Outcomes and prognostic factors in African American and black patients with mycosis fungoides/Sézary syndrome: Retrospective analysis of 157 patients from a referral cancer center

Shamir Geller, MD,[a,b] Emily Lebowitz, MD,[c] Melissa P. Pulitzer, MD,[c,d] Steven M. Horwitz, MD,[e] Alison J. Moskowitz, MD,[e] Steve Dusza, DrPH,[a] and Patricia L. Myskowski, MD[a,c]
New York, New York; and Tel Aviv, Israel

Background: The prevalence of mycosis fungoides/Sézary syndrome (MF/SS) is higher in the black population than in the white population in the United States and worse outcomes have been observed in black patients.

Objective: To describe the outcomes and to identify prognostic factors in African American and black patients with MF/SS.

Methods: Clinical features and follow-up data were analyzed in 157 self-identified African American or black patients seen during 1994-2018.

Results: We included 122 patients with early stage MF and 35 patients with advanced-stage disease (median follow-up of 25 months). Overall, >80% of the patients who died from disease or progressed had erythema or hyperpigmentation without hypopigmentation. Patients with hypopigmentation, either as the sole manifestation or in combination with other lesions, had better overall survival (P = .002) and progression-free survival (P = .014). Clinical stage, TNMB classification, plaque disease, and elevated serum lactate dehydrogenase were also significantly associated with outcomes. Demographic and socioeconomic parameters were not associated with prognosis.

Limitations: A retrospective study at a single cancer center.

Conclusion: MF/SS manifestations and outcomes in African American and black patients are heterogeneous. Demographic and socioeconomic factors do not seem to have a prognostic role, while clinical characteristics might help in the stratification of risk of progression and shorter

From the Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York[a]; Department of Dermatology, Tel Aviv Sourasky Medical Center[b]; Weill Cornell Medical College, New York[c]; Department of Pathology, Memorial Sloan Kettering Cancer Center, New York[d]; and Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York.[e]

Funding sources: Supported in part through the National Institutes of Health National Cancer Institute Cancer Center support grant P30 CA008748.

Conflicts of interest: Dr Horwitz has received research funding, grant support, honoraria and consulting fees from ADCT Therapeutics, Aileron, Forty-Seven Infinity/Verastem Kyowa-Hakka-Kirin, Millennium/Takeda, and Seattle Genetics; research and grant support from Celgene and Trillium; and honoraria and consulting fees from Affimed, Angimmune, Beigene, Corvus, Innate Pharma, Kura, Merck, Miragen, Mundipharma, Portola, and Syros Pharmaceutical. Dr Moskowitz received honoraria from Seattle Genetics; served as a consultant or in an advisory role for Seattle Genetics, Kyowa Hakko Kirin Pharma, Miragen Therapeutics, Takeda Pharmaceuticals, ADC Therapeutics, Cell Medica, Bristol-Myers Squibb, and Erytech PharmaResearch; and received funding through her institution from Incyte, Seattle Genetics, Merck, and Bristol-Myers Squibb. Dr Geller, Dr Lebowitz, Dr Pulitzer, Dr Dusza, and Dr Myskowski have no conflict of interest to declare.

Previously presented at the European Organisation for Research and Treatment of Cancer (EORTC-CLTF) meeting in Athens, Greece, on September 26th, 2019.

Accepted for publication August 30, 2019.

Reprint requests: Shamir Geller, MD, Dermatology Service, Memorial Sloan Kettering Cancer Center, 16 East 60th St, New York, NY 10022. E-mail: shamirgeller@gmail.com.

Published online September 6, 2019.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2019.08.073

survival, allowing for individually tailored therapeutic interventions. (J Am Acad Dermatol 2020;83:430-9.)

Key words: African American; cutaneous lymphoma; hyperpigmented MF; hypopigmented MF; MF; racial disparity; skin of color; survival analysis.

Racial disparities in cancer survival in the United States are well documented; however, the underlying causes are not well understood.[1,2] The incidence of cutaneous T-cell lymphoma (CTCL) and mycosis fungoides/Sézary syndrome (MF/SS) is higher in the United States in the black population than in the white population.[3-5] The prognosis of MF/SS has also been shown to be significantly associated with race in several retrospective cohorts and population-based registries, showing poorer survival in black patients.[6-11] Black patients frequently have an earlier onset of MF/SS[7,11-14] and are diagnosed at more advanced disease stages than white patients.[12,13] Demographic factors along with differences in socioeconomic status, clinicopathologic characteristics, disease biology, and treatments have been proposed to play a role in these MF/SS disparities.

CAPSULE SUMMARY

- Aggressive behavior of mycosis fungoides/Sézary syndrome (MF/SS) in black patients has been reported.
- MF/SS outcomes are heterogeneous in African American and black patients. Inferior outcomes are associated with clinical characteristics and not with demographic and socioeconomic parameters. African American and black patients with MF/SS shouldn't be treated more aggressively as a group.

The goal in this study was to identify the clinical factors associated with outcomes in African American and black patients with MF/SS who sought treatment at a referral cancer center. Understanding the prognostic factors in this specific population can help ensure the use of the most appropriate individually tailored treatment plan and might help to close the racial survival gap in MF/SS.

METHODS

Patient selection and data collection

After approval by the institutional review board at Memorial Sloan Kettering Cancer Center (MSKCC), self-identified African American or black patients with MF/SS diagnoses during 1992-2017 were identified through a search of our institutional database. We identified patients on the basis of race/ethnicity data self-reported upon admission to and registration at MSKCC in accordance with the US Census Bureau's race and ethnicity categories. Medical records were reviewed and patients were included in the study if a diagnosis of MF/SS had been confirmed clinically and histopathologically by a dermatologist and a dermatopathologist at MSKCC.[15-17] Patients who were found to be positive for human T-cell lymphotropic virus I or II were excluded from analysis because human T-cell lymphotropic virus–associated adult T-cell lymphoma and leukemia can be misdiagnosed as MF and represents a distinct disease process. For all cases meeting inclusion requirements, an extensive chart review was performed, and the following data was collected from the time of initial presentation at MSKCC for MF/SS: age at diagnosis of MF/SS, sex, race, ethnicity, country of birth, lesion morphology, clinical variant of MF, and clinical and TNMB classification stage. The following laboratory values at presentation were recorded: serum lactate dehydrogenase (LDH), white blood cell count, absolute lymphocyte count, and absolute eosinophil count. Initial pathology reports were reviewed for presence of folliculotropism and large cell transformation, as well as for $CD4^+$ and $CD8^+$ T-cell phenotype immunohistochemistry staining status on skin biopsy.

Socioeconomic status

Using patients' residential ZIP codes at the time they sought treatment, we recorded median household income and percentage of individuals living below the poverty line. Median household income was categorized as quartiles: ≤$37,999, $38,000-$47,999, $48,000-$63,999, or ≥$64,000; poverty level was categorized as ≤20% or >20%. We utilized the US Census Bureau's 2012-2016 American Community Survey 5-year estimates to assess socioeconomic status, as previously described.[18,19] Health care coverage information was extracted from electronic medical records.

Statistical analysis

The date of the first diagnostic biopsy was considered as the date of MF/SS diagnosis. Duration of follow-up was calculated from the date of initial consultation for MF/SS at MSKCC to the date of most recent visit or date of death. Overall survival

Abbreviations used:

CI:	confidence interval
DSS:	disease-specific survival
HR:	hazard ratio
LDH:	lactate dehydrogenase
MF/SS:	mycosis fungoides/Sézary syndrome
MSKCC:	Memorial Sloan Kettering Cancer Center
OR:	odds ratio
OS:	overall survival
PFS:	progression-free survival

(OS) was calculated from the date of initial presentation at MSKCC with MF/SS to date of death from any cause or date of last follow-up. Disease-specific survival (DSS) was calculated from the date of initial presentation to date of death from MF/SS, date of death from another cause, or date of last follow-up. Progression-free survival (PFS) was defined as the time from initial presentation at MSKCC to date of a documented progression to a more advanced clinical stage or death from MF/SS. Descriptive statistics were used to describe the patient characteristics and clinical characteristics of their disease. χ^2 and Fisher's exact tests and logistic regression were used to assess associations between demographic or clinical characteristics and early versus late stage disease at presentation. Univariate and multivariate analyses of survival and disease progression risk were performed by using Kaplan Meier analysis and Cox proportional hazards models. Log-rank tests were used to assess equality of Kaplan Meier survival estimates. All tests were 2-sided, and P values <0.05 were considered statistically significant. Statistical analyses were performed by using SPSS Statistics software (IBM, Armonk, NY) and Stata version 14.1 (Stata Corporation, College Station, TX).

RESULTS

Characteristics of the study population

Of the 157 patients, a majority were female (n = 97, 60.6%), 142 (90%) were non-Hispanic, and 8 (5%) were Hispanic; for 7 (5%) patients, ethnicity was unknown (Table I). Thirty-one patients (20%) were born outside of the United States. The median (range) age at diagnosis was 49 (12-88) years, with no significant age difference between male and female patients. Eight patients (5%) were ≤18 years when they sought treatment at our institution. Median delay from onset of skin symptoms to diagnosis was 4 years. Median referral delay from diagnosis to presentation at our institution was 2.2 months, and 70% of patients sought treatment at our institution within 6 months of their diagnosis. At the initial evaluation, 122 patients (78%) had early stage MF (clinical stages IA-IIA), mostly (51%) stage IB, while 35 (22%) had advanced-stage MF (IIB-IV).

Patients with early stage MF were more likely to have hypopigmented lesions than patients with advanced-stage disease (odds ratio [OR] 12.64, 95% confidence interval [CI] 3.65-43.78; $P < .001$); less likely have $CD4^+$ versus $CD8^+$ immunophenotype per tissue immunohistochemistry (OR 0.06, 95% CI 0.01-0.48; $P = .008$); and less likely to have an elevated eosinophil count (OR 0.07, 95% CI 0.01-0.38; $P = .002$), white blood cell count (OR 0.05, 95% CI 0.01-0.26; $P < .001$), or LDH (OR 0.08, 95% CI 0.03-0.23; $P < .001$). Early versus advanced-disease cases did not differ by age at diagnosis, sex, ethnicity, birthplace, health insurance, income, or poverty rate by residential ZIP code.

Survival and prognostic factors

Eight patients (5%) were lost to follow-up after a single consult (1 patient with advanced-stage and 7 with early stage disease). For the other 149 patients, median (range) follow-up was 25 (0.5-306) months. Of the 115 patients who had early stage disease, 12 (10%) progressed to advanced stages, and 6 (5%) died of cutaneous T-cell lymphoma after a median (range) follow-up of 74 (9-98) months. Of the 34 patients with advanced-stage disease at their initial evaluation, 5 patients (15%) progressed to a higher clinical stage, and 12 (35%) died of lymphoma. There were 34 deaths observed over the course of follow-up, and 18 deaths were disease related. Overall death and disease-specific death were not associated with sex, birthplace, ethnicity, diagnosis delay, referral delay, health care coverage, income, or poverty rate. Age at diagnosis and health care visit were not associated with disease-specific death.

Survival analysis was performed by using univariable Cox proportional hazards regression (Table II). Older age at diagnosis was associated with shorter OS but not with DSS. No association was found between survival and sex or any other demographic and socioeconomic factor. Overall clinical staging and TNMB classifications were associated with survival. Hypopigmented lesions were seen in 45% of patients, and the presence of hypopigmented lesions, whether as the only presentation or concurrently with hyperpigmentation or erythema, was associated with longer OS (HR 0.04, 95% CI 0.006-0.32; $P = .002$). No disease-specific deaths were recorded among patients with hypopigmented lesions. Among the 94 cases for which we had immunohistochemistry results on initial diagnostic biopsy, no deaths (0/29) were recorded in patients with $CD8^+$ disease, while 30% (19/63) of the patients with $CD4^+$ disease died ($P < .001$); 11 of them died

Table I. Clinical characteristics of 157 African American and black patients with mycosis fungoides/Sézary syndrome

Patient characteristic	Value
Age at diagnosis, y, mean (range)	47.9 (12-88)
Female-to-male ratio (n female:n male)	1.6 (97:60)
Diagnosis delay from onset of symptoms, mon, mean (range)	4.0 (0.1-30)
Referral delay from diagnosis, y, mean (range)	2.2 (0-156.3)
Birth place, n (%)	
United States	68 (43)
Non−United States	31 (20)
Unknown	58 (37)
Ethnicity, n (%)	
Non-Hispanic	142 (90)
Hispanic	8 (5)
Unknown	7 (5)
Health care coverage, n (%)	
Medicaid	21 (13)
Medicare	24 (15)
Private/HMO	105 (67)
Unknown	7 (5)
Median household income by ZIP code, n (%)	
$1-37,999	33 (21)
$38,000-47,999	29 (18)
$48,000-63,999	26 (17)
≥$64,000	60 (38)
Unknown	9 (6)
Poverty rate by ZIP code, n (%)	
≤20%	93 (59)
>20%	55 (35)
Unknown	9 (6)
Most severe type of skin lesions, n (%)	
Patches	84 (53)
Plaques	48 (31)
Tumors and nodules	15 (10)
Erythroderma	9 (6)
Unknown	1 (0)
Color of lesions, n (%)	
Erythematous	44 (28)
Hypopigmented	71 (45)
Hyperpigmented	83 (53)
Unknown	5 (3)
Follicular involvement, n (%)	17 (11)
Ulceration, n (%)	2 (1)
Clinical stage, n (%)	
IA	31 (20)
IB	80 (51)
IIA	11 (7)
IIB	14 (9)
IIIA + IIIB	4 (2)
IVA + IVB	17 (11)
Immunophenotype per IHC on initial skin biopsy, n (%)	
$CD4^+$	64 (41)
$CD8^+$	30 (19)
Unknown	63 (40)
Large cell transformation, n (%)	23 (15)
Initial treatment, n (%)	
Topical steroids alone	21 (13)
Topical nitrogen mustard alone	3 (2)
Phototherapy NB-UVB/PUVA	68* (43)/10† (6)
Radiation local/TSEB	2 (1)/11 (7)
Oral bexarotene	11 (7)
Oral methotrexate	2 (1)
Romidepsin	6 (4)
Brentuximab	2 (1)
Chemotherapy	8 (5)
Observation	1 (<1)
Lost to follow-up	8 (5)
Unavailable	4 (3)

HMO, Health maintenance organization; *IHC*, immunohistochemistry; *NB-UVB*, narrowband ultraviolet B; *PUVA*, psoralen and ultraviolet A; *TSEB*, total-skin electron beam.
*Combined with oral bexarotene in 5 cases.
†Combined with interferon in 1 case and interferon and oral bexarotene in 1 case.

due to lymphoma. Blood test analysis of samples acquired at presentation showed that elevated white blood cell count and LDH were significantly associated with shorter survival, and elevated eosinophil count was associated with shorter DSS. In a multivariate analysis, diagnosis delay from onset of symptoms was independently associated with longer OS (HR 0.87, 95% CI 0.79-0.95; $P = .002$) and DSS (HR 0.86, 95% CI 0.77-0.96; $P = .008$). Advanced clinical stages were associated with shorter survival, while sex, age, health care coverage, and income were not.

Disease progression and prognostic factors in early stage MF

Of 115 patients with early stage MF, skin tumors developed in 6 patients (5%), erythroderma developed in 2 (2%), and extracutaneous disease developed in 4 (3%) after a median (range) follow-up of 15 (2-93) months. One patient progressed from clinical stage IA to IB. None of the 12 patients who progressed to advanced-stage disease had sought treatment with us initially with hypopigmented lesions only. One patient had hypo- and hyperpigmented patches; 1 had localized poikilodermatous lesions; and 10 had hyperpigmented lesions, erythematous lesions, or both. Most had plaques (9/12). One progressed case involved presentation with a $CD8^+$ immunophenotype and 7 involved

Table II. Univariate survival analysis of 149 African American and black patients with mycosis fungoides/Sézary syndrome

		Overall survival from presentation		Disease-specific survival from presentation	
Clinical characteristic	**N**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
Age at diagnosis, per year	149	1.024 (1.002-1.046)	**.033**	1.003 (0.975-1.032)	.846
Sex	149				
Female		1.0		1.0	
Male		0.614 (0.311-1.215)	.161	0.864 (0.333-2.245)	.764
Diagnosis delay, per year	133	0.978 (0.922-1.037)	.448	0.991 (0.919-1.067)	.803
Referral delay, per month	144	1.0 (0.999-1.0)	.408	1.0 (0.999-1.0)	.376
Birthplace	91				
United States		1.0		1.0	
Non−United States		1.77 (0.803-3.904)	.157	1.437 (0.485-4.259)	.513
Health care coverage	142				
Private/HMO		1.0		1.0	
Medicaid		1.044 (0.409-2.668)	.928	1.28 (0.444-3.667)	.65
Medicare		0.971 (0.413-2.284)	.947	0.186 (0.024-1.442)	.108
Median household Income*	140				
≤38K		1.0		1.0	
$38-47K		0.588 (0.201-1.721)	.332	0.702 (0.168-2.939)	.628
$48-63K		0.823 (0.298-2.271)	.707	1.095 (0.292-4.102)	.893
≥$64K		0.794 (0.336-1.875)	.599	0.844 (0.256-2.778)	.78
Skin lesions					
Patches	149				
No		1.0		1.0	
Yes		0.131 (0.065-0.263)	**<.001**	0.172 (0.068-0.439)	**<.001**
Plaques	149				
No		1.0		1.0	
Yes		2.058 (1.027-4.126)	**.042**	2.6 (0.971-6.961)	.057
Tumors and nodules	149				
No		1.0		1.0	
Yes		7.634 (3.209-18.162)	**<.001**	10.35 (3.499-30.612)	**<.001**
Erythroderma	149				
No		1.0		1.0	
Yes		6.04 (2.521-14.467)	**<.001**	6.001 (1.878-19.17)	**.002**
Folliculotropic	149				
No		1.0		1.0	
Yes		2.411 (0.852-6.826)	.097	3.336 (0.981-11.346)	.054
Hyperpigmented lesions	145				
No		1.0		1.0	
Yes		1.289 (0.617-2.693)	.5	1.318 (0.486-3.57)	.587
Hypopigmented lesions	145				
No		1.0		1.0	
Yes		0.044 (0.006-0.32)	**.002**	-	-
Clinical stage	149				
IA		1.0		1.0	
IB		0.79 (0.22-2.831)	.717	0.533 (0.033-8.624)	.658
IIA		4.405 (1.222-15.882)	**.023**	12.195 (1.331-111.718)	**.027**
IIB		11.106 (3.033-40.664)	**<.001**	35.857 (3.912-328.689)	**.002**
IIIA/IIIB		—	—	—	—
IVA/IVB		8.939 (2.779-28.758)	**<.001**	19.202 (2.235-164.974)	**.007**
Early and late-stage disease	149				
Early stage (IA-IIA)		0.1		1.0	
Late stage (IIB-IVB)		6.838 (3.385-13.811)	**<.001**	11.365 (4.077-31.68)	**<.001**

Continued

Table II. Cont'd

Clinical characteristic	N	Overall survival from presentation		Disease-specific survival from presentation	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
T stage	149				
T1		1.0		1.0	
T2		1.568 (0.509-4.828)	.433	2.692 (0.319-22.696)	.363
T3		12.043 (3.355-43.231)	**<.001**	32.933 (3.591-302.049)	**.002**
T4		5.825 (1.707-19.877)	**.005**	14.353 (1.617-127.425)	**.017**
N stage	149				
N0		1.0		1.0	
N1-N2		5.362 (2.228-12.906)	**<.001**	9.682 (2.378-39.417)	**.002**
Nx		11.506 (4.43-29.879)	**<.001**	40.566 (10.152-162.101)	**<.001**
N3		9.269 (2.918-29.443)	**<.001**	19.186 (3.157-116.613)	**.001**
M stage	149				
M0		1.0		1.0	
M1		3.979 (0.94-16.841)	.061	7.567 (1.7-33.683)	**.008**
B stage	149				
B0		1.0		1.0	
B1		7.298 (2.127-25.043)	**.002**	-	-
B2		5.196 (2.371-11.388)	**<.001**	5.755 (2.132-15.531)	**.001**
Blood work					
White blood cell count	134				
Within reference range		1.0		1.0	
Elevated		4.564 (1.754-11.878)	**.002**	5.224 (1.579-17.285)	**.007**
Lymphocyte count	134				
Within reference range		1.0		1.0	
Elevated		5.156 (1.135-23.419)	**.034**	3.69 (0.453-30.046)	.222
Eosinophil count	133				
Within reference range		1.0		1.0	
Elevated		1.93 (0.662-5.627)	.229	3.894 (1.241-12.217)	**.02**
LDH	122				
Within reference range		1.0		1.0	
Elevated		7.085 (2.662-18.855)	**<.001**	5.49 (1.782-16.918)	**.003**

Bolded values are statistically significant.
Dashes indicate cases when no death cases occurred.
CI, Confidence interval; *HMO*, health maintenance organization; *HR*, hazard ratio; *LDH*, lactate dehydrogenase.
*Median household income national quartile for patient's residential ZIP code.

$CD4^+$ disease. In total, 6 of 11 (55%) cases that progressed had elevated LDH at presentation. Six (5%) patients who progressed to advanced-stage disease eventually died of cutaneous T-cell lymphoma after a median (range) follow-up of 74 (9-98) months. In univariate analysis, no association was found between PFS and demographic and socioeconomic characteristics. PFS was associated with hypopigmentation (HR 0.15, 95% CI 0.03-0.66; P = .013), plaques (HR 3.50, 95% CI 1.01-11.45; P = .038), and Nx stage (HR 34.641, 95% CI 6.15-195.18; P < .001). Survival curves for these characteristics are shown in Fig 1. Multivariate PFS analysis adjusting for sex, health care coverage, income, age at diagnosis, and diagnostic delay showed that hypopigmented lesions and patch lesions were associated with better PFS, and Nx stage and elevated LDH were associated with worse PFS (Table III).

DISCUSSION

Other than the higher incidence rates of cutaneous T-cell lymphoma and MF/SS in the black population in the United States,[3,4,20,21] black patients with MF/SS have a female predominance[7,11-13] and are diagnosed at a significantly younger age[4,7,11-14] than white patients. Survival analyses of the National Cancer Institute's Surveillance, Epidemiology, and End Results data sets demonstrated that OS and DSS in black patients with MF were significantly worse than OS and DSS in white patients, despite accounting for demographic factors and tumor stage.[6,21] A recent study of the US National Cancer Database showed that black patients with MF had a

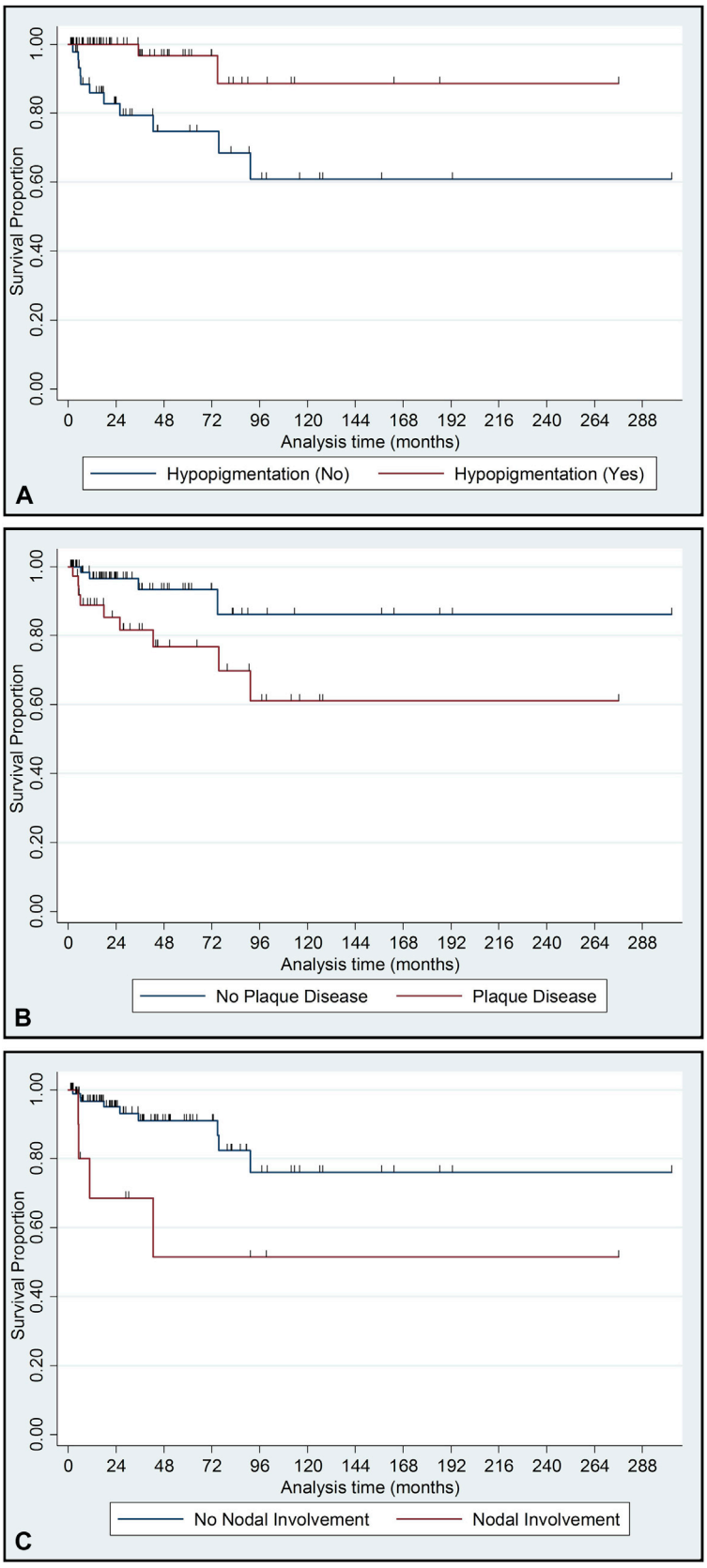

Fig 1. Kaplan-Meier plots of progression-free survival from presentation in African American and black patients with early stage mycosis fungoides. **A**, Hypopigmented lesions (log rank = 0.013). **B**, Plaques (log rank = 0.038). **C**, Lymph node involvement (log rank = 0.02).

Table III. Multivariable overall and progression-free survival analyses in 115 African American and black patients with early stage mycosis fungoides

	Overall survival from presentation		Progression-free survival from presentation	
Characteristic	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Patches	0.09 (0.01-0.75)	**.03**	0.08 (0.01-0.69)	**.02**
Plaques	4.08 (0.66-25.25)	.13	1.51 (0.36-6.36)	.58
Hypopigmented lesions	0.13 (0.01-1.20)	.07	0.10 (0.02-0.63)	**.014**
T stage				
T1	1.0		1.0	
T2	3.04 (0.49-18.87)	.23	0.53 (0.11-2.43)	.41
N stage				
N0	1.0		1.0	
N1-2	3.96 (0.95-16.49)	.06	0.96 (0.17-5.49)	.97
Nx	28.47 (2.29-354.19)	**.009**	61.35 (5.50-648.38)	**.001**
Elevated WBC count	37.80 (1.65-868.41)	**.02**	4.57 (0.19-111.56)	.35
Elevated LDH	7.80 (1.39-43.84)	**.02**	7.80 (1.39-43.84)	**.02**

Analyses were adjusted for sex, insurance type, income, age at diagnosis, and diagnostic delay. Bolded values are statistically significant.
CI, Confidence interval; *HR*, hazard ratio; *LDH*, lactate dehydrogenase; *WBC*, white blood cell.

significantly shorter OS after adjusting for disease characteristics, socioeconomic factors, and types of treatment.[11] It has been concluded that racial disparities in survival are likely secondary to differences in the underlying biology of the disease.[11] It has also been suggested that black patients might require more aggressive initial treatment,[11] and that, in particular, black women with early onset disease should be considered for aggressive therapy, such as allogeneic transplantation.[7] Our experience from the multidisciplinary cutaneous lymphoma clinic at MSKCC shows that African American and black patients with MF/SS seek treatment with diverse clinicopathologic characteristics and have heterogeneous outcomes. Certain subsets of African American and black patients have poor outcomes, while others have an excellent prognosis.

The demographics of our cohort were consistent with previous reports showing an earlier onset of disease[4,11,13,14] and female predominance[11,13,14] among African American and black patients. Unlike previous studies suggesting poor outcomes among black women with early onset disease, our study did not show sex and age to be associated with disease stage, absolute deaths, progression, or survival, other than the expected association of older age at diagnosis with shorter OS.[22] Interestingly, our results demonstrated that African American and black patients with a longer history of symptoms before diagnosis were more likely to have longer survival.

It has been suggested in the literature that socioeconomic differences and a lack of access to medical care might play a role in racial disparities in MF/SS.[6,23] Our study failed to reveal any association between disease severity and outcome with socioeconomic characteristics, including birthplace, health care coverage, median household income, and poverty rate among the studied African American and black patients. Our study included only patients who were seen at MSKCC and, therefore, most likely underrepresents African American and black patients of low socioeconomic status and noninsured patients, limiting the generalizability of our results. However, despite these limitations, 20% of the studied patients were immigrants, 28% had government insurance, 21% resided in areas where the median household income was within the lowest quartile, and 35% resided in an area with a poverty rate of >20%. Despite being performed in a tertiary cancer center, most of the MF/SS patients who seek treatment at our clinic have early stage disease. A definitive diagnosis in early stage MF might be difficult to make; therefore, we excluded cases who were not unequivocally diagnostic. It is possible that we missed patients who did not come to MSKCC because of disease severity or patients with progressive disease who expired before being referred to us. Despite these limitations, we believe our cohort represents the full spectrum of disease severity seen in MF/SS.

Our results showed that the course of MF/SS in African American and black patients is variable. Our results confirmed the prognostic value of the standard staging system and the revised TNMB classification system[24] in this population.

Hypopigmented MF is a variant that predominantly appears in patients with skin of color and usually has an excellent prognosis.[24,25] Hypopigmented lesions might appear as the sole manifestation of MF or with concomitant erythematous and hyperpigmented lesions. Almost half of the studied patients (n = 71; 45%) presented to us with hypopigmented lesions. About half of them (37 patients) had only hypopigmented

lesions, while a mixture of hypo- and hyperpigmented or erythematous lesions was seen in the other half (34 patients). Overall >80% of all cases of death (28/34) and disease progression (22/27) observed in our study occurred in patients with erythema or hyperpigmentation without hypopigmentation. The presence of hypopigmented lesions was highly associated with longer OS (HR 0.04, 95% CI 0.006-0.32; $P = .002$), and none of the patients with hypopigmented lesions died due to disease. Many of the patients with early stage disease had erythematous or hyperpigmented lesions without hypopigmentation (43%), and the absence of hypopigmentation has been shown to be associated with poorer PFS. Clinicians should be careful when evaluating dark skinned patients with MF for hypopigmentation because patients with a history of ulcerated lesions might show depigmented areas in the scarred skin, prior radiation therapy might result in dyspigmentation, and depigmenting skin disorders (eg, vitiligo) might appear concomitantly. Skin biopsy may be recommended to establish or confirm the diagnosis of MF in hypopigmented lesions. Patch versus plaque stage disease and elevated LDH were also significantly associated with disease progression in African American and black patients with early stage disease, supporting previous data on their prognostic value in MF/SS.[24] Among patients with early stage disease, the presence of abnormal lymph nodes per clinical examination (Nx) was independently associated with shorter survival and PFS. The immunophenotype data that was based on immunohistochemistry stain results at presentation was available for 60% of patients. No deaths were recorded among the 29 patients who had $CD8^+$ disease, whereas 30% of the 63 patients with $CD4^+$ MF died. Our findings are in-line with the literature reporting an indolent course in the $CD8^+$ variant of MF and a high prevalence of $CD8^+$ MF among black patients.[26] We did not re-review the immunohistochemistry in this study, and studies with comprehensive immunophenotyping are warranted to better delineate the pathogenic mechanisms behind the association of hypopigmentation, patch-stage disease, and $CD8^+$ phenotype in black patients.[27,28]

Our study highlights the diverse manifestations and heterogenous outcomes of MF/SS in African American and black patients. Demographic and socioeconomic factors did not have prognostic relevance, while certain clinicopathologic features were significantly associated with survival and progression. Decisions on the management and treatment in MF/SS should take into account specific clinical and pathologic prognostic factors and should not be based on demographic parameters or race alone.

REFERENCES

1. Aizer AA, Wilhite TJ, Chen MH, et al. Lack of reduction in racial disparities in cancer-specific mortality over a 20-year period. *Cancer*. 2014;120(10):1532-1539.
2. Kirtane K, Lee SJ. Racial and ethnic disparities in hematologic malignancies. *Blood*. 2017;130(15):1699-1705.
3. Korgavkar K, Xiong M, Weinstock M. Changing incidence trends of cutaneous T-cell lymphoma. *JAMA Dermatol*. 2013;149(11):1295-1299.
4. Wilson LD, Hinds GA, Yu JB. Age, race, sex, stage, and incidence of cutaneous lymphoma. *Clin Lymphoma Myeloma Leuk*. 2012;12(5):291-296.
5. Bradford PT, Devesa SS, Anderson WF, Toro JR. Cutaneous lymphoma incidence patterns in the United States: a population-based study of 3884 cases. *Blood*. 2009;113(21):5064-5073.
6. Nath SK, Yu JB, Wilson LD. Poorer prognosis of African-American patients with mycosis fungoides: an analysis of the SEER dataset, 1988 to 2008. *Clin Lymphoma Myeloma Leuk*. 2014;14(5):419-423.
7. Sun G, Berthelot C, Li Y, et al. Poor prognosis in non-Caucasian patients with early-onset mycosis fungoides. *J Am Acad Dermatol*. 2009;60(2):231-235.
8. Imam MH, Shenoy PJ, Flowers CR, Phillips A, Lechowicz MJ. Incidence and survival patterns of cutaneous T-cell lymphomas in the United States. *Leuk Lymphoma*. 2013;54(4):752-759.
9. Weinstock MA, Reynes JF. The changing survival of patients with mycosis fungoides: a population-based assessment of trends in the United States. *Cancer*. 1999;85(1):208-212.
10. Jang S, Bartnicki S, Gustavson C, Desimone J. Racial differences in survival of patients with Sezary syndrome in the United States: a population-based study of 204 cases. *J Am Acad Dermatol*. 2016;74(5):AB182.
11. Su C, Nguyen KA, Bai HX, et al. Racial disparity in mycosis fungoides: an analysis of 4495 cases from the US National Cancer Database. *J Am Acad Dermatol*. 2017;77(3):497-502.e492.
12. Desai M, Liu S, Parker S. Clinical characteristics, prognostic factors, and survival of 393 patients with mycosis fungoides and Sezary syndrome in the southeastern United States: a single-institution cohort. *J Am Acad Dermatol*. 2015;72(2):276-285.
13. Balagula Y, Dusza SW, Zampella J, Sweren R, Hinds GA. Early-onset mycosis fungoides among African American women: a single-institution study. *J Am Acad Dermatol*. 2014;71(3):597-598.
14. Zampella JG, Hinds GA. Racial differences in mycosis fungoides: a retrospective study with a focus on eosinophilia. *J Am Acad Dermatol*. 2013;68(6):967-971.
15. Olsen E, Vonderheid E, Pimpinelli N, et al. Revisions to the staging and classification of mycosis fungoides and Sezary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC). *Blood*. 2007;110(6):1713-1722.
16. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016;127(20):2375-2390.
17. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005;105(10):3768-3785.
18. Arya S, Binney Z, Khakharia A, et al. Race and socioeconomic status independently affect risk of major amputation in peripheral artery disease. *J Am Heart Assoc*. 2018;7(2).

19. Kreisel K, Flagg EW, Torrone E. Trends in pelvic inflammatory disease emergency department visits, United States, 2006-2013. *Am J Obstet Gynecol*. 2018;218(1):117.e1-117.e10.
20. Criscione VD, Weinstock MA. Incidence of cutaneous T-cell lymphoma in the United States, 1973-2002. *Arch Dermatol*. 2007;143(7):854-859.
21. Weinstock MA, Gardstein B. Twenty-year trends in the reported incidence of mycosis fungoides and associated mortality. *Am J Public Health*. 1999;89(8):1240-1244.
22. Lebowitz E, Geller S, Flores E, et al. Survival, disease progression and prognostic factors in elderly patients with mycosis fungoides and Sezary syndrome: a retrospective analysis of 174 patients. *J Eur Acad Dermatol Venereol*. 2019;33(1):108-114.
23. Bradford PT. Skin cancer in skin of color. *Dermatol Nurs*. 2009; 21(4):170-177, 206; quiz 178.
24. Scarisbrick JJ, Kim YH, Whittaker SJ, et al. Prognostic factors, prognostic indices, and staging in mycosis fungoides and Sezary syndrome: where are we now? *Br J Dermatol*. 2014; 170(6):1226-1236.
25. Rodney IJ, Kindred C, Angra K, Qutub ON, Villanueva AR, Halder RM. Hypopigmented mycosis fungoides: a retrospective clinicohistopathologic study. *J Eur Acad Dermatol Venereol*. 2017;31(5):808-814.
26. Martinez-Escala ME, Kantor RW, Cices A, et al. $CD8^{+}$ mycosis fungoides: a low-grade lymphoproliferative disorder. *J Am Acad Dermatol*. 2017;77(3):489-496.
27. El-Shabrawi-Caelen L, Cerroni L, Medeiros LJ, McCalmont TH. Hypopigmented mycosis fungoides: frequent expression of a CD8+ T-cell phenotype. *Am J Surg Pathol*. 2002;26(4):450-457.
28. Geller S, Lebowitz E, Pulitzer M, Myskowski PL. Understanding racial disparities in mycosis fungoides through international collaborative studies. *Br J Dermatol*. 2019; 180(5):1263-1264.