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Distance from a Comprehensive Cancer Center: A Proxy for Poor Cervical Cancer Outcomes?†

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Abstract

Objective—To evaluate the potential relationship between outcomes in cervical cancer patients based on distance from our Comprehensive Cancer Center (CCC).

Methods—A retrospective cohort study of cervical cancer patients was performed. Abstracted data included: demographics, clinicopathologic variables, treatment, and survival. Analyses both by quartiles and distance < 100 and ≥ 100 miles from our institution were performed. Data were analyzed using SAS version 9.2.

Results—390 patients living a median distance of 58.1 miles (range 1.2–571 miles) from our CCC were identified. Patients were generally white (n=249), non-smokers (n=226), with Stage IB disease (n=222), squamous histology (n=295) and underwent primary surgical therapy (n=229). Patients were divided into both quartiles as well as two strata: < 100 and ≥ 100 miles for comparison. Progression-free survival (PFS) and overall survival (OS) favored patients living closer to our center with a lower median OS for patients living ≥ 100 miles (65.4vs. 99.4 months; p=0.040). Cox proportional hazard modeling noted that advanced stage was predictive of inferior PFS and OS, while other clinical covariates including age, BMI, race, smoking status and histology had a variable impact on outcomes and distance greater than 100 miles was associated with a higher risk of death (hazard ratio [HR]=1.68, 95% confidence interval [CI] 1.11–2.54).

Conclusion—Overall survival for patients living greater than 100 miles from our CCC was worse when compared to patients in closer proximity. Outreach efforts and utilization of navigators may help decrease the impact of geographic and racial disparities on outcomes.

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Keywords

Cervical cancer; disparities; survival outcomes; distance

Introduction

Nearly 13,000 new cases of cervical cancer are diagnosed annually in the United States, with an estimated 4,120 disease-related deaths predicted for 2016 (1). A recent report from the Health Disparities Taskforce of the Society of Gynecologic Oncology notes the presence of disparities in outcomes and care across the spectrum of gynecologic cancers, including cervical cancer (4). While racial disparities in cervical cancer were addressed in this report, the majority of this report and research on disparities in gynecologic cancers has been on ovarian cancer. In addition to race and socioeconomic status, distance from a high-volume hospital is a risk factor that has been identified as a barrier to compliance with National Comprehensive Cancer Network (NCCN) treatment guidelines for ovarian cancer, putting patients at increased risk for non-standard treatment and poorer survival outcomes (2, 3). Importantly, racial disparities in outcomes are minimized or eliminated when black and white patients with ovarian cancer are primarily managed equally in high volume tertiary referral centers or when barriers to access to care are minimized, as in the US military health care system (5,6).

Improving access to health care has been identified as one of the U.S. Department of Health and Human Services top four initiatives for Healthy People 2020 (7). Distance traveled to a high-volume care center may represent a modifiable barrier to access to health care. Prior studies have explored the contribution of geographic location to disparities in gynecologic cancer treatment; however, investigation of the effect of such spatial disparities on cervical cancer treatment and outcomes is limited (8). Two prior retrospective studies looking at sociodemographic characteristics of women with cervical cancer have shown limited or no association between distance traveled for care and outcomes (9, 13). Previously, while we noted some differences between white and black women with cervical cancer, overall survival was similar for patients managed at our comprehensive cancer center (CCC) (10). We did not evaluate any potential impact on distance from our CCC in this previous work. Accordingly, we performed a retrospective cohort study to evaluate the potential impact on clinical outcomes in cervical cancer patients based on distance from our NCI-Designated CCC.

Methods and Materials

This retrospective cohort study was carried out in accordance with the standards of the Institutional Review Board at the University of Alabama at Birmingham (UAB). Cervical cancer patients were identified using the UAB Gynecologic Oncology clinic database. A total of 390 cervical cancer patients who were diagnosed between 1999 and 2011, met eligibility criteria. All patients diagnosed with FIGO stage IA1 through IVA cervical cancer, of any histologic type, who had a documented address of primary residence, were included in this study. Patients were excluded if they did not meet these criteria, if medical records

did not supply sufficient data for evaluation, or if distance of primary residence was an extreme outlier within the dataset, namely patients that had moved out of state since therapy and our records did not demonstrate their address during primary therapy. Information including patient demographic characteristics, location of primary residence, primary therapy, recurrence and recurrence therapy information was collected. Geographic distance between patients and the UAB CCC was calculated in miles. Patients were subsequently divided into quartiles (> 0 to 19.2 miles, > 19.2 to 58.7 miles, > 58.7 to 98.3 miles, and > 98.3 miles). A preliminary analysis suggested no difference in outcomes for patients in the first three quartiles, therefore, patients were divided into two groups: < 100 miles ($n=297$) and ≥ 100 miles ($n=93$). Progression-free survival (PFS) was calculated from the time of diagnosis to disease recurrence or death, defined by clinical, histologic, or radiographic evidence of tumor recurrence or distant metastasis at any time after initial treatment. Overall survival (OS) was calculated from the time of diagnosis to the date of last known follow up or death from any cause.

Chi-square tests were used to compare patient characteristics between patients who lived < 100 miles and ≥ 100 miles from the NCI designated CCC. Cox proportional hazards regression was used to estimate the association between PFS and OS and selected patient characteristics including: age, race, histology, smoking status, BMI, tumor stage, and distance from our CCC. SAS version 9.2 (SAS Institute, INC., Cary, NC) and Statistical Package for the Social Sciences (SPSS) version 21 (IBM, Armonk, NY) were used to conduct the statistical analyses. P-values of < 0.05 was considered statistically significant.

Results

A total of 390 women met eligibility criteria for this study. The median distance of residence for all patients from our CCC was 58.9 miles (min, max: 1.2, 571 miles). Patients were divided into two strata by distance of < 100 and ≥ 100 miles (Table 1) with the two strata generally similar in demographic, tumor and treatment characteristics. When comparing women that lived closer than 100 miles versus greater, the majority of women were white (63.3 % vs. 64.5%; $p=0.447$), had squamous histology (78.5% vs. 66.7%, $p=0.055$), had similar stages at diagnosis with most having Stage I lesions (61% vs. 71%, $p=0.377$) and were never smokers (55.2% vs. 66.7%, $p=0.083$). The general pattern of spatial distribution of patients was depicted using a heat map (Figure 1).

Similar rates of recurrence were noted for patients in both strata based on distance less than and greater than 100 miles. Specifically, the recurrence rates for patients living less than 100 miles was 29.3% (87 of 297 patients) versus 29.0% (27 of 93 patients) ($p=0.657$) for those living further away. Unknown recurrence status was similar between groups, 1.7% versus 3.2 % ($p=0.657$) for patients living closer and further away respectively (Table 2). Recurrence therapies for the two groups were similar, with most patients (37.9% vs. 37.0%) receiving palliative chemotherapy; however, patients living <100 miles away were more likely to undergo radiation therapy for recurrence (13.8% vs. 0%), and those living ≥ 100 miles away were more likely to undergo other treatments such as an pelvic exenteration (25.9% vs 9.0%).

Although not statistically significant, median PFS for patients living ≥ 100 miles was less than those living < 100 miles away (72.1 vs. 92.3 months, $p=0.266$) (Figure 2). However, median OS for patients living ≥ 100 miles was worse than for those living <100 miles away (65.5 vs. 99.4 months, $p=0.040$) (Figure 3). Cox proportional hazard modeling noted that white race conferred a significantly lower risk for recurrence (hazard ratio [HR]=0.52, 95% confidence interval [CI] 0.34–0.79), while locally advanced stage disease including: Stage IB2 (HR 1.92, 95% CI 1.08–3.39), Stage IIA (HR 2.84, 95% CI 1.26–6.43), Stage IIB (HR 2.33, 95% CI 1.28–4.23), Stage IIIB (HR 3.44, 95% CI 1.65–7.18) and Stage IVA (HR 4.53, 95% CI 2.10–9.76) demonstrated higher risks of recurrence. Histology, smoking status, age, BMI and distance from our CCC were not associated with a higher risk of recurrence.

Likewise, age, body mass index, and race did not significantly affect overall survival, although non-squamous histology (HR 1.61, 95% CI 1.04–2.51) and current smoking (HR 1.70, 95% CI 1.18–2.45) were associated with worse survival. As expected, higher tumor stage was inversely associated with survival, with Stage IIIA (HR 4.19, 95% CI 1.78–7.82), Stage IIIB (HR 3.88, 95% CI 2.12–7.09) and IVA (HR 4.15, 95% CI 2.05–8.40) as well as distance greater than 100 miles from our CCC (HR 1.68, 95% CI 1.11–2.54) all having a statistically significant lower OS.

Discussion

In our retrospective cohort, we discovered significant survival differences for patients living ≥ 100 miles from our CCC. Despite having similar stage at first diagnosis, smoking status, BMI and histology, the median OS for patients living further than 100 miles away was approximately 34 months less than for patients living closer. Although not statistically significant, median PFS for patients living ≥ 100 miles was 20 months less than those living < 100 miles away. Importantly, unknown recurrence status, a potential source of bias for patients living further away and at greater risk for lost-to-follow-up, was similar for the two groups. Our study also demonstrated a higher risk of recurrence for non-white patients, which is consistent with previously published data on race and cervical cancer outcomes (11, 21).

Geographic distance from high-volume cancer centers has been shown to affect access to health care, utilization of care, and cancer survival outcomes in ovarian cancer (8, 11, 12). While geographic disparities have been previously studied for other gynecologic malignancies, there is limited data in cervical cancer. In a retrospective study of women receiving care for cervical cancer in Oklahoma, Gunderson et al. showed no difference in OS or PFS between women who traveled less than or more than 30 miles for treatment (9). Although a recent review of cervical cancer treatment for women from Maryland noted racial difference in treatment modalities, no impact of distance travelled for care was reported (13). The same group did, however, find that Medicare and uninsured patients with gynecologic cancer, including 34 with cervical cancer, traveled the greatest distance for care and that distance was directly correlated to completion of recommended therapy (14). In an evaluation of barriers to care for cervical cancer patients, Ramondetta et al. found that lack of access to reliable transportation was associated with higher stage at time of diagnosis, but did not specifically look at distance traveled for cancer care (15).

The poorer outcomes of patients living further away from a CCC as found in our study could be explained by multiple factors. While women all received initial treatment at our CCC (either surgery or radiation therapy), completion of their full treatment course for those requiring chemoradiation may be less likely for patients in the group living further away. Finding reliable transportation to drive greater than an hour to our facility may also be more difficult. It is difficult to determine whether patients receive high quality chemotherapy and radiation therapy at other locations across the state. Furthermore, communication about treatment planning between our CCC and those local providers is hampered by lack of streamlined electronic health records. Patients with recurrence in the group living further away may have received suboptimal initial treatment. The overall survival difference could also be explained by suboptimal treatment at the time of recurrence at outside facilities.

Studies evaluating geographic differences and survival outcomes in ovarian cancer patients have pointed to disparities in provider supply and access to health care as potential predictors for poorer survival (11, 16, 17, 6). Additionally, outreach efforts and utilization of patient navigators have been shown to improve geographic and racial disparities present in underserved populations (18). Ensuring early and uniform access to providers with expertise in the management of cervical cancer is the best way to ensure high-quality care (19). Navigation systems have been shown to improve access to tertiary care centers with fewer interruptions in treatment (20). Finally, improving electronic medical record efficiency and telecommunication systems to streamline care between rural areas and tertiary care centers, may also contribute to lessening the disparity related to distance from cancer centers (19). While our study is strengthened by review of data from a large-volume CCC, it is limited by the inherent biases associated with a retrospective study. Specific weaknesses of our study include the inability to account for potential confounding variables including medical comorbidities, patient socioeconomic status, economic trends over the study period, patient ability or willingness to travel, or the location and practices of rural clinics providing radiation or chemotherapies outside of the our system. Additionally, our small sample size may have contributed to an underpowered study, limiting our ability to detect statistically significant differences in outcomes.

Cervical cancer patients living a greater distance from our CCC appear to have inferior survival when compared to patients living within 100 miles. This difference in outcomes may be explained by differences in the patient characteristics in these two groups and the variability of facilities providing cancer treatment in our state. These results warrant further discussion of the importance of treating gynecologic cancer at high-volume tertiary care centers, or creating satellite cancer centers to increase access to care for women living in geographically remote areas. Analyses of statewide cancer data may allow determination of potential differences in patients referred to our institution, versus those referred to other regional institutions with similar services available. Additionally, future evaluation of the cost-effectiveness and feasibility of implementing interventions to improve access to care for patients in geographically isolated communities is needed. This could include utilizing patient navigators, partnering with primary care and advanced practice providers to improve gynecologic care in rural communities, and creating satellite cancer centers for oncologists to provide care in more geographically diverse areas.

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Research Highlights

- 1.** Cervical cancer patients living further from a CCC had worse overall survival.
- 2.** Standard clinical covariates had variable impacts on recurrence and survival
- 3.** Mechanisms to mitigate geographic disparities are needed and warrant further evaluation.

Figure 1.
Geographic distribution heat map of patient residences

Figure 2.
Progression-free survival based on distance from NCCN cancer center

Figure 3.
Overall survival based on distance from NCCN cancer center

Table 1

Population Characteristics based on Distance from Cancer Center

Patient Characteristics	Distance <100 miles N (%) (N=297)	Distance 100 miles N (%) (N=93)	P value
Mean Age ($\pm$ SD)	45.94 ($\pm$ 13.1)	44.24 ($\pm$ 11.8)	0.265
Mean BMI ($\pm$ SD)	28.62 ($\pm$ 8.5)	28.7 ($\pm$ 10.2)	0.952
Race			0.447
Black	90 (30.3)	24 (25.8)	
White	189 (63.3)	60 (64.5)	
Other	12 (4.0)	4 (4.3)	
Unknown	6 (2.0)	5 (5.38)	
Smoking			0.083
Never	164 (55.2)	62 (66.7)	
Current	112 (37.7)	21 (22.3)	
Former	13 (4.4)	6 (6.5)	
Unknown	8 (2.7)	4 (4.3)	
Stage			0.377
IA1	7 (2.4)	2 (2.2)	
IA2	13 (4.4)	3 (3.2)	
IB1	113 (38.0)	43 (46.2)	
IB2	48 (16.2)	18 (19.3)	
IIA	16 (5.4)	4 (4.3)	
IIB	52 (17.5)	8 (8.6)	
IIIA	6 (2.1)	1 (1.1)	
IIIB	32 (10.8)	7 (7.5)	
IVA	9 (3.0)	6 (6.5)	
Unknown	1 (0.34)	1 (1.1)	
Histology			0.055
Squamous	233 (78.5)	62 (66.7)	
Adenocarcinoma	38 (12.8)	15 (16.1)	
Adenosquamous	8 (2.7)	5 (5.4)	
Other	5 (1.7)	6 (6.5)	
Unknown	13 (4.4)	5 (5.4)	
Primary Therapy			0.221
Surgery	167 (56.0)	62 (66.7)	
XRT	13 (4.4)	3 (3.2)	
XRT + Chemo	114 (38.4)	26 (28.0)	
Chemotherapy	3 (1.0)	2 (2.2)	

Table 2

Recurrence Characteristics based on Distance from Cancer Center

	Distance <100 miles (N=297)	Distance 100 miles (N=93)	P Value
Recurrence	N(%)	N(%)	0.657
No	205 (69.0)	63 (67.7)	
Yes	87 (29.2)	27 (29.0)	
Unknown	5 (1.7)	3 (3.2)	
Recurrence Therapy	(N=87)	(N=27)	0.027
XRT	12 (13.8)	0 (0)	
XRT + Chemotherapy	12 (13.8)	3 (11.1)	
Chemotherapy	33 (37.9)	10 (37)	
Other	7 (9.0)	7 (25.9)	
None	23 (26.4)	6 (22.2)	
Unknown	0 (0.0)	1 (3.7)	

XRT = Radiation therapy