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Cervical cancer survival for patients referred to a tertiary care center in Kentucky ☆

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ABSTRACT

Objectives. To identify prognostic factors influencing cervical cancer survival for patients referred to a tertiary care center in Kentucky.

Methods. A cohort study was performed to assess predictive survival factors of cervical cancer patients referred to the University of Kentucky from January 2001 to May 2010. Eligibility criteria included those at least 18 years-old, cervical cancer history, and no prior malignancy. Descriptive statistics were compiled and univariable and multivariable Cox proportional hazard analysis were performed.

Results. 381 patients met entry criteria. 95% were Caucasian (N = 347) and 66% (N = 243) lived in Appalachian Kentucky. The following covariates showed no evidence of a statistical association with survival: race, body mass index, residence, insurance status, months between last normal cervical cytology and diagnosis, histology, tumor grade, and location of primary radiation treatment. After controlling for identified significant variables, stage of disease was a significant predictor of overall survival, with estimated relative hazards comparing stages II, III, and IV to stage I of 3.09 (95% CI: 1.30, 7.33), 18.11 (95% CI: 7.44, 44.06), and 53.03(95% CI: 18.16, 154.87), respectively. The presence of more than two comorbid risk factors and unemployment was also correlated with overall survival [HR 4.25 (95% CI: 1.00, 18.13); HR 2.64 (95% CI 1.29, 5.42), respectively].

Conclusions. Residence and location of treatment center are not an important factor in cervical cancer survival when a tertiary cancer center can oversee and coordinate care; however, comorbid risk factors influence survival and further exploration of disease comorbidity related to cervical cancer survival is warranted.

Background

Cervical cancer is the third most common gynecologic malignancy diagnosed in the United States with approximately 12,200 new cervical cancer cases and 4210 deaths projected for 2010 [1]. Ethnic, racial, and geographic disparities in diagnosis, treatment, and outcome for cervical carcinomas are well described [2,3]. Related to geography, the Appalachian region of the United States, which includes the eastern counties of Kentucky, experiences an undue burden of cervical cancer. Many Appalachian communities are considered "medically underserved" and are characterized as primarily white, rural, and of lower socioeconomic status [3–5]. Specifically, Kentucky has one of the highest per capita incidence of cervical carcinoma in the United States and the second highest incidence across five Appalachian States with an age-adjusted rate of 10.7 per 100,000 population [4].

While cervical cancer disparities in Kentucky are well documented, the majority of published studies focus on cervical cancer risk and incidence [5,6], or the relationship between survival and demographic variables [7–10]. To date, there is a knowledge gap between recurrence and survival of cervical cancer in Kentucky and other Appalachian regions that adjusts for clinicopathologic variables and comorbidities. Further, the literature does not provide adequate research that accounts for differences among treatment sites (tertiary referral center versus community center), while controlling for clinical risk factors and comorbidities. It is possible that differences in survival between treatment facilities may be due to variations in patient demographic characteristics, clinicopathologic factors, and/or differences in guideline concordant treatment provided among treatment centers [11]. The aim of this study is to identify factors that influence cervical cancer recurrence and survival in Kentuckians who receive at

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least part of their treatment at a tertiary care center, while controlling for confounding variables. Knowledge of these factors may foster hypothesis generation for initiatives that may further bridge the cervical cancer disparity treatment gap for the Commonwealth of Kentucky.

Methods

Institutional Review Board approval was obtained from the University of Kentucky. Cervical cancer patients presenting to the University of Kentucky between January 2001 and May 2010 were identified using the University of Kentucky Cervical Cancer Database. This comprehensive database includes all cervical cancer patients presenting for evaluation and/or treatment. While inclusion criteria were a current or past history of cervical cancer and age over 18 years, individuals were excluded from the study if they were pregnant at the time of diagnosis, under 18 years-old, had a severe mental or physical handicap, or had a history of any cancer other than cervical cancer except non-melanoma skin cancer.

Patient information was obtained and updated using the hospital electronic medical record, Gynecologic and Radiation Oncology clinic charts, Kentucky Cancer Registry Data, and by contacting non-University of Kentucky physicians for patients no longer receiving follow-up care at the institution. In an attempt to control for known and suspected confounding variables, a variety of socioeconomic, demographic, clinicopathologic, and treatment variables were considered. Socioeconomic and demographic factors included were race, body mass index (BMI), smoking status, insurance status, education, employment, and residence. Race was defined as white and other. BMI was calculated using weight in kilograms divided by height in meters squared (kg/m^2). Residence was defined as Appalachian or non-Appalachian, using the Appalachian Regional Commission classification of county (www.arc.gov) and rural/urban status was classified according to rural–urban continuum codes (Beale Codes) [12].

Additionally, clinicopathologic and treatment variables included: comorbid risk factors, length of time elapsed since last cervical cytologic screening prior to the Papanicolaou smear that precipitated the cancer diagnosis, stage, location of primary external radiation, radiation treatment factors, length of time needed to complete radiation therapy, and chemotherapy. Comorbid risk factors were quantified by the number of conditions listed in the medical record and included, but were not limited to hypertension, coronary artery disease as well as other cardiovascular disease, diabetes, collagen vascular disease, pulmonary disease, venothromboembolic disease, and psychiatric disorders. This project was initiated prior to the publication of the 2009 staging system. Thus, stage was determined by the 1995 International Federation of Gynecology and Obstetrics (FIGO) classification [13].

Overall survival (OS) was calculated using the time from diagnosis until the date last seen by a physician or date of death from any cause. Disease-specific survival (DSS) was calculated using the time from diagnosis until the date last seen by a physician or date of death from cervical cancer. Progression-free survival (PFS) was calculated using the time from diagnosis until the time to disease progression, recurrence, or death due to any cause. In all cases, patients were considered censored at the time of last follow-up.

Data analysis was performed using the statistical package R© version 2.10.1 (R Project, Boston, MA). Descriptive statistics were summarized as frequency counts and percentages. Bivariable associations were assessed using Kaplan–Meier survival curves and log-rank tests. Forward stepwise selection Cox proportional hazards regression models were built for the outcomes of overall survival, disease-specific survival, and progression-free survival. Statistical significance was set at $\alpha = 0.05$. The proportional hazards (PH) assumption was tested using the likelihood ratio test for each predictor interacting with time. For categorical variables, log-minus-log survival plots provided additional assessment of PH.

Table 1
Demographic and socioeconomic characteristics (N = 381)[a].

Age (years)	
Median (range)	47 (21–88)
<40	111 (29%)
40–55	158 (42%)
56–64	49 (13%)
>64	59 (16%)
Race	
White	347 (95%)
Other	17 (5%)
Insurance	
Private	45 (12%)
Medicaid	119 (33%)
Medicare	53 (15%)
No insurance	145 (40%)
Education	
Grade School	10 (4%)
High School	180 (66%)
College	84 (31%)
Tobacco Use	
Yes	208 (59%)
No	147 (41%)
Residence	
Rural Non-Appalachia	59 (16%)
Urban Non-Appalachia	64 (17%)
Rural Appalachia	220 (60%)
Urban Appalachia	23 (6%)
Employment status	
Employed	140 (40%)
Unemployed	207 (60%)
Body mass index (kg/m^2)	
<18.5	17 (5%)
18.5–24.9	112 (30%)
29.9–30	108 (29%)
30–40	106 (28%)
40–50	22 (6%)
50–60	6 (2%)
>60	1 (0%)
Number of comorbid risk factors	
0	185 (53%)
1–2	156 (44%)
>2	13 (4%)

[a] Due to rounding and missing values, percentages may not equal 100% and totals may not equal 381.

Results

Three hundred and eight-one patients met eligibility criteria. Their demographic, socioeconomic, and clinical outcomes are reported in Table 1. The median age of the entire cohort was 47 years (range: 21–88 years) and the majority were Caucasian, uninsured or Medicaid, unemployed, and from rural Appalachia. Most patients had a BMI $<30\ kg/m^2$ and no comorbid risk factors. The median length of time between the last normal cytologic screen and cancer diagnosis was 70 months (range: 1–780 months). Pathologic data are shown in

Table 2
Pathologic characteristics (N = 381)[a].

Stage	
I	192 (51%)
II	86 (23%)
III	73 (19%)
IV	24 (6%)
Histology	
Squamous cell	273 (73%)
Adenocarcinoma	72 (19%)
Other	22 (6%)
Grade	
1	23 (6%)
2	127 (34%)
3	131 (35%)

[a] Due to rounding and missing values, percentages may not equal 100% and totals may not equal 381.