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Definitive radiation therapy for cervical cancer: Non-white race and public insurance are risk factors for delayed completion, a pilot study

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ABSTRACT

This is a pilot study to assess whether racial disparities exist in time to initiation and completion of external beam pelvic radiation therapy and brachytherapy in cervical cancers treated with definitive chemoradiation.

A retrospective analysis was conducted on all cervical cancer patients treated with definitive radiotherapy between 2006 and 2016 at a single institution. Patient demographics including age, race, insurance status and stage at diagnosis were obtained. Analyses were performed according to the following definitions of wait times: interval from pathologic diagnosis of cervical cancer to (Siegel et al., 2016) initiation of radiation therapy, (Yoo et al., 2017) completion of external beam radiation therapy and (DeSantis et al., 2016) completion of external beam radiation therapy plus brachytherapy if indicated.

Of 50 women, 21 self-identified as white, 25 as black and 4 as Hispanic. Due to small numbers, Hispanic women were included with black women as a non-white group. The average age was 52 years for women in this cohort. Mean days to initiation of radiation therapy were 41.8 days: 33.7 days among white patients versus 47.8 days for non-white patients (p-value 0.101). Mean days from diagnosis to completion of external beam pelvic radiation therapy were 81.3 days: 70.9 days among white patients versus 88.9 days among non-white patients (p-value 0.006). Non-white patients were more likely to have public insurance, which was also associated with a longer time to completion of radiation treatment.

We conclude that non-white patients experienced delays to completing external beam radiation therapy, which was no longer present after adjusting for insurance status.

1. Introduction

Cervical cancer is the most common gynecologic malignancy worldwide. In the United States, about 12,000 women are diagnosed annually and over 4000 die (Siegel et al., 2016). Screening strategies have resulted in a decline in the incidence and mortality of cervical cancer but racial disparities still exist. Black women in particular are twice as likely to die from cervical cancer as white women and the disparity is even greater in the Southern United States (Yoo et al., 2017; DeSantis et al., 2016). In fact, mortality rates when corrected for hysterectomy reveal an even greater disparity between Black and white women (Rositch et al., 2014). Previously underestimated by at least 44%, hysterectomy corrected mortality rates are reported as 10.1 per 100,000 for black women and 4.7 for white women (Beavis et al., 2017).

Several factors including differences in health care access, screening, follow up and treatment have been proposed to contribute to the disparity (Singh and Jemal, 2017; Yang et al., 2018; McDougall et al., 2007). Specifically, studies investigating disparities in standard of care for locally advanced cervical cancer treatment found that black race was associated with a lower likelihood of receiving pelvic external beam radiation therapy (EBRT) with concurrent chemotherapy and brachytherapy(Uppal et al., 2016; Robin et al., 2016). Here we seek to determine if race is a factor in delayed initiation and completion of primary pelvic external beam radiation therapy (EBRT) and brachytherapy in cervical cancer.

2. Methods

Approval for the study was obtained from the Institutional Review Board at Henry Ford Hospital. A retrospective chart review was completed for all patients with a diagnosis of cervical cancer from 2006 to 2016 in a single institution. Patients who had hysterectomy as primary treatment, radiation therapy as an adjuvant or palliative therapy or in whom cervical cancer was not the primary malignancy were excluded. Only patients who underwent primary chemo-radiation therapy under

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Table 1
Patient characteristics.

		Overall (N = 50)	Non-White (N = 29)	White (N = 21)	Comparison p-value
Age (years)		52.0 ± 14.2	51.8 ± 15.1	52.4 ± 13.2	0.871 (T)
Stage	IB	1	1	0	0.613 (CA)
	IB1	2	1	1	
	IB2	9	5	4	
	IIA	5	2	3	
	IIB	25	17	8	
	IIIA	1	0	1	
	IIIB	5	3	2	
	IVB	2	0	2	
Received Chemotherapy	No	6	5	1	0.380 (F)
	Yes	44	24	20	
Received Brachytherapy	No	15	9	6	0.552 (T)
	Yes	35	20	15	
Smoking Status	Never	14	8	6	0.040 (C)*
	Current	27	19	8	
	Former	9	2	7	
Insurance Status	None	3	2	1	0.020 (F)*
	Private	14	4	10	
	Public	33	23	10	
Side Effects	No	24	12	12	0.271 (C)
	Yes	26	17	9	
Tumor Board prior to Treatment	No	23	12	11	0.441 (C)
	Yes	27	17	10	
PET CT Prior to Treatment	No	4	4	0	0.129 (F)
	Yes	46	25	21	
Reason for Delay	None	33	13	20	< 0.001 (F)*
	Insurance	3	3	0	
	Compliance	14	13	1	

Numerical data is given as mean ± standard deviation and categorical data is given as frequency.
(W) = Wilcoxon Rank Sum Test, (T) = *t*-Test, (CA) = Cochran-Armitage Trend Test, (F) = Fisher Exact Test, (C) = Chi-Square Test.
* Statistically Significant, $p < .05$.

Table 2
Time to initiation, duration and completion of external beam radiation therapy and brachytherapy.

	Overall (N = 50)	Non-White (N = 29)	White (N = 21)	Comparison p-value
Days to Initiate Radiation Therapy	41.8 ± 28.7	47.6 ± 30.8	33.7 ± 23.8	0.101 (W)
External Beam Treatment Duration	39.7 ± 7.9	41.3 ± 9.3	37.5 ± 4.8	0.114 (W)
Days to External Beam Completion	81.3 ± 29.0	88.9 ± 30.4	70.9 ± 23.9	0.006 (W)*
Days to EBRT plus Brachytherapy Completion	95.0 ± 24.1	101.5 ± 28.5	86.4 ± 13.1	0.161 (W)
Duration of EBRT plus Brachytherapy	56.7 ± 7.5	56.2 ± 6.2	57.3 ± 9.1	0.683 (T)

All data is summarized as mean ± standard deviation.
(W) = Wilcoxon Rank Sum Test, (T) = Two-Sample *t*-Test.
* Statistically Significant, $p < .05$.

Table 3
Time to completion and duration of therapy based on insurance status.

	Insurance Type		Comparison P-value
	Private (N = 14)	Public (N = 33)	
Days to External Beam Completion	66.8 ± 13.8	88.5 ± 32.3	0.019 (W)*
Duration of EBRT plus Brachytherapy	58.8 ± 8.3	55.1 ± 7.1	0.188 (T)

All data is summarized as mean ± standard deviation.
(W) = Wilcoxon Rank Sum Test, (T) = Two-Sample *t*-Test.
* Statistically Significant, $p < .05$.

the care of a gynecologic oncologist were included. Stage at diagnosis, age, insurance status, smoking status, date of pathological diagnosis, date of initiation and date of completion of external beam radiation therapy were abstracted from chart review. Receipt of chemotherapy and/or brachytherapy, duration of brachytherapy and reported chemotherapy and radiation side effects were also abstracted from chart review. Presentation at multidisciplinary tumor board and PET CT imaging prior to treatment were also noted.

Analyses were performed according to the following distinct definitions of wait times: interval from pathologic diagnosis of cervical cancer to (Siegel et al., 2016) initiation of radiation therapy, (Yoo et al., 2017) completion of external beam radiation therapy and (DeSantis et al., 2016) completion of external beam radiation therapy plus brachytherapy. Treatment duration was also calculated as the time from initiation of external beam radiation therapy to completion of brachytherapy. To characterize reasons for delay, patients who had > 3 documented missed appointments or > 3 failed attempts at contact were categorized as delayed due non-compliance and patients who had documented issues with insurance coverage we categorized as delayed due to insurance. Analyses of times to completion were made using 2-sample *t*-tests if the means were normally distributed, if not the Wilcoxon rank sum test was used. Comparisons involving the categorical variables were made using chi-square tests in the absence of sparse data; otherwise, the Fisher exact test was used.

3. Results

A total of 50 women underwent primary external beam pelvic radiation therapy for cervical cancer at our institution over a 10-year

Table 4
Logistic regression of time intervals after adjusting for insurance status, side effects and tumor board presentation.

	P-value after adjusting for insurance status	P-value after adjusting for side effects	P-value after adjusting for tumor board
Days to Initiate Radiation Therapy	0.364	0.135	0.102
External Beam Treatment Duration	0.136	0.177	0.120
Days to External Beam Completion	0.100	0.035*	0.026*
Days to EBRT plus Brachytherapy Completion	0.186	0.075	0.089
Duration of EBRT plus Brachy	0.907	0.675	0.676

All data is summarized as mean ± standard deviation.
(W) = Wilcoxon Rank Sum Test, (T) = Two-Sample *t*-Test.
* Statistically Significant, $p < .05$.

period. Of 50 women, 21 self-identified as white, 25 as black and 4 as Hispanic. Due to small numbers, Hispanic women included with black women as a non-white group. The average age was 52 years for both white and non-white women in this cohort. Non-white women were more likely to be current smokers at the time of diagnosis than white women as summarized in Table 1. The most common stage at diagnosis was Stage IIB for both non-white and white women and there was no significant difference in stage at diagnosis. Chemotherapy and brachytherapy were completed at similar rates between both groups and there was no statistically significant difference in reported side effects in both groups. The frequency of tumor board presentation and PET CT imaging prior to treatment was similar between both groups. Reasons for delay were more likely to be documented as due to compliance or insurance issues in the non-white patients (p-value 0.001). Of the 46 women who were insured, non-white women were more likely to have public insurance than white women, (p-value 0.020) also summarized in Table 1.

Mean days to initiation and completion of radiation therapy are summarized in Table 2. White women had a mean of 33.7 days from diagnosis to initiation of therapy in comparison to non-white women with a mean of 47.6 days. There was no significant difference in time to initiate therapy. The mean number of days from diagnosis to completion of external beam radiation therapy for all women was 81.3 days with 70.9 days among white patients and 88.9 days among non-white (p-value 0.006). The frequency of brachytherapy completion was similar between both groups. The mean number of days from diagnosis to completion of brachytherapy was noted to be 86.4 days for white patients and 101.5 days for non-white patients (p-value 0.161) and duration of EBRT and brachytherapy both groups was also similar with a mean of 56.9 days.

Time to completion of therapy was also different based on insurance coverage type; the mean time to completion of external beam treatment was 66.8 days for the privately insured vs. 88.5 days for the publicly insured, (p-value 0.019) as outlined in Table 3. When insurance status, tumor board presentation and presence of side effects were adjusted for, only insurance status accounted for the difference in time to completion between both groups as described in Table 4.

4. Conclusion

Here we describe a group of 50 women with received primary chemoradiation for locally advanced cervical cancer. There was no racial difference in receipt of standard of care, defined as chemotherapy, external beam pelvic radiation and brachytherapy. For all patients, a mean of 41.8 days to initiate radiation therapy was noted. There is no standard for time from diagnosis to initiating treatment, however, a study investigating the timeliness of cervical cancer treatment initiation in the National Breast and Cervical Cancer Early Detection Program found the median time to initiation as 21–22 days in 1417 women (Benard et al., 2012). There was no racial difference in time to initiation of therapy and time to completion of treatment was not discussed in that study. The mean time to initiate radiation treatment was almost twice as long in our study for all patients with no difference in race detected. However, the time to complete external beam therapy was longer in our non-white patients. There was no difference in treatment duration between racial groups, suggesting that although time to initiate was not significantly different between groups, it likely contributed to delayed completion. Treatment duration of 56 days or less is recommended by Radiation Therapy Oncology Group and Gynecologic Oncology Group protocols and treatment duration of > 56 days is associated with higher risk of pelvic failure (Song et al., 2013; Petereit et al., 1995). Due to our small cohort of patients, we have limited ability to determine the effects of delayed completion of therapy on mortality rates or overall outcome. This pilot study can be used as a model for larger cohort studies to examine the effects of delayed initiation and completion of therapy on patient outcomes and mortality.

Reasons for delays included non-compliance (at times manifesting as inability to obtain transportation and childcare) insurance coverage issues and even incarceration in one instance. Non-white women in this study were more likely to be non-compliant and have public insurance. Public insurance status may reflect an underinsured population who only received insurance coverage after being diagnosed with cervical cancer. Among the patients who had no insurance (n = 3), treatments for two of these patients were fully funded through our charity care program. All patients with public insurance experienced delayed completion regardless of race and when insurance status was adjusted for, time to completion was similar between racial groups.

Delays determined to be due to insurance status and/or transportation issues often can be mitigated with social worker or patient navigator involvement. Patient navigation programs have proven to be helpful in decreasing delays to resolution of abnormal screening in African-American patients (Roland et al., 2017). To our knowledge, no studies have investigated the role of patient navigation programs in decreasing time to completion of cervical cancer treatment; however, studies have shown an increase in mortality in cervical cancer patients who have public insurance(Churilla et al., 2016). This study outlines a disparity in time to complete standard of care treatment for cervical cancer in non-white patients and those with public insurance. We suggest further studies to determine significant causes for delays and intervention programs to decrease time to completion of treatment for advanced cervical cancer with hopes of closing the gap of racial disparities.

Conflicts of interest

No conflicts of interest to disclose.

References

Beavis, A.L., Gravitt, P.E., Rositch, A.F., 2017. Hysterectomy-corrected cervical cancer mortality rates reveal a larger racial disparity in the United States. Cancer 123 (6), 1044–1050.
Benard, V.B., Howe, W., Royalty, J., Helsel, W., Kammerer, W., Richardson, L.C., 2012. Timeliness of cervical cancer diagnosis and initiation of treatment in the National Breast and Cervical Cancer Early Detection Program. J. Women's Health 21 (7), 776–782.
Churilla, T., Egleston, B., Dong, Y., Shaikh, T., Murphy, C., Mantia-Smaldone, G., et al., 2016. Disparities in the management and outcome of cervical cancer in the United

States according to health insurance status. Gynecol. Oncol. 141 (3), 516–523.
Desantis, C.E., Siegel, R.L., Sauer, A.G., Miller, K.D., Fedewa, S.A., Alcaraz, K.I., et al., 2016. Cancer statistics for African Americans, 2016: progress and opportunities in reducing racial disparities. CA Cancer J. Clin. 66 (4), 290–308.
Mcdougall, J.A., Madeleine, M.M., Daling, J.R., Li, C.I., 2007. Racial and ethnic disparities in cervical cancer incidence rates in the United States, 1992-2003. Cancer Causes Contr. 18 (10), 1175–1186.
Petereit, D.G., Sarkaria, J.N., Chappell, R., Fowler, J.F., Hartmann, T.J., Kinsella, T.J., et al., 1995. The adverse effect of treatment prolongation in cervical carcinoma. Int. J. Radiat. Oncol. Biol. Phys. 32 (5), 1301–1307.
Robin, T.P., Amini, A., Schefter, T.E., Behbakht, K., Fisher, C.M., 2016. Disparities in standard of care treatment and associated survival decrement in patients with locally advanced cervical cancer. Gynecol. Oncol. 143 (2), 319–325.
Roland, K.B., Milliken, E.L., Rohan, E.A., Degroff, A., White, S., Melillo, S., et al., 2017. Use of community health workers and patient navigators to improve cancer outcomes among patients served by federally qualified health centers: a systematic literature review. Health Equity 1 (1), 61–76.
Rositch, A.F., Nowak, R.G., Gravitt, P.E., 2014. Increased age and race-specific incidence of cervical cancer after correction for hysterectomy prevalence in the United States from 2000 to 2009. Cancer 120 (13), 2032–2038.
Siegel, R.L., Miller, K.D., Jemal, A., 2016. Cancer statistics, 2016. CA Cancer J. Clin. 66 (1), 7–30.
Singh, G.K., Jemal, A., 2017. Socioeconomic and racial/ethnic disparities in cancer mortality, incidence, and survival in the United States, 1950–2014: over six decades of changing patterns and widening inequalities. J. Environ. Public Health 2017, 2819372.
Song, S., Rudra, S., Hasselle, M.D., Dorn, P.L., Mell, L.K., Mundt, A.J., et al., 2013. The effect of treatment time in locally advanced cervical cancer in the era of concurrent chemoradiotherapy. Cancer 119 (2), 325–331.
Uppal, S., Del Carmen, M.G., Rice, L.W., Reynolds, R.K., Jolly, S., Bregar, A., et al., 2016. Variation in care in concurrent chemotherapy administration during radiation for locally advanced cervical cancer. Gynecol. Oncol. 142 (2), 286–292.
Yang, D.X., Soulos, P.R., Davis, B., Gross, C.P., Yu, J.B., 2018. Impact of widespread cervical cancer screening: number of cancers prevented and changes in race-specific incidence. Am. J. Clin. Oncol. 41 (3), 289–294 (2018 Mar).
Yoo, W., Kim, S., Huh, W.K., Dilley, S., Coughlin, S.S., Partridge, E.E., et al., 2017. Recent trends in racial and regional disparities in cervical cancer incidence and mortality in United States. PLoS One 12 (2), e0172548.