12-15-2021

Contribution of socioeconomic risk factors within a diverse mycosis fungoides cohort from Detroit, Michigan

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Recommended Citation

Buechler CR, Sagher E, Tisack A, Jacobsen G, Lim HW, McHargue C, Friedman BJ, Mi QS, Ozog DM, and Veenstra J. Contribution of Socioeconomic Risk Factors within a Diverse Mycosis Fungoides Cohort from Detroit, MI. J Am Acad Dermatol 2021.

Research letter

Contribution of socioeconomic risk factors within a diverse mycosis fungoides cohort from Detroit, Michigan

To the Editor: Mycosis fungoides (MF) is the most common form of cutaneous T-cell lymphoma, with Black patients having worse overall and disease-specific survival than White patients,[1] a fact often attributed to economic factors,[2] though no data have yet been published to corroborate this conclusion. Recent work has suggested that socioeconomic factors do not have any role in MF prognosis, with clinical and histopathologic characteristics alone determining outcome.[3] This study aimed to delineate further what factors impact the course of MF among a large, racially and socioeconomically diverse cohort from Detroit, Michigan.

The Henry Ford Health System MF registry, containing 440 patients with MF confirmed via physician note review, was utilized (IRB #13679) (Table I). Data regarding diagnosis, treatment, disease course, and demography were collected (Supplemental Table I, available via Mendeley at

Table I. Population-level characteristics

Characteristic	Value
Age at diagnosis, mean (range)*	55 (7-103)
Female:male ratio (n:n)	0.849 (208:232)
Race/ethnicity, n (%)	
White/Caucasian	221 (50.2)
Black/African American	176 (40)
Hispanic or Latino	5 (1.14)
Middle Eastern or North African	6 (1.36)
Asian	11 (2.5)
American Indian/Alaska Native	0 (0)
Native Hawaiian/Pacific Islander	0 (0)
Other	3 (0.68)
Unknown	18 (4.09)
Insurance status, n (%)†	
None	12 (2.73)
Private	325 (73.9)
Medicare	254 (57.7)
Medicaid	47 (10.7)
Other	9 (2.05)
Unknown	1 (0.227)
Household income, median (range)	$56,212 ($21,013-$147,303)
Delay in diagnosis from symptom onset, median‡	3-4 years
Clinical stage at diagnosis, n (%)	
IA	162 (36.8)
IB	136 (30.9)
IIA	3 (0.68)
IIB	17 (3.86)
IIIA + IIIB	14 (3.18)
IVA + IVB	9 (2.05)
Unknown	99 (22.5)
Required escalation of therapy, n (%)§	239 (54.3)
Frequency of HFHS dermatology follow-up, n (%)‖	
No visits to HFHS dermatologist	52 (11.8)
Routine current	135 (30.7)
Sporadic current	103 (23.4)
Routine historic	59 (13.4)
Sporadic historic	91 (20.7)
Comorbidities, n (%)	
Heart disease	116 (26.4)
Hypertension	273 (62.0)
Hyperlipidemia	237 (53.9)
Diabetes	110 (25.0)
Obesity	209 (47.5)
Solid tumor cancer¶	84 (19.1)
Leukemia/lymphoma other than MF	19 (4.32)
Other of significance	58 (13.2)
None	73 (16.6)
Pathology variant, n (%)	
CD8 predominant	39 (8.86)
Large cell transformation	24 (5.45)
Hypopigmented	60 (13.6)
Folliculotropic	27 (6.14)
LDH at diagnosis, median	<250
CD4:CD8 ratio, mean (range)	4.52 (0.3-98.5)
Nodal disease ever present, No. (%)	38 (8.64)
Metastatic visceral disease ever present, No. (%)	6 (1.36)

Continued

Table I. Cont'd

HFHS, Henry Ford Health System; *LDH*, lactate dehydrogenase; *MF*, mycosis fungoides.

*Mycosis fungoides diagnosis was identified via HFHS Metriq Cancer Registry and Epic SlicerDicer tool and confirmed with either physician documentation or a definitive pathology report in the HFHS electronic medical record from January 1, 2001 to December 31, 2019.

†Some patients held more than one insurance type. No private exchanges in Michigan offer medical plans that are also classified as Medicaid.

‡Mean time to diagnosis was collected in an ordinal fashion, as follows: <3 months, 3-6 months, 7-12 months, 1-2 years, 3-4 years, 5-6 years, 7-8 years, 9-10 years, 11-12 years, 13-14 years, >14 years, Unknown.

§Defined as need for treatment beyond topical steroids and narrow band UV-B light.

‖Regularity of dermatologic care was measured at time of last follow-up or time of death, and was defined as Current Routine (at least twice per year in past 2 years), Current Sporadic (once per year or less in past 2 years), Historic Routine (at least twice per year >2 years ago), or Historic Sporadic (once per year or less >2 years ago).

¶Excludes non-melanoma skin cancer.

Table II. Mycosis fungoides regression analysis, HR (95% CI)

	Progression		Disease-specific survival		Progression-free survival	
Variable	**Univariable**	**Stepwise multivariable**	**Univariable**	**Stepwise multivariable**	**Univariable**	**Stepwise multivariable**
Black race	1.13 (0.69-1.86)	¶	**0.29 (0.09-0.87)***	¶	1.01 (0.63-1.60)	¶
Male gender	0.93 (0.56-1.53)	¶	1.60 (0.62-4.12)	¶	0.99 (0.62-1.57)	¶
Diagnosis age	1.01 (1.00-1.03)	¶	**1.07 (1.03-1.10)‡**	**1.14 (1.06-1.23)‡**	**1.02 (1.00-1.04)***	¶
Private insurance	0.73 (0.43-1.25)	¶	0.75 (0.28-1.99)	¶	0.62 (0.38-1.01)	¶
Medicare insurance	1.19 (0.70-2.02)	¶	2.69 (0.78-9.32)	¶	1.20 (0.73-1.97)	¶
Medicaid insurance	**2.06 (1.07-3.95)***	**3.56 (1.56-8.12)†**	1.06 (0.24-4.60)	‖	**2.08 (1.14-3.80)***	**3.13 (1.46-6.69)†**
Median income in thousands (by zip code)	0.99 (0.99-1.00)	¶	1.00 (0.99-1.02)	¶	1.00 (0.99-1.01)	¶
Heart disease	1.47 (0.87-2.48)	¶	1.32 (0.50-3.53)	‖	**1.62 (1.00-2.62)***	¶
Hypertension	0.89 (0.53-1.51)	¶	1.08 (0.38-3.04)	¶	0.97 (0.59-1.59)	¶
Hyperlipidemia	0.98 (0.59-1.62)	¶	0.47 (0.18-1.22)	¶	0.89 (0.56-1.41)	¶
Diabetes	1.21 (0.71-2.06)	¶	1.39 (0.53-3.59)	¶	1.17 (0.71-1.91)	¶
Obesity	1.09 (0.66-1.80)	¶	0.66 (0.26-1.67)	¶	1.05 (0.66-1.67)	¶
Solid tumor cancer	0.72 (0.37-1.41)	¶	1.90 (0.71-5.06)	¶	0.90 (0.50-1.62)	¶
Leukemia or lymphoma	1.23 (0.45-3.40)	¶	1.00 (0.13-7.58)	¶	1.04 (0.38-2.85)	¶
Regularity of dermatology care	1.36 (0.87-2.11)	**1.88 (1.07-3.28)***	1.72 (0.73-4.10)	**3.78 (1.07-13.35)***	1.47 (0.97-2.23)	**2.09 (1.23-3.55)†**
MF stage at diagnosis	0.85 (0.66-1.09)	**0.50 (0.36-0.71)‡**	**1.53 (1.23-1.90)‡**	¶	1.02 (0.85-1.22)	**0.66 (0.52-0.84)‡**
LDH at diagnosis ≥250	0.91 (0.34-2.41)	NC	1.37 (0.37-5.11)	NC	1.06 (0.45-2.46)	NC
Required MF hospitalization	**4.16 (2.28-7.62)‡**	**3.77 (1.48-9.59)†**	**59.18 (17.06-205.32)‡**	**70.44 (10.63-466.84)‡**	**6.32 (3.79-10.53)‡**	**3.35 (1.46-7.72)†**
MF treatment escalated	**3.04 (1.49-6.18)†**	**3.82 (1.61-9.04)†**	8.03 (1.06-60.65)	¶	**3.19 (1.63-6.24)‡**	**2.88 (1.27-6.52)***
CD4:CD8 ratio >10	2.17 (0.86-5.50)	NC	4.01 (1.12-14.34)	NC	**3.06 (1.44-6.49)†**	NC
≥1000 μL Sézary cells	**4.54 (1.96-10.51)‡**	NC	**14.87 (3.49-63.36)‡**	NC	**5.69 (2.63-12.29)‡**	NC
$CD4^+$ $CD26^-$ ≥30%	1.14 (0.34-3.84)	NC	**12.54 (3.29-47.48)‡**	NC	**3.01 (1.33-6.81)†**	NC
$CD4^+$ $CD7^-$ ≥40%	1.99 (0.47-8.45)	NC	**22.34 (5.72-87.24)‡**	NC	**5.54 (2.24-13.66)‡**	NC
CD8 predominant pathology	0.29 (0.04-2.12)	¶	1.61 (0.21-12.57)	‖	0.52 (0.13-2.15)	¶
Large cell transformation	**3.56 (1.69-7.52)‡**	**3.51 (1.44-8.52)†**	2.88 (0.66-12.61)	¶	**3.49 (1.73-7.05)‡**	¶
Positive TCR skin rearrangement	1.47 (0.75-2.90)	NC	6.34 (0.82-48.76)	NC	1.60 (0.84-3.04)	NC
Positive TCR blood rearrangement	0.96 (0.48-1.92)	NC	4.05 (0.86-19.11)	NC	1.08 (0.56-2.08)	NC
Hypopigmented variant	0.49 (0.20-1.22)	¶	§	‖	0.42 (0.17-1.03)	¶
Folliculotropic variant	1.14 (0.41-3.14)	¶	0.96 (0.13-7.23)	‖	1.23	¶
Nodal disease present	**5.60 (3.13-10.01)‡**	**2.87 (1.16-7.07)***	**17.20 (6.72-44.02)‡**	**51.53 (4.54-584.80)†**	**6.68‡**	**4.93 (2.31-10.52)‡**
Visceral disease present	**5.90 (2.13-16.35)‡**	¶	**18.28 (5.98-55.88)‡**	¶	**7.67‡**	¶
Years from onset to diagnosis	**0.93 (0.88-0.98)***	**0.91 (0.85-0.98)†**	**0.75 (0.58-0.99)***	¶	**0.87***	**0.83 (0.73-0.95)†**

HR, Hazard ratio; *LDH*, lactate dehydrogenase; *MF*, mycosis fungoides; *NC*, Non-Calculable due to missing status in at least 25% of the study patients; *TCR*, T-cell receptor.

Disease-specific survival was calculated from diagnostic biopsy to either death or most recent mycosis fungoides (MF) specialist follow-up (dermatology, oncology, radiation oncology). Progression-free survival was calculated from diagnostic biopsy to the first documented progression in disease stage or death; or, for those without documented progression, the most recent MF specialist follow-up. All variables evaluated with univariable analysis were applied to the stepwise multivariable Cox regression modeling except those with a missing status in at least 25% of the study patients (lactate dehydrogenase at diagnosis >250, CD4:CD8 ratio >10, >1000 μL Sézary cells, $CD4^+$ $CD26^-$ >30%, $CD4^+$ $CD7^-$ >40%, positive T-cell receptor skin rearrangement, and positive T-cell receptor blood rearrangement). Insurance categories were included as yes/no variables in the Cox regression modeling, and patients were allowed to hold multiple insurance types. HR>1 indicates shorter progression-free time, disease-specific survival, or progression-free survival. HR<1 indicates longer progression-free time, disease-specific survival, or progression-free survival. Statistically significant values are in bold.

*$P < .05$.

†$P < .01$.

‡$P < .001$.

§The hypopigmented variant could not be applied to the univariable Cox regression analysis because MF-specific death did not occur in any patients with hypopigmented MF.

‖For MF-specific death, the CD8 predominant pathology, hypopigmented and folliculotropic variants, could not be applied to the stepwise modeling as none of the modeled patients with those conditions had MF-specific death. The Medicaid insurance and heart disease variables were too unstable to participate in the stepwise modeling due to the limited number of MF-specific deaths among the modeled patients with these variables.

¶Values did not add a significant amount of predictability to the model.

https://data.mendeley.com/datasets/52s2th2hmg/1) and analyzed for factors predicting disease-specific survival, progression, and progression-free survival (PFS) via univariable and multivariable stepwise Cox proportional hazards regression models. For full methodology, see supplemental material.

Medicaid insurance was a significant independent predictor of progression and shorter PFS (Table II). This study is the first to find that this indicator of lower socioeconomic status is independently associated with increased risk for poor outcomes in MF, regardless of race. The predictive value of socioeconomic factors is likely based on access to care, access to medication, health literacy, and bias inherent in a provider or health system. In our dataset, those with Medicaid insurance experienced a longer median diagnostic delay (5-6 years compared to 3-4 years), indicating potential access issues. Unsurprisingly, median household income determined by zip code provided no predictive value, reflecting its inefficiency in measuring individual-level socioeconomic status within socially diverse regions. Previous work has highlighted the variability of MF as a proportion of cutaneous T-cell lymphoma cases between continents as an indicator of environmental contributions to MF pathophysiology[4] such factors could affect outcomes even among inner city and suburban populations if exposures vary substantially. Detroit is heavily segregated, with environmental exposures and health risks disproportionately affecting those with heightened economic vulnerability, making this a possibility.

A higher disease stage at diagnosis and increased diagnostic delay each decreased the risk of future progression and increased PFS (Table II), indicating that disease that has long remained indolent without treatment is likely to remain stable and that treatment-naïve patients with advanced disease generally improved or remained stable upon receiving care. Many of the defining factors of disease progression were associated with MF-specific death, progression, and PFS (Table II), reaffirming the predictive value of established staging criteria.[3] We also confirmed the better prognostic characteristics of the hypopigmented and $CD8^+$ predominant variants and found no prognostic value of folliculotropism, supporting its exclusion from staging criteria and corroborating the recent work by Charli-Joseph et al.[5]

The contribution of socioeconomic factors to the course of MF proved substantial in our database. Though continued research is needed as to the cause of this phenomenon, patients with lower socioeconomic status as indicated by Medicaid insurance should receive consideration for more frequent follow-up and a lower threshold for therapeutic escalation to guard against its effects.

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Funding sources: Supported in part by the William Clay Ford Jr and Lisa V Ford Foundation. Funds for statistical support provided through the Graduate Medical Education office at Henry Ford Hospital.

IRB approval status: Reviewed and approved by Henry Ford Health System IRB (#13679).

Key words: CTCL; environmental; health disparity; lymphoma; medical dermatology; mycosis fungoides; socioeconomics; T cell/CTCL/MF.

Reprints not available from the authors.

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Conflicts of interest

None declared.

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https://doi.org/10.1016/j.jaad.2021.12.016