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The influence of neighborhood socioeconomic status and ethnic enclave on endometrial cancer mortality among Hispanics and Asian Americans/Pacific Islanders in California

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Abstract

Purpose—We investigated the role of neighborhood socioeconomic status (nSES) and residence in ethnic enclaves on mortality following endometrial cancer (EC) diagnosis among Hispanics and Asian Americans/Pacific Islanders (AAPI).

Methods—Using California Cancer Registry data, enhanced with census block group information on ethnic enclave and nSES, we examined 9,367 Hispanics and 5,878 AAPIs diagnosed with EC from 1988 to 2011. Cox proportional hazard models were used to estimate associations between all-cause and EC-specific mortality with nSES and ethnic enclaves, adjusting for subject sociodemographic and tumor characteristics.

Results—Hispanics in the lowest SES neighborhoods had a 39% and 36% increased risk of all-cause and EC-specific mortality, respectively, compared to Hispanics in the highest SES neighborhoods. AAPIs in the lowest SES neighborhoods had a 37% increased risk of all-cause mortality compared to AAPIs in the highest SES neighborhoods. Living in an ethnic enclave was associated with lower all-cause mortality risk for AAPIs.

Conclusions—Mortality risk varied by nSES and ethnic enclave among Hispanics and AAPIs. Women living in lower SES communities experienced significantly higher risk, highlighting the need to identify the specific neighborhood factors underlying these associations so that community-based interventions may be properly targeted.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Keywords

Endometrial neoplasms; Hispanic Americans; Asian Americans; California; Registries; Proportional hazards models; Mortality; Residence Characteristics; Social class

Introduction

Endometrial cancer (EC) is the most commonly diagnosed gynecologic cancer among women in the United States (U.S.) and EC mortality rates have increased in the past two decades in all racial/ethnic groups, including Hispanics and Asian Americans/Pacific Islanders (AAPI) [1, 2].

Little is known about modifiable factors that impact cancer survival among AAPI and Hispanic populations and these two groups have not been comprehensively studied at the population-level in regard to endometrial cancer mortality.

There is growing recognition of the importance of neighborhood contextual factors in cancer outcomes [3] with studies demonstrating significant associations with neighborhood social environments across the cancer continuum [4]. Neighborhood SES (nSES) and ethnic enclave have been documented as particularly relevant factors in cancer survival [4–11]. Despite the potential for these data to inform community-based interventions, to our knowledge, neighborhood factors have not been systematically evaluated as factors influencing EC survival. Neighborhood factors may operate through pathways such as social stress, social support, and access to health care and other resources [4]. nSES and ethnic composition have been shown to be significantly associated with survival for other types of cancers and these associations seem to be race/ethnicity-dependent [11]. There is translational potential in learning whether neighborhood characteristics are associated with EC survival as interventions can be designed to improve survival for not only the rapidly growing AAPI and Hispanic population, but for all patients with EC. For example, we may find that residing in ethnic enclaves confers survival benefit and further studies focusing on these neighborhoods might show that this is due to greater co-ethnic and in-language social support. These elements could then be incorporated into survivorship programs.

California is home to the largest populations of Hispanics and AAPIs in the U.S., with approximately 15 million Hispanics and over 5 million AAPIs [12, 13]. Together with the availability of high-quality population-based statewide cancer registry data and small area-level neighborhood data, California represents the ideal setting to evaluate the impact of neighborhood factors on survival following EC diagnosis. Therefore, we systematically investigated the relationships between nSES and ethnic enclaves on mortality among Hispanic and AAPI women diagnosed with EC in California. We hypothesized that nSES and ethnic enclaves impact EC mortality independent of demographic and clinical factors among these populations.

Materials and methods

Study population

Data were obtained on all Hispanic and AAPI women diagnosed with primary invasive EC in California from 1 January 1988 through 31 December 2011. We used site codes C541 and C549 based on the *International Classification of Diseases for Oncology*, third edition [14].

We obtained information on age at diagnosis, stage at diagnosis (localized, regional, distant, or unknown), tumor grade (well, moderate, poor/undifferentiated, or other), histological subtype (endometrioid, adenocarcinoma not otherwise specified [NOS], serous, adenocarcinoma with squamous differentiated, mixed cell, clear cell, mucinous adenocarcinoma, or other), treatment modalities within the first 12 months after diagnosis (surgery, adjuvant chemotherapy and/or radiotherapy), calendar period of diagnosis (1988–1992, 1993–1997, 1998–2002, 2003–2006, 2007–2011), marital status (married, not married, unknown), and whether the patient was diagnosed and/or treated at a National Cancer Institute (NCI)-designated cancer center (yes/no).

Data on nSES and ethnic enclave were obtained by linkage to data from the California Neighborhoods Data System at the level of the census block group as previously described [15]. In brief, we determined nSES by cases' residential census block group using an index derived from principal components analyses of indicator variables of SES that included education, unemployment, income, housing, poverty, and occupation using 1990, 2000, and 2010 U.S. Census, and 2007–2011 American Community Survey data [16]. Indices characterizing Hispanic and AAPI ethnic enclaves were created by principal components analysis of selected measures from the U.S. Census in 1990 and 2000 [15]. The Hispanic enclave index included percent of the population that was foreign born, percent recent immigrants, percent of all households that were linguistically isolated, percent of Spanish-speaking households that were linguistically isolated, percent of the total population with limited English proficiency, percent of Spanish-speaking population with limited English proficiency, and percent of the population that was Hispanic. The AAPI enclave index included percent of the population that were recent immigrants, percent of AAPI language-speaking households that were linguistically isolated, percent of API language speakers with limited English proficiency, and percent of the population that was AAPI. Linguistically isolated households were defined as having no person over age 14 years who spoke English only or who spoke English “very well.” Limited English proficiency was defined as speaking English “not well” or “not at all.” Each California block group was assigned nSES and ethnic enclave scores that were categorized into quintiles based on the statewide distribution. Each EC case was assigned the nSES and ethnic enclave of her neighborhood census block group of residence at the time of diagnosis. For EC cases diagnosed from 1988 to 2005, nSES was based on 1990 and 2000 Census data [16], while for cases diagnosed from 2006 to 2011, nSES was based on 2007–2011 American Community Survey data [17]. For EC cases diagnosed from 1988 to 1995, ethnic enclave was based on the 1990 Census, whereas for EC cases diagnosed from 1996 to 2011, ethnic enclave was based on the 2000 Census.

Vital status and cause of death information were obtained up to 31 December 2014. After excluding 64 cases diagnosed by death certificate only or autopsy, or with inconsistent dates of diagnosis and/or follow-up, 15,245 women with invasive EC were included in this study. This project was a part of the Greater Bay Area Cancer Registry protocol, which was approved by the Institutional Review Board of the Cancer Prevention Institute of California.

Statistical analysis

We examined the proportion of distant cases (stage III/IV at diagnosis) in the lowest SES neighborhoods compared to the highest SES neighborhoods for each racial/ethnic group. We used Cox proportional hazards models to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) of the associations between contextual neighborhood factors with all-cause and EC-specific mortality. Analyses were conducted separately for Hispanics and AAPIs. For deceased cases, survival time was measured in days from the date of diagnosis to the date of death from any cause for all-cause mortality analyses or to the date of death from EC for EC-specific mortality analyses. Cases who died from other causes were censored at the time of death for analyses of cancer-specific death. Cases alive at the study end date (31 December 2014) were censored at this time or at the date of last follow-up (i.e., last known vital status).

Multivariable Cox regression models included variables significant at $p < 0.05$ in the unadjusted models: tumor grade and histological subtype, treatment (surgery and adjuvant chemotherapy), calendar period of diagnosis, age at diagnosis, marital status, NCI-designated cancer center, ethnic enclave, and nSES. Even though adjuvant radiotherapy was not significant in univariate models, it was included in the models because it has been previously associated with survival [18]. We verified the proportional hazards assumption by testing the correlation between weighted Schoenfeld residuals and logarithmically transformed survival time. Given that proportional hazards varied by stage at diagnosis, stage was included as a stratifying variable in all Cox regression models. We also investigated potential interactions between ethnic enclave and nSES on mortality risk. To address clustering of neighborhood measures, all models were adjusted for census block group using a robust sandwich estimate for the covariance matrix with summed score residuals for block group [19]. Statistical analyses were carried out using SAS 9.4 (SAS Institute, Cary, North Carolina). All p-values reported were two-sided.

Results

Study characteristics of the 15,245 EC cases (Hispanics = 9,367 and AAPIs = 5,878) are shown in Table 1. The mean age of diagnosis was 59.8 years for Hispanics and 58.6 years for AAPIs. The majority of Hispanic and AAPI women were diagnosed with localized disease (69%). Endometrioid endometrial carcinoma was the most common histologic subtype (49 and 53% for Hispanics and AAPIs, respectively), followed by adenocarcinoma NOS (28 and 27% for Hispanics and AAPIs, respectively). The percentage of cases who did not receive surgery as the first course of therapy was slightly higher for Hispanics compared to AAPIs (8 vs. 6%) and the use of adjuvant therapy (chemotherapy and/or radiotherapy) was comparable between the two racial/ethnic groups. The majority of Hispanics resided

predominantly in low SES neighborhoods (Q1–Q3: 75%). In contrast, roughly half of AAPIs resided in high SES neighborhoods (Q4–Q5: 52%). A large proportion of cases in both groups lived in the highest ethnic enclave areas (37% for Hispanics and 52% for AAPIs).

Among Hispanic women, 9.0% of cases in the lowest nSES group had distant disease compared to 5.9% in the highest nSES group. Among AAPI women, the difference across nSES was smaller, with 7.5% of cases in the lowest nSES having distant disease compared to 6.5% in the highest nSES group. For ethnic enclave, differences in stage distribution were somewhat more pronounced among Hispanics than AAPIs: 9.0% of Hispanics in the high enclave group had distant disease versus 6.3% in the low enclave group, whereas 6.9% of AAPIs in the high enclave group had distant disease as compared to 6.7% in the low enclave group.

For Hispanic women with EC, those living in the lowest SES neighborhoods had 39 and 36% increased risks of all-cause and EC-specific mortality risk, respectively, compared to those living in the highest SES neighborhoods (Q1 vs. Q5: HR 1.39, 95% CI 1.19, 1.62 and HR 1.36, 95% CI 1.04, 1.78, respectively) (Table 2). For AAPIs women with EC, living in the lowest SES neighborhoods had 37% higher all-cause mortality risk than those living in the highest SES neighborhoods (Q1 vs. Q5: HR 1.37, 95% CI 1.14, 1.64, Table 2). There was a somewhat elevated risk of EC-specific mortality among AAPI women living in the lowest versus highest SES neighborhoods, but the estimate did not reach statistical significance (HR 1.22, 95% CI 0.93, 1.60).

For AAPIs, living in the highest ethnic enclave areas was associated with modestly lower all-cause mortality risk (HR 0.88, 95% CI 0.77, 1.00) and EC-specific mortality risk (HR 0.88, 95% CI 0.72, 1.07) (Table 2). For Hispanics, ethnic enclave was not significantly associated with either all-cause or EC-specific mortality risk, although the HR for EC-specific mortality for the fourth quintile was reduced (HR 0.87, 95% CI 0.72, 1.04). When we examined ethnic enclave and nSES combined, the HRs for all-cause mortality for Hispanics living in low nSES areas were elevated regardless of living in either high (HRs 1.26, 95% CI 1.15, 1.39) or low (1.19, 95% CI 1.06, 1.34) ethnic enclaves. However, the increased EC-specific mortality risk for Hispanics living in low SES neighborhoods was no longer statistically significant when combined with the enclave measure (Table 2). The all-cause mortality risk for AAPIs living in low nSES and low enclave areas was higher than in the low nSES and high enclave areas (HR 1.25, 95% CI 1.01, 1.56 vs. HR 1.08, 95% CI 0.91, 1.28). When these variables were combined, we no longer observed lower all-cause mortality risk for AAPIs living in ethnic enclaves (Table 2).

We observed that 5.7% of Hispanic and 4.7% of AAPI cases were lost to follow-up, meaning they had a date of last follow-up of 2 or more years. To address the potential influence of loss to follow-up on our results, we conducted a subgroup analysis excluding cases that were lost to follow-up and found similar results (data not shown). We conducted a second similar analysis, assuming all advanced stage cases that were lost to follow-up died of EC, and the results were also essentially unchanged (data not shown).

Discussion

Living in a low SES neighborhood was associated with increased risk of both EC and all-cause mortality among Hispanics, and all-cause mortality among AAPIs with EC. Our finding of higher risk of death among women with EC residing in the lowest vs. highest SES neighborhoods is consistent with previous studies of other cancer sites in California that have found neighborhood SES to impact cancer mortality [5, 6, 20, 21]. However, to our knowledge, no study has demonstrated this association for EC among these two rapidly growing racial/ethnic groups. Socioeconomic differences in cancer survival may be partially explained by differences in access to timely and high-quality treatment. A previous U.S. study showed that lower income (used as a proxy for lower SES) among non-Hispanic (NH) White and NH Black women with EC was independently associated with more advanced disease, fewer hysterectomies as first treatment, and lower survival, while accounting for other sociodemographic and clinical characteristics [22]. The impact of SES on mortality is thought to be multifactorial, influencing cancer development, progression, and outcomes. It has been proposed that improving access to high-quality care is critical in enabling early diagnosis and optimal treatment for vulnerable women with EC [22].

Living in an ethnic enclave was associated with lower overall mortality risk among AAPI EC cases, but not among Hispanics. We also observed increased all-cause mortality for AAPIs living in neighborhoods that were both low ethnic enclave and low nSES areas. We are not aware of any prior study that has examined the relationship between living in an ethnic enclave and EC mortality, although some studies have reported that residence in these neighborhoods was associated with survival differences for other types of cancers, especially among Hispanics [4, 11].

The literature to date on cancer outcomes and the social environment generally finds that patients living in low SES neighborhoods have lower cancer survival; however, the findings for ethnic enclaves are much more variable [4, 11]. The impact of neighborhood characteristics on survival may vary greatly by cancer site and race/ethnicity [11]. For instance, Patel et al. [9] observed a small survival advantage among foreign-born Hispanic cases with non-small cell lung cancer living in lower SES and higher enclave neighborhoods relative to those living in lower SES and lower enclave neighborhoods in California. However, Keegan et al. [8] did not observe differences in survival when they analyzed the joint effect of neighborhood SES and enclave among Hispanic women with breast cancer in the same state. A recent study from Texas found that living in high-density Hispanic neighborhoods was generally associated with increased breast cancer mortality [7]. It is possible that for some cancers the protective role of residence in ethnic enclaves, operating through the mechanisms such as social cohesion and support, may be outweighed by the detrimental effects of other factors related to lower SES such as lack of access to high-quality care.

This study had several limitations. For Hispanics, we do not have information on detailed ethnic subgroups. For the AAPIs, the number of cases in specific ethnic groups was too small to allow for analysis of detailed ethnic origin. We did not have information on nativity (foreign-born or U.S.-born). We also lacked data on individual-level SES. However, studies

have demonstrated that both individual-level and census-based measures of SES are related to health outcomes in similar ways [23]. Census-based measures of SES may uncover risk factors and inequalities in outcome not revealed by individual-level SES [24]. Health insurance status, which may be used as an indicator for individual-level SES, was not consistently collected until about the year 2000, and therefore could not be used in our study. We lacked some clinical information that is not routinely collected by cancer registries, such as body mass index, comorbidities, relapse, and detailed treatment modalities. In addition, the percentage of Hispanic and AAPI women with EC, who migrated out of California, was unknown. Some cases may go back to their countries of origin to seek more affordable treatment or support from relatives. Nevertheless, our study showed that the proportion of women lost to follow-up was small and did not influence our results. Furthermore, studies have shown that the proportion of cases who emigrate is usually small and do not impact mortality substantially [25]. Lastly, ethnic enclave variables were not available at the block group for EC cases diagnosed close to the 2010 period; thus, the 2000 Census data were used. We expect any misclassification in ethnic enclave assessment to be non-differential and would underestimate the association.

Our study had several strengths. Reporting of malignant neoplasms is mandatory in California; therefore, we captured information on virtually all patients with EC during the study period. Case information was obtained from a statewide population-based cancer registry with a very large number of Hispanic and AAPI cases during a long period of observation, which allowed us to examine mortality risk in these diverse populations. Our neighborhood SES measure encompassed many factors including income, education, unemployment, poverty, and housing. To our knowledge, this is the first study to evaluate the separate and combined effects of neighborhood SES and ethnic enclave on the mortality risk of Hispanic and AAPI women with EC in the U.S.

This large population-based study identified important variations in mortality risk across neighborhoods characterized by nSES and ethnic enclave among Hispanic and AAPI women with EC. These findings emphasize the need to better understand the factors driving these contextual socioeconomic disparities within these two racial/ethnic groups. Identifying the specific underlying mechanisms can help to inform interventions for reducing the burden of EC.

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Table 1
 Sociodemographic and clinical characteristics of Hispanic and Asian American/Pacific Islander women diagnosed with endometrial cancer in California, 1988–2011

Characteristics	Hispanic		AAPI	
	n	%	n	%
Total	9,367	100.0	5,878	100.0
Age at diagnosis (years)				
Mean	59.8		58.6	
Year of diagnosis				
1988–1992	1,171	12.5	584	9.9
1993–1997	1,386	14.8	793	13.5
1998–2002	1,760	18.8	1,173	20.0
2003–2006	1,896	20.2	1,215	20.7
2007–2011	3,154	33.7	2,113	35.9
Stage at diagnosis				
I—localized	6,423	68.6	4,027	68.5
II—regional	1,807	19.3	1,208	20.6
III/IV—distant	689	7.4	394	6.7
Unknown	448	4.8	249	4.2
Grade				
Well	3,744	40.0	2,365	40.2
Moderate	2,863	30.6	1,788	30.4
Poor/undifferentiated	1,917	20.5	1,292	22.0
Other	843	9.0	433	7.4
Histologic subtype				
Endometrioid	4,626	49.4	3,112	52.9
Adenocarcinoma, not otherwise specified	2,654	28.3	1,578	26.8
Serous	456	4.9	284	4.8
Adenocarcinoma with squamous differentiation	479	5.1	221	3.8
Mixed cell	337	3.6	221	3.8
Clear cell	147	1.6	97	1.7

Characteristics	Hispanic		AAPI	
	n	%	n	%
Mucinous adenocarcinoma	100	1.1	94	1.6
Other	568	6.1	271	4.6
Surgery treatment				
No	749	8.0	360	6.1
Yes	8,616	92.0	5,516	93.8
Radiation treatment				
No	7,130	76.1	4,465	76.0
Yes	2,235	23.9	1,410	24.0
Chemotherapy treatment				
No	8,282	88.4	5,146	87.5
Yes	1,006	10.7	710	12.1
Marital status				
Married	4,825	51.5	3,687	62.7
Not married	4,210	44.9	1,997	34.0
Seen at NCI-designated cancer center				
Yes	1,230	13.1	704	12.0
No	8,137	86.9	5,174	88.0
Neighborhood SES				
Q1 Lowest	2,912	31.1	626	10.7
Q2	2,298	24.5	995	16.9
Q3	1,843	19.7	1,210	20.5
Q4	1,362	14.5	1,502	25.6
Q5 highest	952	10.2	1,545	26.3
Ethnic enclave				
Lowest (Q1-3)	3,287	35.1	1,369	23.3
Q4	2,370	25.3	1,318	22.4
Highest (Q5)	3,507	37.4	3,077	52.4

Q quintile, SES socioeconomic status, AAPI Asian American/Pacific Islander, NCI National Cancer Institute. Unknown levels of the variable are excluded from the table, so number of cases may not add up to total cases

Table 2

Associations between neighborhood SES and residence in an ethnic enclave residence with mortality among Hispanic and Asian American/Pacific Islander women with endometrial cancer in California, 1988–2011

	All-cause mortality			Endometrial cancer mortality		
	Hispanic (<i>n</i> = 9,367)		AAPI (<i>n</i> = 5,878)	Hispanic (<i>n</i> = 9,367)		AAPI (<i>n</i> = 5,878)
	Deaths	HR ^a (95% CI)	Deaths	HR ^a (95% CI)	Deaths	HR ^a (95% CI)
Neighborhood SES						
Q5: highest	298	1.00	352	1.00	97	1.00
Q4	454	1.10 (0.95, 1.28)	361	1.21 (1.04, 1.40)	159	1.13 (0.86, 1.47)
Q3	604	1.12 (0.96, 1.29)	323	1.23 (1.05, 1.44)	221	1.20 (0.92, 1.56)
Q2	796	1.27 (1.09, 1.47)	276	1.22 (1.04, 1.44)	286	1.31 (1.00, 1.71)
Q1: Lowest	1,071	1.39 (1.19, 1.62)	206	1.37 (1.14, 1.64)	393	1.36 (1.04, 1.78)
Ethnic enclave						
Lowest (Q 1–3)	1,044	1.00	376	1.00	381	1.00
Q 4	805	1.01 (0.91, 1.13)	343	1.03 (0.88, 1.19)	271	0.87 (0.72, 1.04)
Highest (Q 5)	1,302	1.01 (0.90, 1.12)	770	0.88 (0.77, 1.00)	479	0.94 (0.79, 1.13)
Combined neighborhood SES and enclave						
High SES, low enclave	569	1.00	195	1.00	204	1.00
High SES, high enclave	156	1.09 (0.90, 1.30)	508	0.97 (0.82, 1.15)	43	0.86 (0.60, 1.23)
Low SES, low enclave	475	1.19 (1.06, 1.34)	181	1.25 (1.01, 1.56)	177	1.19 (0.97, 1.46)
Low SES, high enclave	1,951	1.26 (1.15, 1.39)	605	1.08 (0.91, 1.28)	707	1.14 (0.96, 1.34)

Bold value denotes confidence intervals that exclude one

Q quintiles, HR hazard ratios, CI confidence intervals, AAPI Asian American/Pacific Islander, SES socioeconomic status

^aMultivariate models adjusted for age (continuously) and grade, histologic subtype, surgery treatment, radiation treatment, chemotherapy treatment, year of diagnosis, marital status, and NCI hospital (all categorically); stratified by stage at diagnosis and adjusted for clustering level by block group