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Social Vulnerability and Racial Disparities in Overall Survival Among Endometrial Cancer Patients

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SOCIAL VULNERABILITY AND RACIAL DISPARITIES IN OVERALL SURVIVAL AMONG ENDOMETRIAL CANCER PATIENTS

by

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ABSTRACT

Introduction. Social vulnerability (SV) refers to potential negative effects on communities caused by external stresses on human health. The CDC/ATSDR Social Vulnerability Index (SVI) scores communities on 15 social indicators in 4 themes: (1) socioeconomic status (SES), (2) household composition and disability, (3) minority status and language, and (4) housing type and transportation. An overall score ranging from 0 (least vulnerable) to 1 (most vulnerable) is calculated to estimate vulnerability. We investigated whether SV as measured by the SVI can explain why black endometrial cancer (EC) patients survive less well than do white EC patients.

Methods. We studied the survival of 918 EC patients, 293 (32%) Black, and 625 (68%) Non-Black (90% White), treated from 2007-2022 at a tertiary-care cancer center in the Deep South. Demographic, clinical, and survival data were retrieved from electronic medical records. OS at 5 years was computed for Black and non-Black patients using Cox proportional hazards models. The relationship between level of social vulnerability (high, medium, or low tertile) and OS was assessed for each group by comparing the percent in the highest tertile for Blacks and non-Blacks.

Results. Black EC patients had about double the percentage of high SV (67% vs 32%, $p<0.0001$) than did non-Black EC patients; and Black patients did not survive as well

as non-Black patients. Blacks did worse than Whites for all themes, with all comparisons highly statistically significant: Theme 1: 71.3% vs 37.3%; Theme 2: 67.2% vs 50.2%; Theme 3: 17.4% vs 7.4%; Theme 4: 44.4% vs 23.2%. Within races, multivariate analysis showed that high SES vulnerability (Theme 1) was associated with worse OS for non-Black EC patients (HR 2.9, 95% CI 1.4-6.2), but not for Black patients (HR 0.97, 95%CI 0.28-3.28), independent of the other factors in the model. Other themes did not yield statistically significant findings.

Conclusions. Higher social vulnerability among Black as compared to non-Black patients, was associated with lower OS. Non-Black patient survival was primarily driven by SES vulnerability. Further investigation of racial differences in social vulnerability components is warranted to understand the dynamics of race and SES determination of disparities in endometrial cancer survival.

Keywords: Endometrial Cancer, Social Vulnerability, Racial Disparities

DEDICATION

I would like to thank my parents, Rudi and Inge, for the endless support to my journey, for believing in me despite the circumstances. I dedicate this to my wife, Emily, who is always there for me even on the though days when no other people knows what happened behind the scenes. To my mentors, John, Jerry, and Becca, thank you for the guidance, fruitful collaborations, and endless support in our projects.

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ATSDR	Agency for Toxic Substances and Disease Registry
BMI	Body Mass Index
CCI	Charlson-Deyo Comorbidity Index
CI	Confidence Interval
CDC	Centers for Disease Control and Prevention
EC	Endometrial Cancer
G1-2	Grade I-II
G3	Grade III
HR	Hazard Ratio
ICD	International Classification of Diseases
ICD-9	Ninth Edition of International Classification of Diseases
ICD-10	Tenth Edition of International Classification of Diseases
IRB	Institutional Review Board
MMMT	Multiple Mixed Mullerian Tumor
OS	Overall Survival
PEComa	Perivascular Epithelioid Cell tumors
Ref	Reference
SDOH	Social Determinants of Health
SES	Socioeconomic Status
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

SV	Social Vulnerability
SVI	Social Vulnerability Index
T1	Theme 1
T2	Theme 2
T3	Theme 3
T4	Theme 4
UAB	University of Alabama at Birmingham
UPSC	Uterine Papillary Serous Carcinoma

INTRODUCTION

Cancer of the uterine corpus, 95% of cases classified as Endometrial cancer (EC), is the most common gynecologic cancer and ranks fourth among all cancers in women, with an estimated 66,200 new cases and 13,030 deaths in 2023 [1,2]. EC primarily affects postmenopausal women and more than 90% present with post-menopausal vaginal bleeding[3,4]. EC rates have continued to climb, despite the overall decline in cancer incidence rate in the United States[1,5,6].

Racial disparities of EC survival are appreciable. Although the age-adjusted incidence is 31% lower among Black women than among White women, the mortality rate in Black women is 80% higher than in White women, with a huge gap of five-year survival, 81% versus 63% for Black compared to White women[1,2,7,8]. This gap places endometrial cancer a close second (21%) after melanoma (22%) among cancers having large black-white survival differences[1]. This racial disparity is observed for endometrioid and non-endometrioid cancers, with a lower 5-year survival rate for Black women[9]. Previous studies showed that disparities occurred because Black women tend to be diagnosed at a later stage and have more unfavorable prognoses, but the etiology of disparities is multifactorial and complex[3,4,10,11].

Factors associated with diminished EC survival include higher age at diagnosis, higher BMI, more advanced stage, non-endometrioid histopathology, Black race, higher Charlson-Deyo Comorbidity Index (CCI) score, and history of cancer[4,7]. Complementary

to these factors is the association of racial disparities with health outcomes measured by Social Determinants of Health (SDOH)[12]. SDOH have been associated with disparities in cancer presentation and health outcomes for a variety of cancers including endometrial cancer[2,4,11]. SDOH consist of complex relationships of social, cultural, and financial factors that influence the entire trajectory of health[4]. One of the means to measure and quantify SDOH is through an index by the Centers for Disease Control and Prevention (CDC) called the Social Vulnerability Index (SVI). This is a publicly available index online database tool comprised of 4 themes of 15 components to identify communities at risk[13-15]. Although the SVI was originally intended to identify vulnerable communities and assess readiness to deal with environmental hazards, it has been broadly used in outcomes research studies in surgery, obstetrics, cancer, and cardiology[13,15-19].

Social vulnerability is an important determinant of access to health care. But it is unknown whether the SVI corresponding to area of residence is associated with EC survival. The relationship between race, social vulnerability, and survival of EC patients is incompletely understood. Thus, we sought to investigate the impact of social vulnerability on survival from endometrial cancer. We hypothesized that women residing in an area with high SVI level have a worse survival than those who are not, our primary objective. Secondary objectives were to identify the relationship between race and overall survival in EC patients as well as investigate how race and SVI independently and together are associated with EC overall survival. The use of SVI as a measure of SDOH to predict EC patient survival could shed light on the impact on ways to decrease continuing disparities among EC patients.

METHODS

Study Design

This study was a single-center retrospective cohort study of EC patients diagnosed from 2007-2021 and treated at the University of Alabama at Birmingham (UAB) Hospital and O'Neal Comprehensive Cancer Center. All patients having histological diagnosis of epithelial-derived uterine cancer, including endometrioid, clear cell, and uterine papillary serous endometrial cancer, as well as carcinosarcoma, seen at UAB Gynecologic Clinic between 2007 and 2022, were studied. Exclusion criteria were patients missing data of importance such as address and zip code, as well as patients with any of these diagnoses: stromal or mesenchymal sarcoma (such as low-grade and high-grade endometrial stromal sarcoma), undifferentiated uterine sarcoma, uterine leiomyosarcoma (epithelioid and myxoid variants), uterine tumor resembling ovarian sex cord tumor, rhabdomyosarcoma, and perivascular epithelioid cell tumors (PEComas). Study participants were identified using the International Classification of Diseases (ICD), ninth (ICD-9) and tenth (ICD-10) versions, electronic medical records, and local databases of gynecologic oncology patients who came to clinic. This manuscript was written with reference to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[20]. This study was evaluated and approved by the UAB Institutional Review Board (IRB- 300006290).

Social Vulnerability Index

To calculate the SVI for each patient, the CDC/Agency for Toxic Substances and Disease Registry (ATSDR) SVI 2018 database, the latest version available during data collection, was used. Scores for 15 social indicators were based on American community survey data from 2014 to 2018. As shown in Figure 1, SVI indicators are categorized into 4 themes: (1) socioeconomic status (SES) based on income ($21,870 for the head of household with the addition of $7,710 per every additional person defined poverty), employment status, and less than high school education); (2) household composition and disability (aged 65 or older, aged 17 or younger, civilian with a disability, and single parent household); (3) minority status and language (minority race or ethnicity and speak English less than well), and (4) housing type and transportation (living in a multiunit structure, mobile home, crowding, group quarter, and having no vehicle)[14].

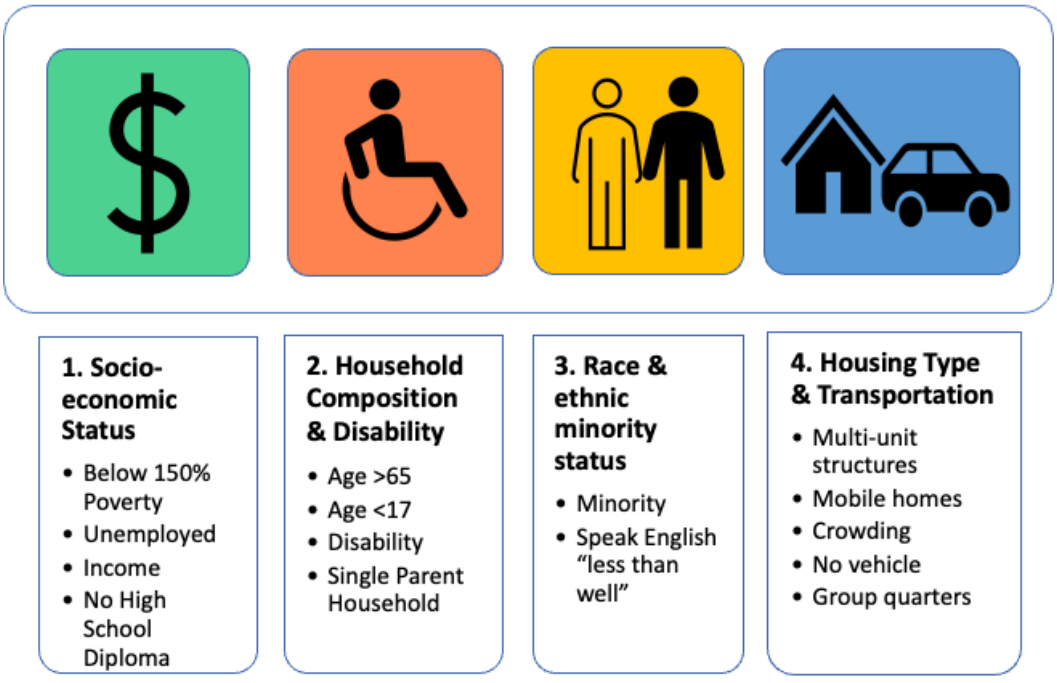

Figure 1. Social Vulnerability Index themes and components.

The CDC/ATSDR Social Vulnerability Index interactive map was used to find the SVI for each subject. Each patient's address and zip code were obtained from the electronic medical record and inputted to the interactive map to find the specific census tract assigned to that address. Knowing the census tract of each patient, scores for all four themes were obtained. SVI scores are generated at the census tract level and are calculated based on the sum of rankings of the indicators, according to relative vulnerability compared to other counties in the same population[14,16]. The overall score is a continuous variable ranging from 0 to 1, with a high number indicating high vulnerability. There are no accepted criteria or cutoffs to classify SVI scores as high, medium, or low. In this study we classified SVI scores in tertiles, as high, medium, or low, corresponding to the upper, middle, and lower tertiles, respectively.

Data Management and Analysis

Descriptive statistics summarizing patient characteristics include age at diagnosis, body mass index (BMI), histology, staging, race, vital status, and SVI categories and its 4 themes (socioeconomic status, household composition and disability, race and ethnic minority status, housing type and transportation). Chi-square tests compare patient characteristics between races across SVI categories. Patients self-identified as African American were categorized as Black, while patients of other races, more than 90% White, were categorized as non-Black. Cox proportional hazards regression models were used to estimate the association between SVI and survival with and without adjustment for factors *a priori* known to be associated with EC survival, including Black race, age at diagnosis,

histopathology, body mass index (BMI), and stage at diagnosis[4,7]. Stratification for race was performed to evaluate effect modification. All significance tests were performed at alpha level 0.05. All statistical analyses were performed using JMP Pro 16 software and SAS v 9.4 (SAS Institute, NC) software.

RESULTS

Sample Demographics

A total of 1043 pathology-confirmed endometrial cancer (EC) patients seen in clinic from 2007-2022 were screened for this study. As shown in Figure 2, 125 patients were dropped because critical information was missing: address or zip code (99 patients), race (16 patients), age at diagnosis (4 patients), and BMI (3 patients). Three others were excluded for statistical reasons. A total of 918 women remained for the analyses in this study.

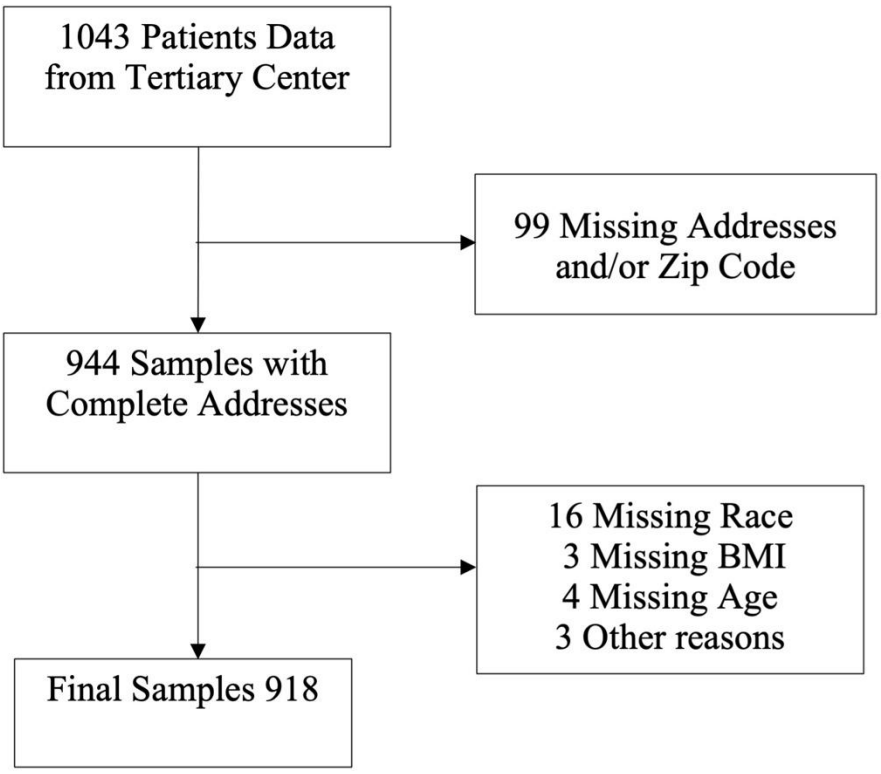

Figure 2. Flowchart of sample collections.

Demographic and socioeconomic characteristics are shown in Table 1. Many enrolled patients (n=371, 40%) were 60-69 years old, and 293 (32%) patients were Black. A total of 635 (69%) patients were obese, with 260 (28%) categorized as obese class 3 (BMI of 40 kg/m^2 or more). Most patients (n=641,70%) had endometrioid type endometrial cancer histopathology, predominantly grade 1 and 2 (n=575, 63%). Other types of histopathology account for less commonly findings, such as PEComa, neuroendocrine tumor, or mixtures of 2 histologies. The vast majority of patients (n=899, 98%) had been successfully surgically staged, and the majority had stage I or II endometrial cancer (n=731, 80%). By the end of the follow up period, 123 patients (13.4%) had passed away.

Table 1. Characteristics of patients with endometrial cancers diagnosed from 2007 – 2022 (N=918)

Variable	Overall		Non-Black		Black		
	N	**%**	**n**	**%**	**n**	**%**	***p*-value**
Age at Diagnosis, years							
<50	91	9.9	65	10	26	8.9	0.1369
50-59	207	23	150	24	57	20	
60-69	371	40	237	38	134	46	
>=70	249	27	173	28	76	26	
BMI							
> **Obese (>=30 kg/m^2)**	635	69	414	66	221	75	**0.0009**
Obese Class 3 (>=40 kg/m^2)	260	28	151	24	109	37	
Obese Class 2 (35-40 kg/m^2)	176	19	123	20	53	18	
Obese Class 1 (30-35 kg/m^2)	199	22	140	22	59	20	
> **Overweight** (25-30 kg/m^2)	188	21	137	22	51	17	
> **Normal** (18.5-25 kg/m^2)	95	10	74	12	21	7.2	
Histology							
> **Endometrioid**	641	70	474	76	167	57	**<0.0001**
Endometrioid G1-2	575	63	437	70	138	47	

Endometrioid G3	66	7.2	37	5.9	29	9.9	
> **Non-Endometrioid**	277	30	151	24	126	43	
Clear Cell	24	2.6	14	2.2	10	3.4	
Uterine Papillary Serous Carcinoma (UPSC)	156	17	87	14	69	24	
Carcinosarcoma (MMMT)	77	8.4	39	6.2	38	13	
Other	20	2.2	11	1.8	9	3.1	
Staging,							
I-II	731	80	509	81	222	76	0.1598
III	122	13	79	13	43	15	
IV	46	5	27	4.3	19	6.5	
Unknown	19	2	10	1.6	9	3.1	
Deceased							
Yes	795	87	75	12	48	16	0.0733
No	123	13	550	88	245	84	
Social Vulnerability Index (SVI)							
SVI 2018							
High	396	43	201	32	195	67	**<0.0001**
Moderate	201	22	250	40	71	24	
Low	321	35	174	28	27	9.2	
Theme 1 (Socioeconomic)							
High	442	48	233	37	209	71	**<0.0001**
Moderate	171	19	246	39	59	20	
Low	305	33	146	23	25	8.5	
Theme 2 (Household Composition)							
High	510	56	313	50	197	67	**<0.0001**
Moderate	126	14	205	33	76	26	
Low	281	31	106	17	20	6.8	
Theme 3 (Race and Ethnic Minority Status)							
High	97	11	46	7.4	51	17	**<0.0001**
Moderate	346	38	278	45	197	67	
Low	475	52	301	48	45	15	
Theme 4 (Housing Type and Transportation)							
High	265	30	135	23	130	44	**<0.0001**
Moderate	311	36	204	35	95	32	
Low	299	34	243	42	68	23	

More than one-third of patients were living in an area of high SVI (n=396, 43%). Theme 1 (socioeconomic status) and Theme 2 (household composition) were consistent drivers of high SVI (n=442, 48% and n=510, 56% respectively). Theme 3 (minority status and language) was associated with low SVI (n=475, 52%), while Theme 4 (housing type and transportation) had a relatively balanced distribution with moderate SVI level the main category (n=311, 36%).

Black patients showed a higher (75%) proportion of obese patients than did non-Black patients (66%), with more patients categorized as obese class 3 (37% vs 24%) for Black than non-Black patients. Endometrioid histology was more common among non-Black patients (76%) than among Black patients (57%). Notably, Black, and non-Black patients differed in SVI, with a higher proportion (67% versus 32%) of upper tertile (high) SVI among Black patients, a highly significant result ($p<0.0001$).

Table 2a. Patient demographics by Social Vulnerability Index categories.

Variable	SVI						
	Low		Mid		High		*p*-value
	n	%	n	%	n	%	
Age at Diagnosis, years							
<50	18	9	34	10.6	39	9.9	0.8128
50-59	39	19.4	76	23.7	92	23.2	
60-69	83	41.3	141	40.8	157	39.7	
>=70	61	30.4	80	24.9	108	27.3	
Race							
Black	27	13.4	71	22.1	195	49.2	**<0.0001**
Non-Black	174	86.6	250	77.9	201	50.8	
BMI							
Obese Class 3 (>=40 kg/m^2)	43	21.4	79	24.6	138	34.9	**0.0005**
Obese Class 2 (35-40 kg/m^2)	40	19.9	58	18.1	78	19.7	
Obese Class 1 (30-35 kg/m^2)	35	17.4	82	25.6	82	20.7	
Overweight (25-30 kg/m^2)	58	28.9	65	20.3	65	16.4	
Normal (18.5-25 kg/m^2)	25	12.4	37	11.5	33	8.3	
Histology							
Endometrioid G1-2	136	67.7	201	62.2	238	60.1	**0.0246**
Endometrioid G3	18	9	16	5	32	8.1	
Clear Cell	3	1.5	9	2.8	12	3	
UPSC	30	14.9	67	20.9	59	14.9	
MMMT	13	6.5	21	6.5	43	10.9	
Other	1	0.5	7	2.2	12	3	
Staging,							

I-II	160	79.6	261	81.3	310	78.3	0.0922
III	30	14.9	35	10.9	57	14.4	
IV	8	4	22	6.9	16	4	
Unknown	3	1.5	3	0.9	13	3.3	
Deceased							
Yes	19	9.5	44	13.7	60	15.2	0.1353
No	182	90.6	277	86.3	336	84.9	

Table 2b. Patient demographics by Social Vulnerability Index theme 1 (socioeconomic) and theme 2 (household composition and disability) categories

Variable	Theme 1 (Socioeconomic)							Theme 2 (Household Composition)						
	Low		Mid		High		*p*-value	Low		Mid		High		*p*-value
	n	%	n	%	n	%		n	%	n	%	n	%	
Age at Diagnosis, years														
<50	14	8.2	35	12	42	9.5	0.8213	12	9.5	23	8.2	55	11	0.8767
50-59	35	21	73	24	99	22		25	20	63	22	119	23	
60-69	71	42	118	39	182	41		54	43	117	42	200	39	
>=70	51	30	79	26	19	27		35	28	78	28	136	27	
Race														
Black	25	15	59	19	209	47	**<0.0001**	20	16	76	27	197	39	**<0.0001**
Non-Black	146	85	246	81	233	53		106	84	205	73	313	61	
BMI														
Obese Class 3 (>=40 kg/m^2)	40	23	74	24	146	33	**0.0414**	28	22	74	26	157	31	**0.0074**

Obese Class 2 (35-40 kg/m^2)	32	19	56	18	88	20		16	13	62	22	98	19	
Obese Class 1 (30-35 kg/m^2)	34	20	71	23	94	21		29	23	58	21	112	22	
Overweight (25-30 kg/m^2)	40	23	70	23	78	17		27	21	63	22	98	19	
Normal (18.5-25 kg/m^2)	25	15	34	11	36	8.1		26	21	24	8.5	45	8.8	
Histology														
Endometrioid G1-2	120	70	188	62	267	60	0.0553	88	70	183	65	303	59	0.1834
Endometrioid G3	16	9.4	16	5.3	34	7.7		5	4	23	8.2	38	7.5	
Clear Cell	3	1.8	9	3	12	2.7		2	1.6	7	2.5	15	2.9	
UPSC	22	9.4	63	21	71	16		23	18	46	16	87	17	
MMMT	9	5.3	23	7.5	45	10		7	5.6	17	6.1	53	10	
Other	1	0.6	6	2	13	2.9		1	0.8	5	1.8	14	2.8	
Staging,														
I-II	138	81	248	81	345	78	0.6952	106	84	213	76	411	81	0.1921
III	23	14	39	13	60	14		15	12	46	16	61	12	
IV	8	4.7	14	4.6	24	5.4		4	3.2	18	6.4	24	4.7	
Unknown	2	1.2	4	1.3	13	2.9		1	0.8	4	1.4	14	2.8	
Deceased														
Yes	12	7	44	14	67	15	**0.0143**	13	10	33	12	77	15	0.2208
No	159	93	261	86	375	85		113	90	248	88	433	85	

Table 2c. Patient demographics by Social Vulnerability Index theme 3 (race and ethnic minority status) and theme 2 (housing type and transportation) categories

Variable	Theme 3 (Race and Ethnic Minority Status)							Theme 4 (Housing Type and Transportation)						
	Low		Mid		High		*p*-value	Low		Mid		High		*p*-value
	n	%	n	%	n	%		n	%	n	%	n	%	
Age at Diagnosis, years														
<50	39	11	41	8.6	11	11	0.7275	30	9.7	30	10	27	10	0.996
50-59	84	24	102	22	21	22		68	22	63	21	60	23	
60-69	137	40	196	41	38	39		128	41	123	41	106	40	
>=70	86	25	136	29	27	28		85	27	83	28	72	27	
Race														
Black	45	13	197	42	51	53	**<0.0001**	68	22	95	32	130	49	**<0.0001**
Non-Black	301	87	278	59	46	47		243	78	204	68	135	51	
BMI														
Obese Class 3 (>=40 kg/m^2)	91	26	142	30	27	28	0.5071	76	24	81	27	91	34	**0.0121**
Obese Class 2 (35-40 kg/m^2)	71	21	87	18	18	19		50	16	63	21	44	17	
Obese Class 1 (30-35 kg/m^2)	68	20	104	22	27	28		71	23	55	18	61	23	
Overweight (25-30 kg/m^2)	73	21	96	20	19	20		84	27	63	21	41	16	
Normal (18.5-25 kg/m^2)	43	12	46	9.7	6	6.2		30	9.7	37	12	28	11	
Histology														
Endometrioid G1-2	248	72	264	56	63	65	**0.0003**	201	65	182	61	167	63	0.4723
Endometrioid G3	21	6.1	42	8.8	3	3.1		23	7.4	25	8.4	17	6.4	
Clear Cell	5	1.5	14	3	5	5.2		8	2.6	5	1.7	9	3.4	
UPSC	50	15	91	19	15	16		50	16	53	18	43	16	

MMMT	16	4.6	51	11	10	10		27	8.7	27	9	20	7.6	
Other	6	1.7	13	2.7	1	1		2	0.6	7	2.3	9	3.4	
Staging,														
I-II	278	80	379	80	74	76	0.4846	255	82	243	81	208	79	0.9079
III	45	13	59	12	18	19		38	12	37	12	37	14	
IV	17	4.9	27	5.7	2	2.1		14	4.5	13	4.4	13	4.9	
Unknown	6	1.7	10	2.1	3	3.1		4	1.3	6	2	7	2.6	
Deceased														
Yes	44	13	64	14	15	16	0.7846	39	13	40	13	33	13	0.9342
No	302	87	411	87	82	85		272	88	259	87	232	88	

Table 3. Unadjusted hazard ratio and adjusted hazard ratio for endometrial cancer patients based on Social Vulnerability Index with the stratification of race.

Variable	**Univariate analysis**				**Multivariate analysis**				**Black**				**Non-Black**			
	HR	**Low CI**	**High CI**	***p*-value**	**HR***	**Low CI**	**High CI**	***p*-value**	**HR****	**Low CI**	**High CI**	***p*-value**	**HR****	**Low CI**	**High CI**	***p*-value**
SVI High	1.8	1.1	3	**0.0289***	1.6	0.92	2.8	0.099	0.9	0.3	2.6	0.79	1.94	1.02	3.69	**0.0427***
SVI Moderate	1.5	0.9	2.6	0.127	1.6	0.93	2.8	0.087	1.1	0.3	3.9	0.839	1.59	0.84	3.02	0.157
SVI Low	Ref				Ref				Ref				Ref			
T1 High	2.4	1.3	4.5	**0.0049***	2.4	1.24	4.5	**0.0089***	1	0.3	3.3	0.955	2.9	1.35	6.2	**0.0062***
T1 Moderate	2.3	1.2	4.4	**0.0108***	2.4	1.27	4.7	**0.0073***	1.1	0.3	4	0.935	2.74	1.28	5.88	**0.0097***
T1 Low	Ref				Ref				Ref				Ref			

T2 High	1.5	0.9	2.8	0.155	1.4	0.73	2.5	0.331	0.3	0.1	0.8	**0.0147***	2.26	1.03	4.98	**0.0429***
T2 Moderate	1.2	0.6	2.2	0.651	1.1	0.58	2.2	0.717	0.4	0.1	1.2	0.087	1.54	0.64	3.69	0.334
T2 Low	Ref				Ref				Ref				Ref			
T3 High	1.3	0.7	2.4	0.332	1.2	0.66	2.3	0.503	1.3	0.5	3.6	0.615	1.57	0.6	4.15	0.361
T3 Moderate	1.2	0.8	1.7	0.469	0.8	0.5	1.2	0.256	1.2	0.5	2.7	0.749	0.69	0.42	1.14	0.151
T3 Low	Ref				Ref				Ref				Ref			
T4 High	1	0.6	1.6	0.99	0.9	0.54	1.5	0.645	0.5	0.3	1.2	0.122	1.43	0.74	2.76	0.289
T4 Moderate	1.1	0.7	1.8	0.607	1	0.65	1.6	0.922	1	0.5	2	0.922	1.03	0.57	1.86	0.92
T4 Ref	Ref				Ref				Ref				Ref			

Social Vulnerability Level

Tables 2a, 2b, and 2c show the bivariate analysis of age at diagnosis, race, BMI, histology, staging, and deceased status based for low, moderate, and high social vulnerability. As shown in Table 2a, there was a higher proportion of Black patients in the high overall SVI category (49%) than in the moderate SVI (22%) and low SVI (13%) categories. This difference was observed for every theme shown in Tables 2b and 2c. Obese class 3 patients were more common in the high SVI group (35%) compared to the moderate and low groups (25% and 21%, respectively). This pattern was seen for Themes 1, 2, and 4, but not in Theme 3 (Tables 2b and 2c). The high overall SVI group had a lower percentage of endometrioid grade I-II (G1-2) histology, although this difference was not consistent across SVI themes. There was no significant difference in age at diagnosis, stage, or deceased status according to overall SVI score or individual themes.

Overall Survival

Table 3 presents the association between overall survival and SVI level (low, medium, or high tertile). In the univariate analysis, high overall SVI level (HR=1.79, 95% CI 1.09-2.99) as well as high and moderate Theme 1 scores (HR=2.42, 95% CI 1.31-4.49; HR 2.30, 95%CI 1.21-4.36, respectively) are highly associated with lesser survival. The other themes demonstrated positive associations that were not statistically significant.

Following adjustment for age at diagnosis, BMI, histopathology, race, and staging, both high and moderate socioeconomic status (HR 2.35, 95% CI 1.24-4.47, and HR 2.44, 95% CI 1.27 – 4.69, respectively) remained significantly associated with overall survival

of EC patients. In Table 3, multivariable analysis adjusting for age at diagnosis, BMI, histopathology, and staging, with stratification by race is shown. Among Black patients SVI was not significantly associated with survival, with the exception of high Theme 2 on household composition and disability (HR 0.28, 95% CI 0.10-0.78). However, Theme 2 was not statistically significant before stratification (1.36, 95% CI 0.73-2.54). Conversely, among non-Black EC patients, high overall SVI (HR 1.94, 95% CI 1.02-3.69), high and moderate Theme 1 (HR 2.9, 95% CI 1.35-6.2; HR 2.74, 95% CI 1.28-5.88, respectively) as well as high Theme 2 (HR 2.26, 95% CI 1.03-4.98) were consistently and significantly associated with worse survival (Figure 3).

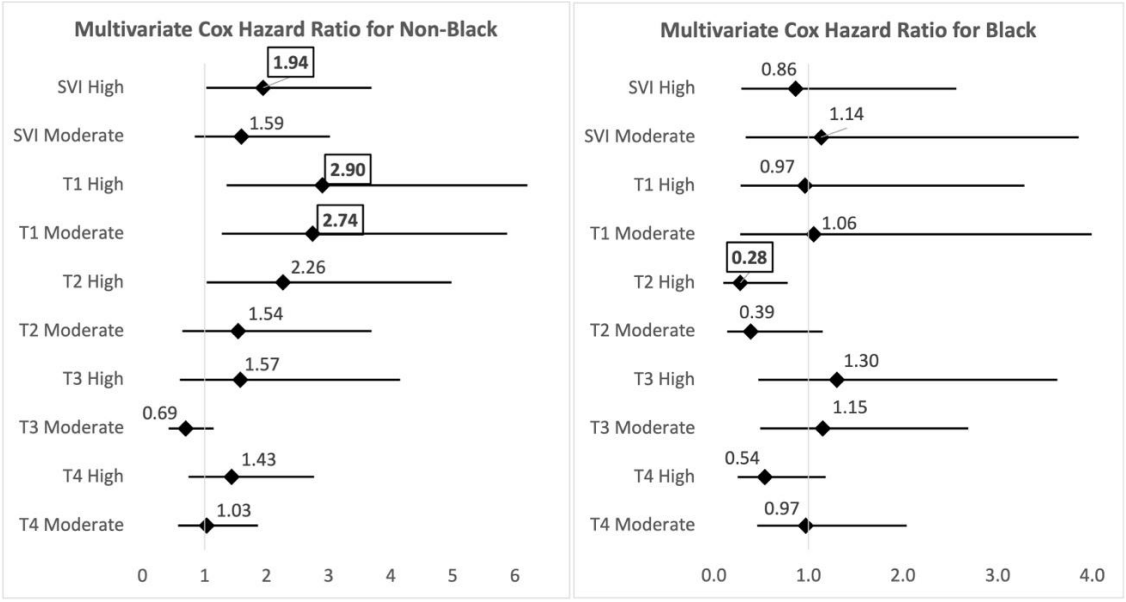

Figure 3. Adjusted hazard ratio for endometrial cancer patients based on Social Vulnerability Index with the stratification of race. Figures divided into non-Black (left) and Black (right) while adjusting for age at diagnosis, BMI, histopathology, and staging. T1: theme 1(socioeconomic status); T2: theme 2 (household composition); T3: theme 3 (race and ethnic minority status); T4: theme 4 (housing type and transportation)

DISCUSSION

Principal Findings

Our findings suggest that EC patients residing in geographic areas with census-tract level high general social vulnerability, as well as high and moderate levels of socioeconomic status vulnerability, had a higher risk of death over 5 years (Table 3). Although some studies found no association between socioeconomic deprivation and survival in endometrial cancer[21,22], we found 1.3-1.4 times increased risk of death for patients with highly vulnerable socioeconomic status compared to those with lower vulnerability. Studies from Germany and England found that lower SES is associated with cancer-specific mortality among endometrial cancer patients[23,24]. A previous study found a strong association and incremental impact of social vulnerability for mortality related to cancer[16]

We found survival disparities according to SVI level and for all four themes comparing Black with non-Black EC patients. Black patients generally resided in areas with higher social vulnerability. Racial and ethnic disparities have been observed in adherence to endometrial cancer treatment with Black race and low neighborhood SES associated with 12% and 27% less adherence compared to White patients and higher neighborhood SES[25]. Moreover, high social vulnerability along with low socioeconomic status were observed among Black patients compared to other races[16]. We hypothesize that disparities of SVI level distribution caused the skewed distribution of SVI between Black

and non-Black patients, with Black patients having a greater tendency to be in moderate and high vulnerability (p<0.0001) areas. Non-Black patients in high and moderate socioeconomic vulnerability groups are 1.7-1.9 times more likely to die from endometrial cancer, but this risk was not found among Black patients with the same vulnerability level. Although our stratified results did not demonstrate significance for Black patients, previous studies of disparities in EC survival showed Black patients tend to have worse survival than other races[1,2,8,9]. Therefore, regardless of SVI level, disparities exist among Black individuals.

Clinical and Research Implications

Our study has several implications moving forward as researchers strive to identify the optimal metric to relate social vulnerability factors to social determinants of health. We categorized patients into tertiles within general SVI level and for Themes 1 to 4, then stratified their risk of death from endometrial cancer. This approach provides a practical and concise risk stratification that enables clinicians to determine which patients have high risk of death from EC based on their area of residence. By knowing the Theme 1 (socioeconomic status) category to which the patient belongs, clinicians could become attuned to higher risk of death among non-Black EC patients. Considering the widely and publicly accessible data from CDC, calculation of SVI is widely applicable in the United States.

As SDOH consists of a wide range of components, identifying which component has the greatest significance had been challenging. By knowing which theme and

component is most closely related to survival, targeted efforts addressing specific SVI components could be explored in an effort to decrease vulnerability and enhance survival. Further directions of study could analyze SVI components in detail by breaking down each determinant of the themes. Implications of the SVI determining survival for other cancers could differ. Extrapolation of our results for survival from other gynecologic cancers could be strongly supported by different approaches and perspectives of other cancer types.

Strengths and Limitations

This is an early study that addresses use of SVI to quantify Social Determinants of Health (SDOH) in order to understand survival disparities among EC patients. Previous studies have linked SDOH with EC without quantifying the SDOH[4]. We were able to study a high percentage of Black patients, compared to other disparity studies, and at a higher percentage than the national average[25-27]. Our study includes only patients seen at our Comprehensive Cancer Center in the Deep South. The demographics of our subjects include a much higher percentage of Black subjects than in previous studies addressing racial disparities in Black[25,26]. Our source population spanned 436 census tracts, a geographically wide and diverse area, thereby increasing generalizability of our results. The ratio of census tracts per sample is much higher than in similar studies with a larger number of samples[15]. Our clinical data enabled incorporation and association of demographic factors with survival, as well as identifying themes most closely related to survival. This analysis adds value to the growing literature of SVI utility beyond its original goal, assessment of emergency preparedness. Since the SVI is publicly available

through the CDC website, it can be applied to a large, diverse populations across the United States.

This study has several limitations. First, our study analyzed overall survival of endometrial cancer patients but included no other clinical endpoints, such as progression-free survival, time to progression, disease free survival, or other measures[28]. Associations with other clinical endpoints could be important to include in further studies. Second, our study is a single-center study which could limit generalizability of our results. Previous studies used national databases when mapping the SVI[16,19]. Third, the definitive criteria to categorize SVI as high versus medium or low, is not well-established, therefore, our data could be presented or interpreted differently by other investigators. We classified SVI into tertiles)[29], whereas other investigators may use more groups (quartiles, quintiles)[16,19] or continuous[15] variables. Fourth, inclusion of other races such as Latina, Asian, Native Hawaiian or Pacific Islander, as well as American Indian or Alaska Native was not possible in our study, with insufficient numbers of these groups in Alabama.

CONCLUSION

The Social Vulnerability Index (SVI) enables us to quantify the impact of social determinants of health (SDOH) to explain endometrial cancer survival disparities. Women residing in areas of social vulnerability have worse EC survival. Theme 1 (socioeconomic status vulnerability) was most closely associated with poor survival. However, it is noteworthy that disparities in EC survival among Black patients exist regardless of SVI level. Further investigation of racial differences in social vulnerability components is warranted to better understand the dynamics of race and SES, in an effort to address health disparities in endometrial cancer survival.

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