a commercial data retrieval company (Equifax, McLean, VA) was employed to obtain last known date alive or date of death.

Survival probabilities were estimated by the method of Kaplan and Meier (9). All-cause mortality was the variable used, because an additional analysis of our study population showed that death certificates failed to mention scleroderma as an underlying or contributory cause in ~35% of cases (10). Expected survival probabilities for age- and race-matched Michigan women were calculated using published hazard figures, by age and race, for the Michigan female population (11). Survival time comparisons, adjusted for age at diagnosis, were performed using Cox proportional hazards regression (12). Age at diagnosis was included as a continuous variable in all models. Interactions between age at diagnosis and race or organ involvement (gastrointestinal, pulmonary, renal, and muscle) were tested; none were statistically significant. The proportional hazards assumption for race, age at diagnosis, and organ involvement was validated using standard graphical methods (13).

RESULTS

Overall, 533 eligible women with scleroderma, diagnosed in Michigan between 1980 and 1991, were identified, of whom 514 were either black or white. The remaining 19 women of other races or for whom race was unspecified (n = 11) were excluded. As previously described, 395 women (77%) met the ACR criteria for scleroderma and were considered to have definite cases, and 119 (23%) had sclerodactyly and at least 1 other CREST feature and were considered to have probable cases. Further classification identified 157 women (30.5%) with diffuse scleroderma, 241 (46.9%) with limited scleroderma, and 116 (22.6%) with scleroderma of unspecified extent (Table 2). For the incidence and survival analyses, the 346 patients diagnosed between 1985 and 1991, inclusive, were included. For the other analyses, inclusion of the women who were diagnosed between 1980 and 1984 did not change the proportions, by race, of women with diffuse and limited disease.

Comparison of black and white women with regard to the extent of scleroderma and age at diagnosis resulted in several notable differences. Diffuse scleroderma was much more common among black women (49.6% versus 24.9%; $P < 0.001$) (Table 2), and age at

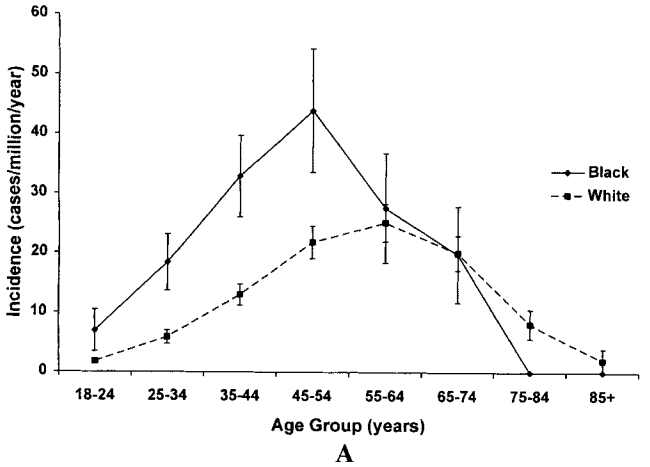
Table 2. Distribution of patients with limited, diffuse, or unspecified scleroderma, by race.*

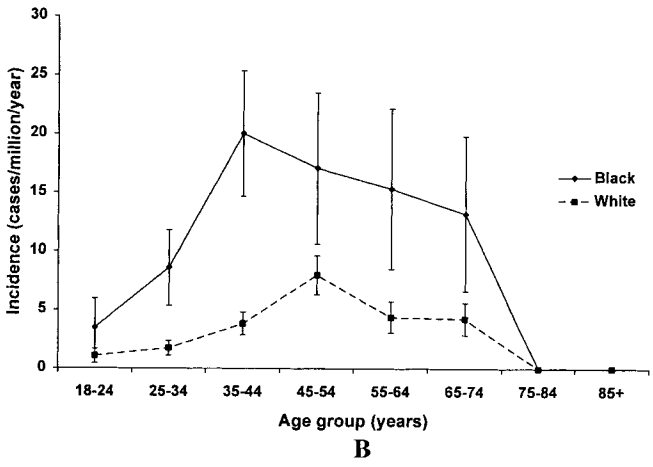
	Black, no. (%)	White, no. (%)	Total, no. (%)
Diffuse	58 (49.6)	99 (24.9)	157 (30.5)
Limited	25 (21.4)	216 (54.4)	241 (46.9)
Unspecified	34 (29.1)	82 (20.7)	116 (22.6)
Total	117 (100.0)	397 (100.0)	514 (100.0)

* Diffuse disease was defined according to skin changes in the trunk, thighs, or upper arms, or was labeled as diffuse by the physician. Limited disease was labeled by the physician as either CREST (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, telangiectasias) or as limited, or was applied to patients with Raynaud's phenomenon/sclerodactyly/telangiectasias without diffuse involvement. The term unspecified disease was applied when there were insufficient chart data to determine the extent of skin involvement.

Table 3. Age of patients at diagnosis, by race

Age	Black, no. (%)	White, no. (%)	Total, no. (%)
All scleroderma			
18–24	10 (8.6)	13 (3.3)	23 (4.5)
25–34	24 (20.5)	44 (11.1)	68 (13.2)
35–44	30 (25.6)	74 (18.6)	104 (20.2)
45–54	25 (21.4)	98 (24.7)	123 (23.9)
55–64	17 (14.5)	91 (22.9)	108 (21.0)
65–74	10 (8.6)	64 (16.1)	74 (14.4)
75–84	1 (0.8)	12 (3.0)	13 (2.5)
≥85	0 (0.0)	1 (0.3)	1 (0.2)
Mean ± SD age	44.5 ± 14.2	51.5 ± 14.3	49.9 ± 14.6
Total	117 (100.0)	397 (100.0)	514 (100.0)
Diffuse scleroderma			
18–24	6 (10.3)	5 (5.1)	11 (7.0)
25–34	12 (20.7)	10 (10.1)	22 (14.0)
35–44	17 (29.3)	23 (23.2)	40 (25.5)
45–54	9 (15.5)	31 (31.3)	40 (25.5)
55–64	8 (13.8)	14 (14.1)	22 (14.0)
65–74	6 (10.3)	16 (16.2)	22 (14.0)
75–84	0 (0.0)	0 (0.0)	0 (0.0)
≥85	0 (0.0)	0 (0.0)	0 (0.0)
Mean ± SD age	43.4 ± 15.2	48.6 ± 13.3	46.7 ± 14.2
Total	58 (100.0)	99 (100.0)	157 (100.0)
Limited scleroderma			
18–24	2 (8.0)	4 (1.9)	6 (2.5)
25–34	4 (16.0)	23 (10.7)	27 (11.2)
35–44	5 (20.0)	39 (18.1)	44 (18.3)
45–54	9 (36.0)	54 (25.0)	63 (26.1)
55–64	4 (16.0)	54 (25.0)	58 (24.1)
65–74	1 (4.0)	32 (14.8)	33 (13.7)
75–84	0 (0.0)	9 (4.2)	9 (3.7)
≥85	0 (0.0)	1 (0.5)	1 (0.4)
Mean ± SD age	45.7 ± 11.6	52.6 ± 14.0	51.8 ± 13.9
Total	25 (100.0)	216 (100.0)	241 (100.0)





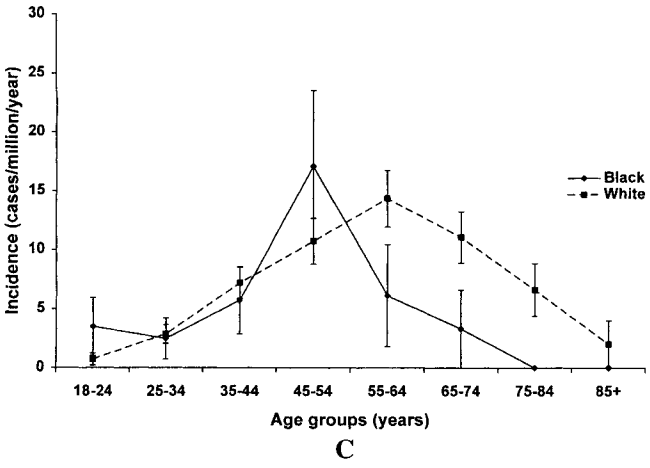


Figure 1. Age-specific incidence of scleroderma in Michigan women, 1985–1991, by race. **A,** All scleroderma. **B,** Diffuse scleroderma. **C,** Limited scleroderma. Bars indicate 1 standard error above and below the point estimate.

diagnosis was also significantly lower among black women (mean 44.5 years versus 51.5 years; $P < 0.001$) (Table 3). When disease frequencies were stratified by age at diagnosis, early onset of both diffuse and limited disease among black women was apparent (Table 3). However, these values were unadjusted for population frequencies in each age/race category, as were the incidence estimates reported below.

The estimated overall incidence of scleroderma between 1985 and 1991 (14.1 per million per year; 95% CI 12.7–15.6) was comparable to previously reported estimates (3). However, black women (22.5 per million per year; 95% CI 17.4–27.6) exhibited a significantly higher average annual incidence of scleroderma ($P < 0.001$) than did white women (12.8 per million per year; 95% CI 11.3–14.3). This difference was most prominent among women who were <54 years old (Figure 1A).

Diffuse scleroderma was more common among black women at all ages, particularly in the 35–44-year-old age group (Figure 1B). In contrast, the age-specific incidences for limited scleroderma were more similar, except that the peak age at diagnosis for black women occurred earlier and the age-specific incidences among white women were greater at all ages over 55 years (Figure 1C). Consistent with previous findings, and in contrast to the cohort of black women, there was also a small group of white women who developed scleroderma after the age of 75 (Figures 1A and C).

Tables 4 and 5 list the most important clinical features of scleroderma and their frequencies, by diffuse/limited status and by race, respectively. Patients with diffuse disease were significantly more likely to have pericarditis, pleural effusions, myositis/myopathy, and renal insufficiency, and to have experienced a hypertensive crisis. Raynaud's phenomenon, telangiectasias, and sicca syndrome were significantly more com-

Table 4. Percentage of patients (n = 514) with each disease manifestation, by disease extent*

	Diffuse	Limited	*P*
Calcinosis	21.0	27.0	0.18
Raynaud's phenomenon	88.5	97.5	<0.001
Esophageal dysmotility	40.1	38.2	0.70
Telangiectasias	43.3	84.2	<0.001
Digital ulcers/pitting	52.9	53.9	0.83
Digital infarcts	7.0	12.0	0.10
Sicca syndrome†	6.4	13.3	0.03
Pericarditis	7.6	3.3	0.05
Pulmonary hypertension	7.6	7.5	0.95
Pulmonary fibrosis	20.4	23.2	0.50
Pleural effusions	26.1	15.8	0.01
Myositis/myopathy	17.8	10.0	0.02
Peripheral arthritis (hands)	19.1	24.9	0.18
Renal insufficiency	15.9	8.3	0.02
Hypertensive crisis	7.0	1.7	0.01

* Variable scored as not present if not explicitly stated in the medical record. See Table 2 for definitions.
† Sicca syndrome, Sjögren's syndrome, or keratoconjunctivitis.

Table 5. Percentage of patients (n = 514) with each disease manifestation, by race*

	Black	White	*P*
Calcinosis	16.2	22.2	0.16
Raynaud's phenomenon	82.1	93.4	<0.001
Esophageal dysmotility	30.8	36.8	0.23
Telangiectasias	29.9	62.0	<0.001
Digital ulcers/pitting	54.7	48.4	0.23
Digital infarcts	1.7	12.1	<0.001
Sicca syndrome†	6.0	11.6	0.08
Pericarditis	9.4	3.5	0.009
Pulmonary hypertension	15.4	5.3	<0.001
Pulmonary fibrosis	24.8	22.7	0.63
Pleural effusions	28.2	17.4	0.01
Myositis/myopathy	20.5	12.1	0.02
Peripheral arthritis	18.0	23.4	0.21
Renal insufficiency	15.4	9.1	0.05
Hypertensive crisis	2.6	3.3	0.70

* Variable scored as not present if not explicitly stated in the medical record.
† Sicca syndrome, Sjögren's syndrome, or keratoconjunctivitis.

mon among those with limited disease. Calcinosis was noted infrequently in both groups, perhaps due to its being relatively less apparent on physical examination (Table 4).

Among black women, pericarditis, pulmonary hypertension, pleural effusions, myositis/myopathy, and renal insufficiency were significantly more common, while Raynaud's phenomenon, telangiectasias, and digital infarcts were observed significantly more frequently among white women (Table 5). Logistic regression was performed to assess the effect of race adjusted for diffuse/limited status. Pericarditis (odds ratio [OR] = 3.5, $P = 0.012$) and pulmonary hypertension (OR = 3.2, $P = 0.007$) were found significantly more frequently among black women, while Raynaud's phenomenon (OR = 5.2, $P \leq 0.001$), telangiectasias (OR = 2.7, $P < 0.001$), and digital infarcts (OR = 4.9, $P = 0.033$) were significantly more common among white women.

Among the laboratory variables, anticentromere antibodies were significantly more frequent in women with limited disease. Interestingly, anti–Scl-70 (anti–topoisomerase I) antibodies were equally prevalent in both the diffuse and limited scleroderma groups. However, a further analysis demonstrated that 3 of 13 black women (23.1%) considered to have limited disease had a positive test for anti–Scl-70 antibodies, suggesting the possibility of failure to appropriately characterize the extent of skin involvement. Consistent with the increased frequencies of myositis/myopathy previously noted, women with diffuse disease were also more likely to have an elevated CPK (Table 6).

Black women were significantly more likely to have had an erythrocyte sedimentation rate (ESR) >40 mm/hour, and to have positive anti-RNP antibodies. Cryoglobulinemia and an elevated CPK were also more common among black women, but the differences were not statistically significant. White women, as expected, were significantly more likely to have anticentromere antibodies than were black women (35% versus 14%) (Table 7). Logistic regression was again performed to assess the effect of race adjusted for diffuse/limited status. Black women were significantly more likely to have positive rheumatoid factor (OR = 2.3, $P = 0.028$) and to have an elevated ESR (OR = 2.8, $P = 0.002$).

Overall survival at 7 years after diagnosis was 76.5% (95% CI 70.4–82.7), and was similar among black

Table 6. Percentage (number) of patients with abnormal laboratory results, by disease extent*

	Diffuse	Limited	*P*
Rheumatoid factor	21.4 (21/98)	27.6 (40/145)	0.28
ESR >40 mm/hour	42.2 (49/116)	35.0 (57/163)	0.22
ANA	91.7 (133/145)	94.6 (209/221)	0.28
Anticentromere	14.2 (18/127)	46.8 (94/201)	<0.001
Anti–Scl-70	18.0 (11/61)	15.2 (12/79)	0.65
Anti-RNP	10.9 (10/92)	15.8 (20/127)	0.30
Anti-Ro	12.5 (10/80)	9.8 (11/112)	0.56
Anti-La	4.9 (4/81)	1.8 (2/111)	0.22
CH50	13.0 (3/23)	14.8 (9/61)	0.84
Cryoglobulins	5.9 (1/17)	5.4 (3/55)	0.95
CPK	31.4 (32/102)	21.0 (29/138)	0.07

* Patients without test results recorded were excluded. ESR = erythrocyte sedimentation rate; ANA = antinuclear antibody; CPK = creatinine phosphokinase.

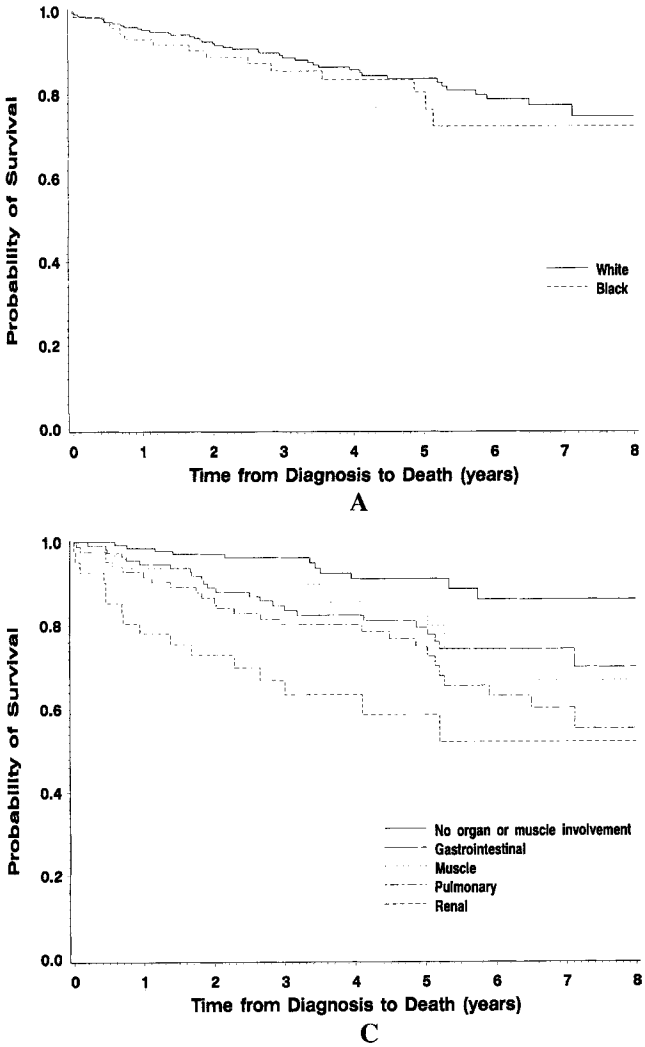
Table 7. Percentage (number) of patients with abnormal laboratory results, by race*

	Black	White	*P*
Rheumatoid factor	30.9 (21/68)	25.8 (60/233)	0.40
ESR >40 mm/hour	58.9 (43/73)	34.0 (91/268)	<0.001
ANA	93.2 (96/103)	91.3 (326/357)	0.54
Anticentromere	14.1 (12/85)	35.4 (114/322)	<0.001
Anti–Scl-70	18.4 (7/38)	18.6 (23/124)	0.99
Anti-RNP	22.4 (15/67)	12.7 (23/206)	0.05
Anti-Ro	10.7 (6/56)	11.2 (29.168)	0.92
Anti-La	1.8 (1/56)	3.9 (7/179)	0.44
CH50	19.0 (4/21)	13.2 (11/83)	0.50
Cryoglobulins	11.2 (1/9)	4.9 (4/81)	0.44
CPK	35.6 (26/73)	26.6 (60/226)	0.14

* Patients without test results recorded were excluded. See Table 6 for definitions.

women (72.5%, 95% CI 58.4–86.7) and white women (77.6%, 95% CI 70.7–84.4) (P = 0.455) (Figure 2A). However, the risk of death subsequent to the diagnosis of scleroderma increased significantly with age at diagnosis (RR = 1.64 for a 10-year increase in age, 95% CI 1.35–2.00), and, as noted above, the mean age at diagnosis was lower for black women (44.5 years) than for white women (51.5 years). After adjusting for age at diagnosis, black women had a significantly increased risk of death compared with white women (RR = 1.98, 95% CI 1.06–3.71) (P = 0.033). Survival was also significantly worse among women with diffuse disease compared with those with limited disease (RR = 2.27, 95% CI 1.22–4.21) (Figure 2B). No significant race effect could be demonstrated after adjusting for both age at diagnosis and diffuse/limited status (P = 0.177).

When compared with those women without organ system involvement (7-year survival 86.4%, 95% CI 77.8–94.9), those with gastrointestinal, muscle, pulmonary, or renal involvement experienced decreased sur-



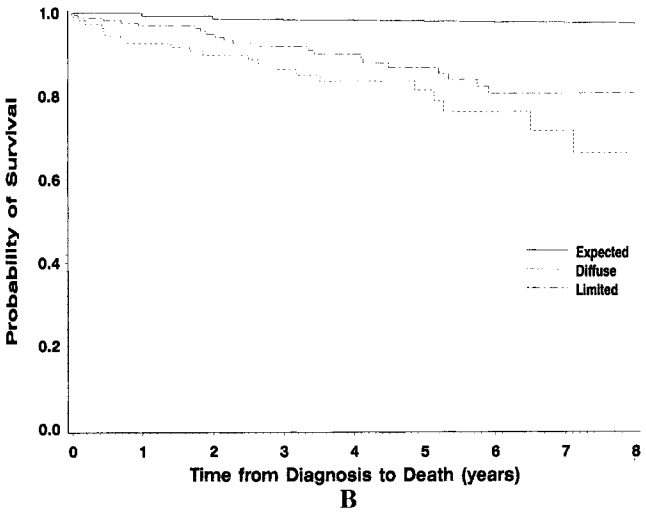


Figure 2. Kaplan-Meier survival probabilities, comparing patients with scleroderma according to **A,** race (75 blacks and 271 whites), **B,** extent of disease (110 diffuse, 166 limited, and expected rate in Michigan women of similar age and race as in the patient population), and **C,** internal organ involvement (146 no involvement, 115 gastrointestinal, 32 myositis/myopathy, 84 pulmonary, and 41 renal). Women with involvement of multiple organ systems were considered redundantly in these calculations.

vival (7-year survival rates 74.4% [95% CI 64.9–83.9], 66.9% [95% CI 45.1–88.6], 60.3% [95% CI 47.1–73.6], and 52.2% [95% CI 32.8–71.5], respectively) (Figure 2C). However, after adjusting for other organ system involvement, as well as age at diagnosis, neither gastrointestinal nor muscle involvement were significant risk factors for mortality ($P = 0.278$ and $P = 0.468$, respectively), while pulmonary (RR = 2.06, 95% CI 1.20–3.54) and renal (RR = 3.65, 95% CI 2.00–6.67) involvement remained as significant risk factors.

DISCUSSION

Although multiple aspects of the epidemiology of scleroderma have previously been described (1), relatively few publications have addressed racial differences in relation to clinical manifestations, incidence, and survival, and none has focused exclusively on women. Due to the relatively large size of our patient population, and to the relatively high proportion of black women, we were able to confirm and expand several earlier observations regarding black-white differences in the manifestations of scleroderma.

Especially interesting was the highly disproportionate proclivity toward diffuse disease among black women compared with white women in our study (50% versus 25%). This result is consistent with the findings of a study by Reveille et al (14), in which, in a series of 156 scleroderma patients in the US, anti–Scl-70 antibodies (a marker for diffuse scleroderma) were found in 37% of the black patients compared with only 17% of the white patients. Further support for the low rate of diffuse disease among white women can be derived from a report by Vayssairat et al (15), who found that only 8.5% of those in their series of 164 consecutive scleroderma patients (162 white; personal communication) had diffuse disease.

The increased percentage of black women with diffuse disease found in our study is also notable in light of the study by McNeilage et al, which compared 68 white Australian patients and 49 Thai patients with scleroderma (16). In that study, 15% of the Australians had diffuse disease compared with 100% of the Thais. More recently, Tan et al have described 19 Native American Choctaws with scleroderma, of whom 11 (58%) had diffuse disease (17). Unfortunately, findings from the large series of Japanese patients reported by Tamaki et al (18) may not be interpreted readily because the investigators used a different classification system (19). However, with this exception, the foregoing studies, combined with our results, suggest that white women have a lower incidence of diffuse disease than do women of color.

Previous estimates of the incidence of scleroderma, primarily among white women, have ranged from 3.6 to 16 per million per year (4,20,21). The overall incidence estimated from our data, 14.1 per million per year, is consistent with this range. The increased incidence of scleroderma among black women contributed to the fact that our estimate was near the upper limit of the range, but it still probably underestimates the true incidence by roughly 20–30% because not all eligible women were identified and participation was not complete.

When differences in the incidence of scleroderma between black and white women are considered, 3 previous studies are pertinent. Medsger and Masi's 1971 study of a series of 86 patients (4) yielded an increase of ~2-fold in incidence among black women. An analysis of US death certificates from 1969–1977 by Hochberg et al also showed that age-adjusted mortality in nonwhite women with scleroderma was nearly twice that of white women (5). In addition, a 1988 study by Steen et al, which assessed a cohort of 442 patients diagnosed between 1963 and 1982, also showed an increased incidence of scleroderma among young black women (3).

The overall incidence of scleroderma among black women in Michigan was higher than in white women: 22.5 per million per year for black women versus 12.8 per million per year for white women, a difference explained almost entirely by the excess of diffuse disease among black women. The age-specific incidence among black women exceeded that of white women at all age groups by 2–5-fold. The ratios were greatest among the 25–34-year and 35–44-year age groups, which contrasts somewhat with the result reported by Steen et al (3), who found the greatest excess of diffuse disease in black women among those who were 15–24 years old.

When grouped into diffuse and limited categories, many of the clinical and laboratory manifestations noted in our study (Tables 4 and 5) occurred at frequencies comparable to generally accepted previous estimates (22), with some exceptions, including more calcinosis than expected in the diffuse disease group and less esophageal dysmotility in both groups, although the latter may relate to the relative stringency with which this diagnosis was accepted during chart review. Among the laboratory variables for patients with diffuse disease, a smaller percentage than expected had anti–Scl-70 antibodies and, conversely, a greater percentage than expected had anticentromere antibodies. These observations may be partly explained by misclassification. A

more important factor, however, may be that the laboratory test results and clinical observations reported in this study reflected the judgment of the treating physicians rather than a summary from a uniformly administered battery of examinations.

When clinical manifestations were considered as a function of race, black women were significantly more likely to have experienced pericarditis, pulmonary hypertension, pleural effusions, myositis/myopathy, and renal insufficiency. White women, largely reflecting the underlying greater incidence of limited disease among them, had significantly higher percentages of digital infarcts. Among the laboratory variables, black women were significantly more likely to have had an ESR >40 mm/hour detected at some point during the course of their disease. Interestingly, 14% of black women were also positive for anticentromere antibodies, which substantially exceeded the 4% found by Reveille et al (14), but only 27 blacks were tested in that study.

Together, these observations suggest a greater severity of disease in black women relative to white women, and appear to be explained by the much higher frequency of diffuse disease among black women. However, by applying logistic regression, potential race effects, independent of diffuse/limited status, were assessed. These analyses demonstrated that black women had an increased risk of developing pericarditis, pulmonary hypertension, and/or an elevated ESR, and white women were more likely to have Raynaud's phenomenon, telangiectasias, and/or digital infarcts. Some of these differences may be explained on the basis of ease of detection, e.g., telangiectasias in whites, but others may connote true racial differences in severity of disease manifestation. Pulmonary hypertension is particularly interesting in this regard, since both the limited and diffuse disease groups of black women had higher frequencies than those of white women. Moreover, although our overall frequency of pulmonary hypertension in patients with diffuse disease was slightly higher than that in patients with limited disease, which contrasts with previous series (22,23), when black and white women were examined separately, pulmonary hypertension was more common among those with limited disease in each group (24).

These results would also suggest that survival would be expected to be decreased among black women in our study, as has been suggested by previous studies. This was first addressed by Masi and D'Angelo in a 1967 study of 53 fatal cases of scleroderma from the Baltimore area (25). Those authors suggested that survival among blacks was decreased, especially among black women. In 1971, Medsger and Masi reported a series of 86 patients (4), which, when combined with 223 scleroderma patients diagnosed in Pittsburgh, again suggested decreased survival among blacks (26). Interestingly, however, 2 studies by Medsger and Masi of 358 *male* US veterans failed to demonstrate that survival among blacks was decreased (27,28).

The survival data from our study support the notion that survival is decreased among black women, but only after adjustment for age at diagnosis. As in previous studies, survival was significantly worse among those women with diffuse disease and/or internal organ involvement (26,29–33). However, after adjusting for both age at diagnosis and diffuse/limited status, there was no longer a significant difference in survival between black and white women. This result suggests that the lack of an unadjusted survival difference between black and white women could be explained by racial differences in age at onset and disease severity. Perhaps more significant is the fact that the combined black-white survival rate at 7 years (76.5%) appeared to be improved compared with previous estimates (27–59%) (4,26,28,29,33,34), although differences in disease criteria limit the validity of direct comparisons.

Selection bias was a potential weakness of our study because the cases identified were neither a complete census nor a random sample of all cases in Michigan. Relevant in this regard is the fact that most of the scleroderma cases (54%) were identified from the University of Michigan and Wayne State University medical centers. In addition, because other institutions and practices required individual patient consent to release medical records, overall rates of participation were lower in those locations. However, the consent rate overall was estimated to be about 75% among eligible women, and no differences in consent rates by age group or disease severity were observed. Consent rate disparities were identified between white women (93%) and black women (68%), and between patients who were alive (89%) and the spouse or relative of deceased patients (71%). The latter effect may have resulted in a bias toward overestimation of survival rates, but was probably tempered to some extent by the preponderance of patients being derived from the state's tertiary referral centers, which likely treat sicker patients with attendant lower survival rates. Bias may have been introduced into the analyses of clinical characteristics because of underascertainment during the period 1980–1984. However, as mentioned above, inclusion of those patients did not change the proportions, by race, of women with diffuse and limited disease.

In summary, our patient cohort represents the largest group of black and white female scleroderma patients studied to date. Our data suggest that black women have a significantly increased incidence of diffuse scleroderma, manifest the disease at a younger age than white patients, are more likely to develop characteristics of aggressive disease, and, after adjusting for age at diagnosis, have a worse prognosis than white patients. Consistent with previous studies, we also demonstrate that survival in both black and white women is adversely influenced by internal organ involvement and the presence of diffuse disease.

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