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Cervical Cancer Survival by Socioeconomic Status, Race/Ethnicity, and Place of Residence in Texas, 1995–2001

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ABSTRACT

Objective: The current study explored whether socioeconomic status (SES), race/ethnicity, and rural residence may be linked to poorer cervical cancer survival by stage at diagnosis.

Methods: Data from 7,237 cervical cancer cases reported to the Texas Cancer Registry from 1995–2001 were used to address the association by stage at diagnosis and cause of death. Zip code-level census data were used to classify residence and to develop a composite variable for SES. Multilevel Cox proportional hazards modeling was used to estimate hazard ratios (HR) and 95% confidence intervals (CI).

Results: Late stage at diagnosis was a strong predictor of cervical cancer mortality (HR = 6.2, 95% CI 5.5-7.2). SES and race/ethnicity were independently associated with stage at diagnosis. Women residing in areas with lower SES had significantly shorter survival times when diagnosed at an early stage (HR = 3.0, 95% CI 2.1-4.3). Hispanic women had a lower probability of dying from cervical cancer during the follow-up period (HR = 0.7, 95% CI 0.6-0.8) after adjusting for confounders. The association between lower SES and poorer survival was consistent across all racial/ethnic groups, suggesting the effect of SES may be more important than race.

Conclusions: SES and race/ethnicity were independently associated with poorer cervical cancer survival in this large Texas sample. Further research is needed to investigate the role of optimal treatment and comorbid conditions in the association between SES and cervical cancer survival.

INTRODUCTION

DESPITE THE PREVENTABLE NATURE of cervical cancer, an estimated 9710 women will be diagnosed and 3700 of these women will die from this malignancy in the United States in 2006.1 Hispanic women have the highest age-adjusted cervical cancer incidence, and African American women have the highest mortality rates compared with non-Hispanic whites.1 Differences in socioeconomic status (SES) by race/ethnicity may explain observed racial differences in cervical cancer incidence and mortality.

SES is best described as a combination of highly correlated yet distinct factors, including income, education, occupation, and place of residence.2

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Data from these factors are commonly used as proxy variables to indicate overall SES. Among studies examining SES indicators and survival,3–11 about one third5–7 found an association between low SES and poorer cervical cancer survival after adjusting for race/ethnicity. In a large cohort study, Singh et al.12 found that cervical cancer mortality increased with increasing poverty and lower education for women in each racial/ethnic group examined. Using data from the Military Healthcare System in which all women had similar access to care, Farley et al.3 found that neither race/ethnicity nor SES were associated with cervical cancer survival. Almost half of all studies addressing race/ethnicity and survival without adjusting for SES9,13–20 concluded that minority race/ethnicity was an important predictor of survival.13,14,16–18 However, failure to adjust for SES may be responsible for the apparent racial gap in survival that was observed.

Fewer studies have addressed rural residence as a proxy measure for access to care and cervical cancer survival.5,21 O’Brien et al.21 found that women living in rural areas in Australia were at higher risk of death than those living in metropolitan areas (standardized mortality ratio 10.1), suggesting lack of access to healthcare services. In contrast, Johnson5 did not find this association among South Carolina women after adjusting for race/ethnicity, age, and poverty (adjusted hazard ratio [HR] = 1.10, 95% confidence interval [CI] 0.81-1.50).

The large population, ethnic diversity, and high proportion of rural areas make Texas an optimal state to study the impact of socioeconomic factors on cervical cancer survival. The purpose of this study is to estimate cervical cancer survival by SES, rural residence, and race/ethnicity while adjusting for confounders using multilevel Cox proportional hazards modeling.

MATERIALS AND METHODS

Data for this population-based cohort study were obtained from the Texas Cancer Registry (TCR), which has a case completeness proportion of 99%.22 Institutional Review Boards from the Texas Department of State Health Services and the University of Texas Health Science Center at Houston reviewed the study protocol and deemed the project exempt. Eligible cases included women ≥18 years reported to the TCR as having an invasive primary cervical cancer diagnosis between January 1, 1995, and June 30, 2001. Women with multiple primary cancers were excluded. Incident cases were linked with the Texas Department of State Health Services mortality data through December 21, 2001, to identify women with an incident cancer who died, along with the date and underlying causes of death. All women in whom cervical cancer was listed as an underlying cause of death were used to estimate cause-specific survival rates. Women who died from other causes were censored.

Exposures: SES, rural residence, and race/ethnicity

Data from the TCR and the U.S. Census 2000 were used to define three primary exposures: SES, rural residence, and race/ethnicity. A composite variable was created for SES using ZIP code-level data for median income, poverty, education, and employment. Poverty was defined as the percent of residents living in the ZIP code of the cervical cancer patient whose incomes were at or below the federal definition of poverty.23 Similarly, low education and unemployment were defined as the percent of women living in the ZIP code of the cervical cancer patient with less than a high school education23 and who were not in the labor force,24 respectively. As all other variables comprising the composite variable are percentages, median income was transformed into a percent for purposes of consistency. Median income was defined as the percent difference between the median household income of residents living in the ZIP code of the cervical cancer patient and the median household income for the state of Texas.23 The four indicator variables were summed to create the final SES composite variable based on an accepted measure of community-level SES.25–27 Analysis of the individual components of the composite variable showed satisfactory internal consistency (Cronbach’s alpha = 0.71). Given that the percent difference ranged from negative to positive values (corresponding to median incomes lesser and greater than the median income for Texas), the final composite variable was brought to a positive distribution by adding the absolute value of the largest negative value to the entire distribution. SES was then categorized into quartiles based on the distribution of the data.
Rural residence was hypothesized to be a proxy measure for access to healthcare, including proximity to urban areas where cancer screening and treatment services are more readily available. Rural residence was also defined using ZIP code-level data from the U.S. Census 2000, which indicates the proportion of the ZIP code denoted as rural. This variable was categorized into five groups based on distribution of the Texas population: urban (0% rural, referent group), midurban (<11.66% rural), rural (11.67%–23.32% rural), midrural (23.33%–69.99% rural) and very rural (>70% rural).

Race/ethnicity was defined by individual data from two variables (race and Spanish/Hispanic origin) abstracted from medical records by TCR staff. This enabled us to classify those with a Spanish/Hispanic origin who may report different racial groups. Race/ethnicity was categorized as white non-Hispanic (referent group), African American, Hispanic, and other race/ethnicity groups (Asian, other, and unknown). Of those classified as Hispanic, 32.3% were Mexican, 57.2% were Spanish, Hispanic, or Latina, 7.2% had a Spanish surname, 2.6% were other Hispanic, 0.4% were Central or South American, 0.2% were Puerto Rican, and 0.1% were Cuban. No African American women reported a Spanish/Hispanic origin.

Outcome: Cervical cancer survival

The primary outcome was months of survival following cervical cancer diagnosis. Subjects were censored at the end of the follow-up on December 31, 2001. Data characterizing stage at diagnoses were obtained from the TCR and reported using the Surveillance, Epidemiology and End Results (SEER) summary staging guide. Stage at diagnosis was classified into two categories: early and late stage. Early stage is classified as localized only and corresponds to International Federation of Gynecology and Obstetrics (FIGO) staging by including stages I, IA1, IA2, and IB. Late stage is classified as regional or invasive carcinoma and likewise corresponds to FIGO stages IIA, IIB, IIA, III, and IV. Stage of diagnosis was evaluated as an effect measure modifier because the impact of poverty, rural residence or race/ethnicity on survival may differ by stage.

Statistical methods

All data were analyzed using the statistical software package Intercooled Stata version 8.0. As stage at diagnosis is a strong predictor of survival, we used multivariate logistic regression to determine if the socioeconomic composite variable, rural residence, and race/ethnicity were associated with late stage at diagnosis. All women who were missing on stage at diagnosis (n = 1241) were excluded from analyses because of the strong impact of stage on survival. Potential confounders included age, year of diagnosis, and cancer cell type.

Multilevel Cox proportional hazards modeling was used to estimate the relative risk of dying from cervical cancer associated with SES, rural residence, and race/ethnicity. The Breslow-Day test for homogeneity, as a measure of effect modification of stage on SES and survival, was significant (chi-square = 7.37, p = 0.001); therefore, all analyses were conducted by stage (early stage I–IB, late stage IIA–IV). An additional model, where stage was treated as a confounder, was also employed. Analyses were conducted for cervical cancer-specific mortality, in which women dying from other causes were excluded. Survival curves were generated using the Kaplan-Meier procedure and compared using the log-rank test. Although cervical cancer cell type was evaluated as a potential confounder due to differences in survival and efficacy of screening among women with adenocarcinoma, it did not meet the operational definition of a confounder in a cohort study. All final models included the primary exposures of interest: composite SES, rural residence, race/ethnicity, and age.

RESULTS

Table 1 provides the descriptive characteristics of all 7237 women diagnosed with primary invasive cervical cancer from January 1, 1995, to June 30, 2001, and reported to the TCR. Of those with data on stage at diagnosis, the majority of patients were diagnosed in the early stage (59.2%) with squamous cell carcinomas (72%). The mean age of women diagnosed with cervical cancer was 50.0 ± 16.2 years, with almost two thirds of women diagnosed before age 55. Over 30% of women diagnosed with cervical cancer reported a Spanish/Hispanic origin, and approximately 14% were African American (Table 1). Twenty-eight percent (n = 2029) of the cohort died during the follow-up period. Almost 73% of women who died with information
on stage at diagnosis were diagnosed with late stage disease.

Table 2 shows the association between the composite SES variable, rural residence, race/ethnicity, and stage of cervical cancer diagnosis. Patients with missing staging information (n = 1169), no available ZIP code data (n = 116), and with other/unknown race/ethnicity (n = 162) were excluded, leaving 5467 women for logistic regression analysis. After adjusting for race/ethnicity, rural residence, and age, women living in ZIP codes with lower SES were more likely to be diagnosed at a later stage. The trend test of greater proportion late stage with decreasing SES was significant (p < 0.001). Rural residence was not associated with being diagnosed at a later stage. Relative to non-Hispanic white women with cervical cancer, African American and Hispanic women were more likely to be diagnosed at a later stage (Table 2).

Table 3 and Figures 1 and 2 present the results from the survival analysis. Patients with missing staging information (n = 1169), no available ZIP code data (n = 116), with other/unknown race/ethnicity (n = 162), and listing competing causes of death (n = 323) were excluded, leaving 5467 women for the Cox proportional hazards modeling and Kaplan-Meier analyses. The demographic profile of women included in the survival analysis was not statistically different from that of women in the full sample. Kaplan-Meier survival curves (Figs. 1 and 2) limited to early and late stage disease, respectively, indicate that lower SES is associated with reduced cervical cancer survival time for women diagnosed in both early (log-rank test chi-square = 35.2, p < 0.001) and late stage disease (log-rank test chi-square = 21.1, p value <0.001). Women diagnosed in late stage disease were 6.2 times (adjusted HR 95% CI 5.5-7.2)
### Table 2. Multivariate Predictors of Late Stage Cervical Cancer Diagnosis among 5790 Women Reported to the Texas Cancer Registry, 1995–2001

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Late stage (%</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5790</td>
<td>2377 (41.1)</td>
<td></td>
</tr>
<tr>
<td>Composite socioeconomic status&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low SES</td>
<td>1442</td>
<td>694 (48.1)</td>
<td>1.4 (1.2–1.7)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Medium SES</td>
<td>1445</td>
<td>622 (43.0)</td>
<td>1.2 (1.1–1.5)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>High SES</td>
<td>1443</td>
<td>553 (38.3)</td>
<td>1.1 (1.0–1.3)</td>
</tr>
<tr>
<td>Very High SES</td>
<td>1460</td>
<td>508 (34.8)</td>
<td>1.0 Ref&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Trend test Z</td>
<td>4.49</td>
<td>0.001&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Rural residence&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;70.00% rural</td>
<td>572</td>
<td>240 (42.0)</td>
<td>1.0 (0.8–1.2)</td>
</tr>
<tr>
<td>23.33%–69.99% rural</td>
<td>973</td>
<td>393 (40.4)</td>
<td>0.9 (0.8–1.1)</td>
</tr>
<tr>
<td>11.67%–23.32% rural</td>
<td>553</td>
<td>221 (40.0)</td>
<td>0.9 (0.7–1.1)</td>
</tr>
<tr>
<td>0.01%–11.66% rural</td>
<td>1576</td>
<td>598 (37.9)</td>
<td>0.8 (0.7–0.9)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urban: 0% rural</td>
<td>2116</td>
<td>925 (43.7)</td>
<td>1.0 Ref</td>
</tr>
<tr>
<td>Trend test Z</td>
<td>0.6</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>790</td>
<td>374 (47.3)</td>
<td>1.3 (1.1–1.6)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1861</td>
<td>838 (45.0)</td>
<td>1.3 (1.1–1.5)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>White non-Hispanic</td>
<td>3139</td>
<td>1165 (37.1)</td>
<td>1.0 Ref</td>
</tr>
</tbody>
</table>

<sup>a</sup>Women excluded from this analysis include those with no available ZIP code data, those of other/unknown race/ethnicity, and those with missing stage at diagnosis.

<sup>b</sup>Late stage includes summary stages IIA–IV.

<sup>c</sup>Odds ratios are adjusted for age and other covariates in the table.

<sup>d</sup><i>p</i> < 0.05.

<sup>e</sup>Ref, reference group.

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**FIG. 1.** Kaplan-Meier survival estimates: Early stage survival of cervical cancer patients by socioeconomic status.
more likely to die than women diagnosed with early stage disease (Table 3).

Lower SES was associated with shorter cervical cancer cause-specific survival time among women with cervical cancer. The trend test for quartiles of the composite SES variable and survival time supports a dose-dependent association for both early and late stage at diagnosis (Table 3). Comparison of the lowest to highest SES quartile and cervical cancer survival time indicates that SES is associated with poor survival for both early and late stage disease (early stage adjusted \( \text{aHR} = 3.0, 95\% \text{ CI} 2.1-4.3 \); late stage \( \text{aHR} = 1.7, 95\% \text{ CI} 1.4-2.1 \)). Moreover, when stage is treated as a confounder in the model, low SES remains associated with poor survival (\( \text{aHR} = 1.9, 95\% \text{ CI} 1.6-2.3, p \text{ for trend} <0.001 \)).

Rural residence was not associated with cervical cancer survival in any stage of diagnosis (Table 3). Furthermore, trend tests do not indicate a dose-dependent relationship between the degree of rural/urban residence and survival. Increased risk estimates for women living in areas that are approximately 23\%-70\% rural are seen across early, late, and all stages of diagnosis (all stages, \( \text{aHR} = 1.2, 95\% \text{ CI} 1.0-1.4 \); early stage \( \text{aHR} = 1.2, 95\% \text{ CI} 0.9-1.7 \); late stage \( \text{aHR} = 1.2, 95\% \text{ CI} 1.0-1.5 \)); however, these estimates did not reach statistical significance.

Race/ethnicity remained associated with survival after adjusting for SES, rural residence, and age. Relative to non-Hispanic white women, African American women were 1.3 times (95\% CI 1.1-1.5) more likely to die of cervical cancer independent of stage (Table 3). Hispanic women, however, had a significant survival advantage (\( \text{aHR} = 0.7, 95\% \text{ CI} 0.6-0.8 \)) relative to non-Hispanic white women that held for all stages at diagnosis (Table 3).

Results of this analysis show that both SES and race/ethnicity affect cervical cancer survival after adjusting for stage at diagnosis and age. In Table 4, we present analysis of SES and cervical cancer survival within the three racial/ethnic groups. SES continued to be associated with cervical cancer survival in each racial/ethnic group, with the most elevated risk among Hispanic women living in areas of low SES (\( \text{aHR} = 2.2, 95\% \text{ CI} 1.5-3.3 \)). Moreover, trend tests reflect a dose-dependent association between SES and survival within each racial/ethnic group (Table 4).
DISCUSSION

Minority race/ethnicity has consistently been documented as a risk factor for later stage of cervical cancer diagnosis. Our study found that a lower composite SES and minority race/ethnicity were associated with late stage at diagnosis. Additionally, lower SES and African American race were associated with poorer survival. Although Hispanic women were more...
likely than non-Hispanic white women to present help at a later stage, Hispanic cervical cancer patients were less likely to die of this disease. Furthermore, the association between lower SES and poorer survival was consistent across all racial/ethnic groups, suggesting the effect of SES may be more important than race.

Our finding that lower SES was associated with poorer survival, particularly among those diagnosed at an early stage, is consistent with the work reported by Mundt et al., Morgan et al., and Johnson, who found that SES may be an important predictor of survival after adjusting for race/ethnicity. Further, our findings concur with those of Singh et al., who found that mortality increased with increasing poverty for women in all racial/ethnic groups. Five other studies found no association with poverty for women in all racial/ethnic groups.

The effect of rural residence as a proxy for access to care may differentially affect stage at diagnosis and survival if access to screening services is different from access to follow-up and treatment services. We report no association between rural residence and stage at diagnosis or survival, which contrasts with the strong association between rural residence and cervical cancer mortality (OR = 19.4) reported by O’Brien et al. in Australia. However, our findings concur with those reported by Johnson for cervical cancer survival in South Carolina. Results of borderline significance for the association between women living in areas that are between 27% and 70% rural with reduced survival may indicate a greater difficulty for these women to receive treatment services. However, adequate treatment data are necessary to explore these preliminary results.

When adjusting for SES, our conclusion that African American women were more likely to be diagnosed at a late or unknown stage and to have shorter survival times, particularly among those diagnosed at a late or missing stage, is consistent with the preponderance of the existing literature yet four studies reported that African American race was not an important predictor of survival after adjusting for socioeconomic factors. Our finding that Hispanic women were less likely to die of cervical cancer compared with non-Hispanic white women within any stage at diagnosis contrasts with the two published studies with sufficient numbers that report Hispanic ethnicity was not an independent predictor of survival.

Strengths and limitations of the study

A limitation to this study is the use of aggregate (census) data as indicators for individual SES and rural residence. However, defining rural residence by ZIP code is not likely to cause misclassification. Census tract residential conditions based on the federal definition of rural and urban areas are not likely to vary greatly for individuals within a ZIP code. This may not be the case for ZIP code-level proxies for SES. Census tract-level data have been used to estimate the potential effects of SES yet these data were not available to us. A recent study by Robert et al. using the same components measures of SES used here, reported that census tract level variables were consistent with the effects of SES using ZIP code-level variables. Our ZIP code-level data may cause some misclassification relative to census tract-level data, yet any misclassification will likely bias the measure of association toward the null. It is possible, however, that we could have differential misclassification if lower SES women were consistently misclassified as higher SES because of their ZIP codes. An analysis of the correlation between the components of our composite SES measure revealed satisfactory correlation (Cronbach’s alpha = 0.71), thus supporting accurate categorization of women in respective SES quintiles.

The use of death certificate information to determine cause of death may contribute to outcome misclassification for our cervical cancer survival analysis. This potential for bias is likely to be nondifferential, as census data are not linked with vital records. Exclusions for missing data (e.g., those diagnosed by death certificate only) may cause selection bias. However, our comparisons between the complete dataset and that used for analyses did not show statistically significant differences in the variables of interest.

Using tumor registry or medical record data to abstract race/ethnicity has the potential for misclassification. However, using data from both the race and Spanish/Hispanic origin variables increases accurate classification of race/ethnicity. Accuracy between medical records and self-report has reported to be moderate (Latinas) to high (whites, Asians, and African Americans). Furthermore, the TCR has strict guidelines outlined
in the Texas cancer reporting handbook for identifying persons of Spanish or Hispanic origin.\textsuperscript{22}

Other intervening variables not measured by this model that may affect the association between SES factors and mortality include treatment and presence of comorbid illnesses.\textsuperscript{38} Like most cancer registries, the TCR was established to provide a population-based estimate of cancer incidence, not to provide validated treatment data. Acquiring information on these variables from outside sources will help to better understand the relationship between factors associated with decreased survival from cervical cancer. We are looking toward future studies that will include data on these variables to supplement the registry data.

Strengths of this study include its large sample size ($n = 7346$), which reduces random error and increases study power. The use of a population-based cancer registry reduces the potential for selection bias by including all cervical cancer cases in Texas. Evidence for case completeness includes the reported TCR completeness proportion of 99\% and the similar number of cervical cancer cases reported per year to the TCR between 1997 and 2001 (1071)\textsuperscript{39} compared with the American Cancer Society annual estimate for Texas in 2001 (1000).\textsuperscript{40}

**Future directions**

Further studies are needed to replicate our finding that Hispanic women with cervical cancer have better survival relative to non-Hispanic white and African American women. The well documented Hispanic paradox\textsuperscript{41–43} indicates that regardless of lower SES, the Hispanic population in the United States has lower mortality rates. Reasons for this advantage may include difference in social support, religion/faith, cultural influences, or health-selective immigration differences between these populations. Health-selective return migration of immigrants may underestimate the mortality rates in the United States,\textsuperscript{44} leading to an underestimation bias in Hispanic mortality rates from research linked to the U.S. Death Index.

To address the possibility that Hispanic women with cervical cancer return to Mexico and are, therefore, underreported as cases in the TCR, we restricted the analysis to exclude women with cervical cancer living along the Texas-Mexico border (El Paso, Starr, Cameron, Hidalgo, and Willacy counties). Hispanics relative to non-Hispanic white women still had a survival advantage ($aHR = 0.8, 95\% CI 0.7-0.9$). This finding indicates that selective migration back to Mexico may not explain the strong protective effect of Hispanic ethnicity on cervical cancer survival.

The findings reported here suggest that disadvantaged groups (e.g., African Americans or people with low SES) may be at higher risk of dying from a preventable (early stage) cancer. Additional research on these high-risk groups is needed to identify the missed opportunities for preventing death among these women. Missed opportunities may take the form of logistical/financial barriers (e.g., having no transportation for treatment, not having insurance, or insurance not covering care), communication barriers (e.g., language barriers between patient and healthcare provider or not understanding options offered for treatment), selective provision of healthcare by race/ethnicity, income, or rural residence (e.g., not offering more aggressive treatment to someone living in rural areas), and individual or cultural differences in reaction to cervical cancer. As the effect of SES was shown to be consistent across all racial/ethnic groups, interventions may be more effective in reducing cervical cancer mortality if these are developed to target women of lower SES rather than by racial/ethnic groups. Interventions can be developed to target high-risk groups, for example, to ensure that state-of-the-art treatment is offered and resources are provided to overcome the impact of logistical or financial barriers.

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