RESEARCH ARTICLE

African American Race and Low Income Neighborhoods Decrease Cause Specific Survival of Endometrial Cancer: A SEER Analysis

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Abstract

Background: This study analyzed Surveillance, Epidemiology and End Results (SEER) data to assess if socio-economic factors (SEFs) impact on endometrial cancer survival. Materials and Methods: Endometrial cancer patients treated from 2004-2007 were included in this study. SEER cause specific survival (CSS) data were used as end points. The areas under the receiver operating characteristic (ROC) curve were computed for predictors. Time to event data were analyzed with Kaplan-Meier method. Univariate and multivariate analyses were used to identify independent risk factors. Results: This study included 64,710 patients. The mean follow up time (S.D.) was 28.2 (20.8) months. SEER staging (ROC area of 0.81) was the best pretreatment predictor of CSS. Histology, grade, race/ethnicity and county level family income were also significant pretreatment predictors. African American race and low income neighborhoods decreased the CSS by 20% and 3% respectively at 5 years. Conclusions: This study has found significant endometrial survival disparities due to SEFs. Future studies should focus on eliminating socio-economic barriers to good outcomes.

Keywords: Endometrial cancer - SEER - socio-economic disparity - cause specific survival

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Introduction

Endometrial cancers are the most common gynecologic cancers of United States (U.S.), with over 35000 cases diagnosed each year (Duong et al., 2011). The incidence is on the rise because of obesity epidemic. Current management includes surgery alone for early endometrial cancers and additional post-operative radiotherapy (Patel et al., 2012) (Koskas et al., 2011) and chemotherapy (Wright et al., 2012) for more advanced cases. Endometrial cancers have excellent outcomes (Wright et al., 2012) with cause specific survival over 90% for earlier stages. Some studies have shown that race is shown to be associated with endometrial outcome (Olson et al., 2012). However, the nature of the socio-economic barriers in good outcome for endometrial cancer has not been well characterized. The Surveillance Epidemiology and End Results (SEER) cancer registry data have been extensively used to build prognostic models for endometrial cancer (Berrington et al., 2011; Felix et al., 2011). This study analyzed SEER data to assess if socio-economic factors (SEFs) impacted on endometrial cancer survival.

Materials and Methods

SEER registries contain public use data. These data can be used for analysis with no internal review board approval needed. SEER registry has massive amount of data available for analysis, however, manipulating the data could be challenging. SEER Clinical Outcome Prediction Expert (SCOPE) (Cheung, 2012) was used to mine SEER data and construct accurate and efficient prediction models (Cheung et al., 2001a; 2001b). The data were obtained from SEER 18 database. SEER*Stat (http://seer.cancer.gov/seerstat/) was used for listing the cases. The filter used was: Race, Sex, Year Dx, Registry, County. Year of diagnosis='2004','2005','2006','2007','2008','2009' AND Site and Morphology. Site rec with Kaposi and mesothelioma='Endometrial'. Patients diagnosed from 2004-2009 were included. This study explored a long list of socio-economic, staging and treatment factors that were available in the SEER database. Endometrial cancer patients treated from 2004-2007 were included in this study. Time to event data were analyzed with Kaplan-Meier method. Kolmogorov-Smirnov's 2-sample tests and Cox proportional hazard models were used for univariate and multivariate analyses, respectively, to identify independent risk factors. Probability $p < 0.05$ was considered statistically significant.

The variable 'SEER cause-specific death' was used as the CSS outcome variable. For univariate and multivariate analyses, the predictors were coded as follows: SEER stage: 0=local/regional, 1=metastatic/un-staged; histology: 0=adenocarcinoma, 1=others; grade:

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0=grade 1-2, 1=grade 3-4 and ungraded; race/ethnicity: 0=non African American, 1=African American; county level % college graduate: 0=more than 25%, 1=less or equal to 25%; and county level family income: 0=more than $50k/year, 1=less or equal to $50k/year.

The areas under the receiver operating characteristic (ROC) curve were computed for predictors using absolute mortality risk. Similar strata were fused to make more efficient models if the ROC performance did not degrade (Cheung et al., 2001a; 2001b).

Results

Figure 1 shows the Kaplan-Meier's estimate for CSS of SEER endometrial cancer patients. For all of the patients, the CSS was over 80%. There were 64710 patients included in this study. The follow up duration (S.D.) was 28.2 (20.8) months. The mean (S.D.) age was 62.4 (12.9) years. The overall risk of death from endometrial cancer was 11%. Only 11 SEER patents younger than 20 years old were diagnosed with endometrial cancer from 2004-2009. Grade was predictive of cause specific survival. The risk of cause specific death was 1.6% for grade I, 6.0% for grade II, 22.4% for grade III and 29.3% for grade IV. Being un-graded had a 20.5% risk of cause specific death as patients with a grade III disease. 4-tiered SEER stage was the simpler predictive model of absolute risk of cause specific death than the 16-tiered AJCC (American Joint Committee on Cancer) model. Furthermore, the SEER stage could be optimized further by SCOPE (Table 1). Race predicted a 12% difference in absolute cause specific survival (ROC area of 0.55). The other two SEFs lower county family income and lower county education attainment were associated with a 2% disadvantage in absolute cause specific survival. The ROC areas of these socio-economic factors were only marginal at 0.51. However, these were already better than Radiation Treatment (ROC area of 0.50). The significant SEFs were also studies by univariate and multivariate analyses.

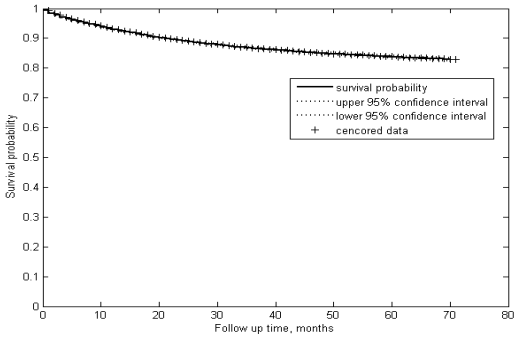

Figure 1. Kaplan-Meier Survival Plot of SEER Endometrial Cancer Patients

For the SEER stage model, the staging was defined as localized, regional, distant or incompletely staged/others. The stage status was highly predictive of cause specific survival (ROC area or 0.81). This 4-tiered staging model was optimized to a 3-tiered model consisted of localized, regional/un-staged versus distant with a ROC area of 0.81.

SEFs were analyzed with the ROC selected biological predictors. SEER staging was the best pretreatment predictor of CSS also for predictive actuarial CSS (Figure 2a), and the other factors included were histology (Figure 2b), grade (Figure 2c), race/ethnicity (Figure 2d), county level % college graduate (Figure 2e) and county level family income (Figure 2f). These were found to be significant univariate pretreatment predictors (Table 1). Under multivariate analysis, county level % college graduate did not maintain statistical significance (Table 1). For the SEFs, at 5 years, African American race and low income neighborhoods decreased the CSS by 20%

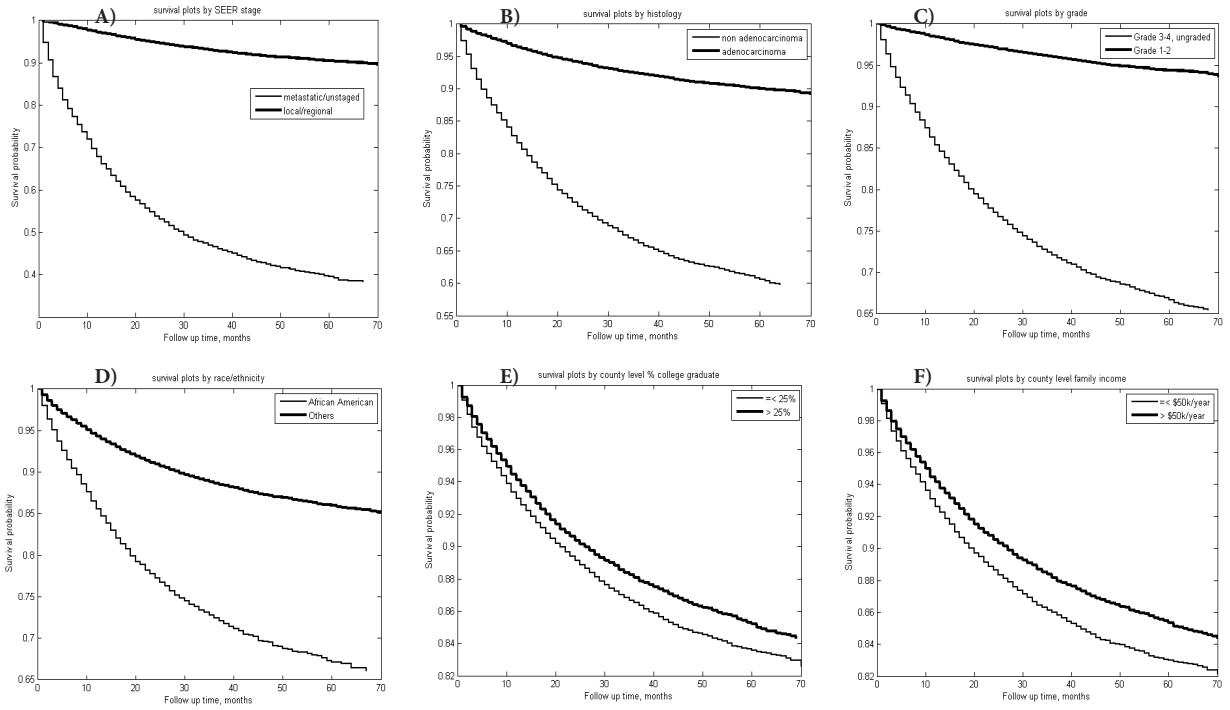

Figure 2. The effects of Univariate Predictors on Cause Specific Survival of Endometrial Cancers. A) SEER stage; B) Histology; C) Grade; D) Race/Ethnicity; E) County Level % College Graduate And F) County Level Family Income

Table 1. Univariate and Multivariate Analyses of Pretreatment Predictors of Endometrial Cancers

		Kolmogorov-Smirnov test			Cox proportional hazard model		
		l	p	k	beta	s.e.	p
SEER stage	0=local/regional 1=metastatic/unstaged	1	1.55E-28	9.54E-01	1.82E+00	2.58E-02	0.00E+00
Histology	0=adenomcarcinoma 1=others	1	7.00E-26	9.08E-01	6.07E-01	2.64E-02	0.00E+00
Grade	0=grade 1-2 1=grade 3-4, ungraded	1	1.12E-28	9.42E-01	1.37E+00	3.35E-02	0.00E+00
Race/ethnicity	0=non African American 1=African American	1	1.41E-19	7.94E-01	3.84E-01	3.12E-02	0.00E+00
County % college graduate	0= more than 25% 1=less or equal to 25%	1	1.57E-02	2.57E-01	2.65E-02	3.32E-02	4.26E-01
County family income	0=more than $50k/year 1=less or equal to $50k/year	1	3.37E-04	3.43E-01	1.04E-01	3.33E-02	1.80E-03

*For significant Kolmogorov-Smirnov Statistics k, l =1. Beta and s.e. were respectively Cox proportional hazard coefficients and standard errors. Probability $p < 0.05$ was considered significant

(Figure 2d) and 3% (Figure 2f) respectively in actuarial risk of death.

Discussion

The effects of socio-economic factors on cause specific survival of endometrial cancers were investigated in this study. This is a part of a larger study surveying the SEER database for SEF disparities. Recently, a 10-15 years long-term study has found moving individuals from low income neighborhoods to higher income ones improved their obesity and diabetes (Ludwig et al., 2011). Against this background, this study aimed at generating hypotheses that could be tested in future clinical trials to remove socio-economic barriers to good endometrial cancer outcome.

Some studies have shown that race is shown to be associated with endometrial outcome (Olson et al., 2012). More studies are needed in this important but under-investigated area. The Surveillance Epidemiology and End Results (SEER) cancer registry data have been extensively used to build prognostic models for endometrial cancer (Berrington et al., 2011; Felix et al., 2011). National Cancer Institute and Center for Disease Control fund SEER to monitor the cancer epidemiology of US. SEER registers about 28% of all of the oncology cases in US. This study used SEER-18 database updated in November of 2011. SEER data have been used widely as a benchmark for studying cancer outcomes in US and in other countries (Ognjanovic et al., 2009; Sultan et al., 2009; Cheung et al., 2010; McDowell et al., 2010; Pappo et al., 2010; Bhatia, 2011; Perez et al., 2011). SEER coverage is selected geographically to well represent U.S. Therefore, SEER data is ideal for identifying potential socio-economic disparity in oncology outcome. In addition to the biological staging factors and the treatment factors, this database also contains a large number of county level socio-economic factors data. In addition to constructing the best predictors of cause specific survival, this study also aimed to identify barriers to good treatment outcome that may be discernable only from a national database.

This study is interested in constructing accurate and efficient models that will aid patient and treatment selection for endometrial cancer patients. To that end, this study examined the ROC models (Hanley and McNeil, 1982) of a long list of potential explanatory factors. When measuring the accuracy of prediction models, ROC analysis takes into account both sensitivity and specificity of the prediction model. Ideal model would have a ROC area of 1 and a random model is expected to have an area of 0.5 (Hanley and McNeil, 1982). For example, a clinical ROC model can be used to predict if a patient receiving the recommended treatment will/will not die from the disease given a cutoff value. In this study, all potential cut points were used to calculate the ROC area.

In order to be consistent over decades, SEER historical stage abstracts the staging into simple but important stages for cancer progression: localized, regional and distant. SEER stage was highly predictive of patient outcome (Figure 1). The model has a ROC area of 0.81. Thus complete staging is important in this disease since it will aid patient selection and council. After optimization, the 4-tiered stage model was reduced to a 3-tiered model based on ROC area calculations. These results show that staging is important because being un-staged was associated with a higher risk of cause specific death. As a reference, the prostate risk model has a ROC area of 0.75 in its accuracy of predicting biochemical failure (Cheung et al., 2001a; 2001b). The ROC area 0.81 implied the information content (i.e. the staging accuracy) of the models was very high but still incomplete. This adds to the uncertainty of the modeling. Staging remains an area for improvement.

This study has found significant endometrial survival disparities due to SEFs univariate and multivariate analyses (Table 1). African American race and low income neighborhoods adversely decreased the CSS of endometrial cancer by an impressive 20% (Figure 2d) and 3% (Figure 2f) respectively. These SEFs remained independently significant even under multivariate analysis with SEER stage, histology and grade which were highly predictive biological factors. Future studies should focus on eliminating these apparent and excessive socio-economic barriers to improve outcomes of endometrial cancers.

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