Race- and Age-Related Disparities in Cervical Cancer Mortality

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ABSTRACT

Background: Although the incidence of cervical cancer among younger Black women is now equivalent to that of White women, it is unknown whether the reduced incidence has affected survival rates among younger Black women. The goal of this study was to assess differences in survival by age and race. **Patients and Methods:** A retrospective cohort study was performed using the National Cancer Database to analyze women with nonmetastatic cervical cancer diagnosed between 2004 and 2014. Women with unknown survival data and those who died within 3 months of diagnosis were excluded. Multivariable logistic regression models evaluated interactions between age and race (Black vs non-Black) for presentation with stage I disease and receipt of optimal treatment. A multivariable Cox regression model was used to evaluate survival differences by age and race. **Results:** Of 55,659 women included, 16.4% were Black. Compared with their non-Black counterparts, fewer Black women presented with stage I disease (37.8% vs 47.8%; $P < .01$) and received optimal treatment (46.2% vs 58.3%; $P < .01$). Fewer Black women had private insurance if they were aged ≤ 65 years (39.6% vs 55.7%; $P < .01$), but not if they were aged ≥ 65 years (11.7% vs 12.4%; $P = .43$). According to multivariable logistic regression, Black women aged ≤ 39 years were less likely to present with stage I disease, with a significant interaction term between age and race ($P < .01$ for interaction). Disparities in overall survival by race were greatest for Black women aged ≤ 39 years (adjusted hazard ratio, 1.32; 95% CI, 1.20–1.46; $P < .01$) but decreased with increasing age interval until no disparity was noted for women aged ≥ 65 years ($P < .01$ for interaction). **Conclusions:** Younger Black women with cervical cancer are at risk for presenting with higher-stage disease and having worse overall survival. These findings may be related to insurance-related disparities and inadequate follow-up for abnormal Papanicolaou test results. Younger Black women with cervical cancer may be a particularly vulnerable population.

J Natl Compr Canc Netw 2021;19(7):789–795
doi: 10.6004/jnccn.2020.7665

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Background

Black women have the highest incidence of and mortality from cervical cancer in the United States.^{1,2} Minority women with cervical cancer are often diagnosed at a higher stage than White women³ and are less likely to receive optimal treatment when controlling for confounding factors.^{4,5} Drivers of these racial inequities in care are numerous but include historical differences in Papanicolaou (Pap) screening and follow-up for abnormal Pap test results^{6,7} and social determinants of health, including inadequate insurance coverage, lack of transportation, and financial strain.^{8,9}

Little is known about cervical cancer among younger Black women in the United States, who are at higher risk than older Black women of being uninsured or underinsured.¹⁰ Although the disparity in cervical cancer incidence among younger Black women versus White women has been eliminated since 2005,¹¹ it is not clear whether this has translated into improved survival for younger Black women. The goal of this study was to assess differences in receipt of optimal treatment for cervical cancer and survival by age and race.

Patients and Methods

We performed a retrospective cohort study of women who were diagnosed with nonmetastatic cervical cancer (stage IA–IVA) and received treatment at a National Cancer Database (NCDB) reporting facility between January 1, 2004, and December 31, 2014 (see supplemental eFigure 1, available with this article at JNCCN.org). The NCDB collects data from approximately 1,500 cancer programs accredited by the American College of Surgeons' Commission on Cancer. Approximately 70% of all US patients diagnosed with cancer are recorded in the NCDB, which is a hospital-based registry.¹²

Women with unknown survival data and those who died within 3 months of diagnosis were excluded, because these women may have died of treatment-related complications rather than cervical cancer (supplemental

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eFigure 1). Histology was defined as squamous cell histology and nonsquamous cell histology. Squamous cell histology was defined as codes 8070, 8071, 8072, 8073, 8074, 8075, and 8076, which are all the existing codes for squamous cell histology according to the ICD-O-3. Stage is entered into the NCDB using the *AJCC Cancer Staging Manual* edition that was in use at time of diagnosis. Race was defined as Black or non-Black race, given previous data suggesting similar survival rates for Hispanic and Asian patients compared with White patients.^{13,14} Optimal treatment was defined as receipt of surgery or radiation therapy (RT), including brachytherapy for patients with stage IA–IB1 or IIA1 disease. For stage IB2, IIA2, or IIB–IVA or node-positive disease, optimal treatment was defined as receipt of RT and chemotherapy.

Statistical analyses were performed using R version 3.5.0 (R Foundation for Statistical Computing). A *P* value of .05 was set as the threshold for statistical significance. Multivariable logistic regression models were used to evaluate interactions between age and race (Black vs non-Black) for presentation with stage I disease, receipt of optimal treatment, and odds of having private insurance. The following baseline variables were included in the model: age (≤ 39 , 40–49, 50–64, or ≥ 65 years), race per age interval (Black or non-Black), stage (I, II, III, or IVA), year of diagnosis (2004–2009 or 2010–2014), histology (squamous or nonsquamous), Charlson-Deyo comorbidity score (0, 1, or ≥ 2), insurance status (private, government, noninsured, or unknown), and facility volume (high or low). High-volume facilities were defined as hospitals that are ranked ≥ 90 th percentile for patient volume, whereas low-volume facilities were defined as those ranked < 90 th percentile. Interaction *P* values were calculated to determine the relationship between race per age interval and odds of having stage I disease, odds of receiving optimal treatment, and odds of having private insurance.

To evaluate the interaction between age and race on survival, a multivariable Cox regression model was used, controlling for age, Black race per age interval, stage, optimal treatment, year of diagnosis, histology, Charlson-Deyo comorbidity score, insurance status, and facility volume. Overall survival (OS) was determined for the study population overall, for those who received optimal treatment, and for those who had nonoptimal treatment. Interaction *P* values were calculated to determine the relationship between race per age interval and OS.

In addition, treatment disparities were further assessed by determining rates of adverse pathology (eg, positive margins or pathologic nodal involvement) among Black and non-Black women who received surgery to determine if rates of postoperative RT differed by race. Completion of RT within 8 weeks was also compared by race using chi-square analysis because prior data showed worse

Table 1. Demographic and Treatment Characteristics of the Study Population

Clinical Factor	Non-Black n (%)	Black n (%)	P Value
Total, N	46,506	9,153	
Age, y			<.01
≤ 39	11,486 (24.70%)	1,960 (21.41%)	
40–49	12,293 (26.43%)	2,308 (25.22%)	
50–64	14,189 (30.51%)	2,959 (32.33%)	
≥ 65	8,538 (18.36%)	1,926 (21.04%)	
Cancer stage			<.01
I	22,235 (47.81%)	3,458 (37.78%)	
II	10,706 (23.02%)	2,282 (24.93%)	
III	12,115 (26.05%)	3,079 (33.64%)	
IVA	1,450 (3.12%)	334 (3.65%)	
Year of diagnosis			<.01
2004–2009	18,603 (40.00%)	3,974 (43.42%)	
2010–2014	27,903 (60.00%)	5,179 (56.58%)	
Histology			<.01
Squamous	24,978 (53.71%)	5,873 (64.16%)	
Nonsquamous	21,528 (46.29%)	3,280 (35.84%)	
Charlson-Deyo comorbidity score			<.01
0	40,315 (86.69%)	7,420 (81.07%)	
1	5,000 (10.75%)	1,271 (13.89%)	
≥ 2	1,191 (2.56%)	462 (5.05%)	
Insurance			<.01
Private	22,198 (47.73%)	3,087 (33.73%)	
Government	18,798 (40.42%)	4,828 (52.75%)	
None	4,483 (9.64%)	990 (10.82%)	
Unknown	1,027 (2.21%)	248 (2.71%)	
Facility volume ^a			<.01
High	20,379 (43.82%)	4,616 (50.43%)	
Low	26,127 (56.18%)	4,537 (49.57%)	
Treatment type			<.01
Surgery	20,301 (43.65%)	2,739 (29.92%)	
Radiotherapy	23,905 (51.40%)	5,792 (63.28%)	
None	2,300 (4.95%)	622 (6.80%)	
Optimal treatment			<.01
Yes	27,117 (58.31%)	4,224 (46.15%)	
No	19,389 (41.69%)	4,929 (53.85%)	

^aHigh-volume facilities were defined as those facilities that are ranked ≥ 90 th percentile for patient volume, and low-volume facilities were considered those ranked < 90 th percentile.

outcomes, including diminished locoregional control and possibly worse OS when RT is completed in > 8 weeks.^{15–18} NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Cervical Cancer also recommend that RT be completed within 8 weeks based on these data.¹⁹

Results

A total of 105,766 women with cervical cancer were diagnosed between 2004 and 2014 and recorded in the NCDB. We excluded 42,185 patients with metastatic disease and 7,922 with unknown survival data or who died within 3 months of diagnosis (supplemental eFigure 1). The final cohort consisted of 55,659 women, 9,153 (16.4%) of whom were Black. Compared with their non-Black counterparts, fewer Black women presented with stage I disease (37.8% vs 47.8%, respectively; $P < .01$) and received optimal treatment (46.2% vs 58.3%; $P < .01$) (Table 1). Fewer Black women had private insurance if aged <65 years (39.6% vs 55.7%; $P < .01$) but not if aged ≥ 65 years (11.7% vs 12.4%; $P = .43$). Figure 1 shows differences in private insurance, stage I disease, and optimal treatment among Black versus non-Black patients by age.

Multivariable logistic regression (Table 2) revealed that the interaction between age and race was significant for presentation with stage I disease, with Black women aged ≤ 39 years being less likely to present with stage I disease (adjusted odds ratio, 0.65; $P < .01$). The interaction between age and race was not significant for receipt of optimal treatment, although Black women of all ages were less likely to receive optimal treatment.

Multivariable Cox regression revealed that disparities in OS by race were greatest for Black women aged ≤ 39 years (adjusted hazard ratio [aHR], 1.32; 95% CI, 1.20–1.46; $P < .01$) but decreased with increasing age interval until no disparity was noted for women aged ≥ 65 years (Table 3). The interaction between age and race was significant ($P < .01$ for interaction) (Figure 2). When the analysis was restricted to women who received optimal treatment, this interaction was no longer significant ($P = .61$). However, there remained a non-significant survival disparity for women aged ≤ 39 years who received optimal treatment (aHR, 1.18; 95% CI, 1.00–1.39; $P = .06$).

Further analysis of treatment disparities revealed similar rates of adverse pathology (eg, positive margins or pathologic nodal involvement) between Black and non-Black women who received optimal treatment with surgery (13.4% vs 13.6%; $P = .81$). However, Black women were less likely to receive postoperative RT for adverse pathology (51.3% vs 59.6%; $P < .01$). Furthermore, Black women who received optimal treatment with RT were less likely to complete treatment in ≤ 8 weeks (45.2% vs 50.0%; $P < .01$).

Discussion

Our findings showed significant differences in optimal treatment and survival by race and age. Younger Black women were less likely to present with stage I disease, and there was a persistent survival disparity in younger Black women in the setting of treatment disparities. Even when they received optimal treatment according to NCCN Guidelines, younger Black women were more likely to experience delays in the receipt of RT and less likely to even undergo RT if adverse pathology was detected at the time of surgery. This is consistent with prior work suggesting that treatment-related disparities may mediate survival differences in Black women with cervical cancer.^{4,20}

Younger Black women in our study were less likely than younger non-Black women to present with stage I disease. This suggests that there remain inadequacies in follow-up for abnormal Pap test results among younger Black women in particular, leading to diagnosis at later stages. Prior studies have shown that minority women have lower rates of follow-up for abnormal Pap test results and lower rates of colposcopy.^{7,21} Younger Black women were also less likely than older Black women to have private insurance in our study. Therefore, it is possible that insurance status may also be contributing to lack of abnormal Pap test follow-up in underinsured younger Black women.

Figure 1. Differences in (A) private insurance, (B) stage I disease, and (C) optimal treatment among Black versus non-Black patients by age.

Table 2. Odds of Stage I Disease, Optimal Treatment, and Private Insurance by Race and Age Interval

Clinical Factor	Stage I Disease		Optimal Treatment		Private Insurance	
	aOR (95% CI)	P Value	aOR (95% CI)	P Value	aOR (95% CI)	P Value
Age, y						
≤39	Ref		Ref		Ref	
40–49	0.55 (0.52–0.58)	<.01	1.07 (1.01–1.14)	.02	1.14 (1.09–1.21)	<.01
50–64	0.32 (0.30–0.33)	<.01	0.90 (0.85–0.95)	<.01	1.14 (1.09–1.21)	<.01
≥65	0.30 (0.28–0.32)	<.01	0.63 (0.59–0.68)	<.01	0.13 (0.12–0.14)	<.01
Effect of Black race per age interval, y						
≤39	0.65 (0.59–0.72)	<.01	0.73 (0.65–0.81)	<.01	0.58 (0.52–0.64)	<.01
40–49	0.79 (0.71–0.86)	<.01	0.68 (0.61–0.75)	<.01	0.62 (0.56–0.68)	<.01
50–64	0.91 (0.83–0.99)	.03	0.76 (0.69–0.83)	<.01	0.57 (0.53–0.62)	<.01
≥65	0.78 (0.70–0.88)	<.01	0.67 (0.60–0.76)	<.01	1.02 (0.88–1.19)	.77
Cancer stage						
I	—	—	Ref		Ref	
II	—	—	0.16 (0.15–0.17)	<.01	0.59 (0.57–0.62)	<.01
III	—	—	0.10 (0.09–0.10)	<.01	0.54 (0.52–0.57)	<.01
IVA	—	—	0.05 (0.04–0.06)	<.01	0.43 (0.39–0.48)	<.01
Year of diagnosis						
2004–2009	Ref		Ref		Ref	
2010–2014	2.17 (2.09–2.26)	<.01	1.25 (1.20–1.30)	<.01	0.89 (0.86–0.92)	<.01
Histology						
Squamous	Ref		Ref		Ref	
Nonsquamous	2.06 (1.99–2.14)	<.01	1.13 (1.09–1.18)	<.01	1.39 (1.34–1.44)	<.01
Charlson-Deyo comorbidity score						
0	Ref		Ref		Ref	
1	1.13 (1.06–1.19)	<.01	1.04 (0.98–1.11)	.22	0.76 (0.71–0.80)	<.01
≥2	1.14 (1.03–1.27)	.02	0.66 (0.58–0.74)	<.01	0.44 (0.39–0.50)	<.01
Insurance						
Private	Ref		Ref		—	—
Government	0.59 (0.56–0.61)	<.01	0.82 (0.78–0.86)	<.01	—	—
None	0.45 (0.43–0.48)	<.01	0.66 (0.62–0.71)	<.01	—	—
Unknown	0.65 (0.57–0.73)	<.01	0.42 (0.37–0.49)	<.01	—	—
Facility volume ^a						
High	Ref		Ref		Ref	
Low	1.06 (1.02–1.10)	<.01	0.76 (0.73–0.79)	<.01	1.35 (1.30–1.40)	<.01
Intercept	1.09 (1.03–1.15)	<.01	6.00 (5.60–6.43)	<.01	1.25 (1.18–1.32)	<.01
Interaction P value	<.01		.36		.01	

Abbreviation: aOR, adjusted odds ratio.

^aHigh-volume facilities were defined as those facilities that are ranked ≥90th percentile for patient volume, and low-volume facilities were considered those ranked <90th percentile.

We also found that disparities in OS by race were greatest for Black women aged ≤39 years and that disparities diminished with increasing age, until no disparity was noted for Black women aged ≥65 years. When restricted to women who received optimal

treatment, the interaction between race and age was no longer significant despite maintaining a large sample size in this analysis (n=31,341). Therefore, our study also highlights the importance of access to quality treatment, because disparities in OS by race and age were noted

Table 3. Overall Survival by Optimal and Nonoptimal Treatment

Clinical Factor	All (N=55,659)		Optimal Treatment (n=31,341)		Nonoptimal Treatment (n=24,318)	
	aHR	P Value	aHR	P Value	aHR	P Value
Age, y						
≤39	Ref		Ref		Ref	
40–49	1.15 (1.09–1.22)	<.01	1.17 (1.07–1.28)	<.01	1.14 (1.06–1.23)	<.01
50–64	1.33 (1.26–1.41)	<.01	1.40 (1.29–1.53)	<.01	1.26 (1.18–1.36)	<.01
≥65	2.03 (1.92–2.15)	<.01	2.14 (1.95–2.34)	<.01	1.92 (1.78–2.06)	<.01
Effect of Black race per age interval, y						
≤39	1.32 (1.20–1.46)	<.01	1.18 (1.00–1.39)	.06	1.35 (1.20–1.52)	<.01
40–49	1.20 (1.10–1.30)	<.01	1.10 (0.95–1.27)	.21	1.21 (1.10–1.34)	<.01
50–64	1.14 (1.06–1.21)	<.01	1.07 (0.95–1.20)	.27	1.16 (1.07–1.25)	<.01
≥65	1.02 (0.95–1.09)	.66	1.02 (0.88–1.17)	.83	1.03 (0.95–1.11)	.53
Cancer stage						
I	Ref		Ref		Ref	
II	1.90 (1.81–1.99)	<.01	2.44 (2.28–2.61)	<.01	1.28 (1.20–1.37)	<.01
III	3.29 (3.14–3.44)	<.01	4.32 (4.05–4.61)	<.01	2.22 (2.09–2.36)	<.01
IVA	5.16 (4.81–5.54)	<.01	5.80 (4.91–6.85)	<.01	3.63 (3.34–3.95)	<.01
Optimal treatment						
No	Ref		—	—	—	—
Yes	0.64 (0.62–0.66)	<.01	—	—	—	—
Year of diagnosis						
2004–2009	Ref		Ref		Ref	
2010–2014	0.81 (0.78–0.84)	<.01	0.85 (0.81–0.90)	<.01	0.80 (0.77–0.83)	<.01
Histology						
Squamous	Ref		Ref		Ref	
Nonsquamous	1.09 (1.05–1.12)	<.01	1.07 (1.01–1.12)	.02	1.11 (1.07–1.16)	<.01
Charlson-Deyo comorbidity score						
0	Ref		Ref		Ref	
1	1.27 (1.22–1.33)	<.01	1.29 (1.20–1.39)	<.01	1.26 (1.20–1.33)	<.01
≥2	1.71 (1.59–1.83)	<.01	1.83 (1.60–2.09)	<.01	1.65 (1.52–1.80)	<.01
Insurance						
Private	Ref		Ref		Ref	
Government	1.34 (1.30–1.39)	<.01	1.38 (1.30–1.46)	<.01	1.30 (1.24–1.37)	<.01
None	1.20 (1.13–1.26)	<.01	1.19 (1.08–1.31)	<.01	1.17 (1.09–1.25)	<.01
Unknown	1.05 (0.95–1.17)	.32	1.11 (0.90–1.36)	.34	1.02 (0.90–1.14)	.80
Facility volume ^a						
High	Ref		Ref		Ref	
Low	1.07 (1.04–1.11)	<.01	1.11 (1.05–1.16)	<.01	1.06 (1.02–1.10)	<.01
Interaction P value	<.01		.61		<.01	

Abbreviation: aHR, adjusted hazard ratio.

^aHigh-volume facilities were defined as those facilities that are ranked ≥90th percentile for patient volume, and low-volume facilities were considered those ranked <90th percentile.

among those who did not receive optimal treatment. We also found that Black women were less likely to receive postoperative RT for adverse pathology and that those who did receive RT were less likely to complete treatment in ≤ 8 weeks. Multiple factors contribute to the ability of patients to receive optimal treatment, including distance to treatment centers, hospital volume of those centers, and patient finances, insurance status, comorbidities, education, and health literacy.^{4,9,20,22–26} Minority women may have more barriers to receiving treatment, including difficulty in assuring transportation, diminished ability to take time away from family or work responsibilities, financial strain, and poor understanding of the importance or significance of treatments.

Because of the retrospective nature of our study, we were unable to determine the exact cause of these treatment-related disparities; however, it is interesting that younger Black women were less likely to have private insurance and had worse OS in our study. We also found that both women with government insurance and uninsured women were at higher risk of mortality. Insurance-related disparities were an important predictor of outcomes among minority women in prior studies.²⁰ In the United States, Black women are more likely than women of other races to be unemployed or to hold low-wage jobs that do not provide health benefits.²⁷ Therefore, >3.3 million Black women (or 1 in 4 nationally) are covered by Medicaid. On the one hand, younger, underinsured Black women, especially those who live in states that did not expand Medicaid with the Affordable Care Act, may encounter delays in obtaining insurance coverage and ultimately cancer screening and treatment.²⁸ On the other hand, older Black women aged ≥ 65 years may not encounter such delays, because many are already enrolled in Medicare. Health insurance coverage among Black women varies in the United States by age: although 98.4% of Black women aged ≥ 65 years are insured, only 87.7% aged 18 to 64 years have coverage.²⁹ In addition, in many states, emergency insurance coverage can be enacted when cervical cancer is diagnosed, but significant delays in receiving coverage may be encountered, with reports of delays of up to 4 months for some patients.²⁶ Furthermore, the complexity of signing up for insurance plans in the United States may impact the ability of minority women to receive timely care. Signing up for emergency coverage after a cancer diagnosis may explain why uninsured women and women with government insurance had similar poor survival outcomes in our study, given that the NCDB does not capture data regarding who received emergency coverage for treatment. Treatment delays in minority women have been associated with increased mortality in prior

Figure 2. Overall survival by race and age interval.

studies.³⁰ Thus, lack of insurance and/or delays in receipt of emergency insurance coverage may also contribute to the survival disparities noted in this study among younger Black women.

Conclusions

This study suggests that younger Black women are at higher risk of presentation with later-stage cervical cancer, suboptimal treatment of cervical cancer, and increased mortality compared with their non-Black counterparts. Multiple factors may contribute to these findings, including inadequate healthcare coverage among younger Black women, who may be a particularly vulnerable population. Improving follow-up for abnormal Pap test results and access to universal health insurance may help reduce treatment and survival disparities in this at-risk population.

Acknowledgments

The authors acknowledge Brandon Mahal, MD, in the Department of Radiation Oncology at Brigham and Women's Hospital, for his contributions in reviewing the manuscript. No compensation was received for his role.

Submitted June 11, 2020; final revision received September 28, 2020; accepted for publication September 29, 2020. Published online April 1, 2021.

Author contributions: Study concept: Alimena, Pachigolla, Feldman, Lee, King. Data curation: Yang, Orio, Lee, King. Formal analysis: Lee, King. Investigation: Alimena, Pachigolla, Lee, King. Methodology: Lee, King. Writing – original draft: Alimena, Pachigolla. Writing – review and editing: All authors.

Disclosures: The authors have disclosed that they have not received any financial considerations from any person or organization to support the preparation, analysis, results, or discussion of this article

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Race- and Age-Related Disparities in Cervical Cancer Mortality

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J Natl Compr Canc Netw 2021;19(7):789–795

eFigure 1: Inclusion and Exclusion Criteria

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Abbreviation: NCDB, National Cancer Database.