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Journal
Obstetrics and Gynecology, 131(5)

ISSN
1099-3630

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Publication Date
2018-05-01

DOI
10.1097/aog.0000000000002591

Peer reviewed

Published in final edited form as:
Obstet Gynecol. 2018 May ; 131(5): 899–908. doi:10.1097/AOG.0000000000002591.

Disparities in Adherence to National Comprehensive Cancer Network Treatment Guidelines and Survival for Stage IB-IIA Cervical Cancer in California

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Abstract

Objective—To evaluate the association of sociodemographic and hospital characteristics with adherence to National Comprehensive Cancer Network (NCCN) treatment guidelines for stage IB-IIA cervical cancer and to analyze the relationship between adherent care and survival.

Methods—This is a retrospective population-based cohort study of stage IB-IIA invasive cervical cancer cases reported to the California Cancer Registry from January 1, 1995, through December 31, 2009. Adherence to NCCN guideline care was defined by year- and stage-appropriate surgical procedures, radiation, and chemotherapy. Multivariate logistic regression, Kaplan-Meier estimate, and Cox proportional hazards models were used to examine associations between patient, tumor, and treatment characteristics and NCCN guideline adherence and cervical cancer-specific 5-year survival.

Results—A total of 6,063 patients were identified. Forty-seven percent received NCCN guideline-adherent care and 18.8% were treated in high-volume centers (≥20 cases per year). On multivariate analysis, lowest socioeconomic status (aOR 0.69, 95% CI 0.57-0.84), low-middle socioeconomic status (aOR 0.76, 95% CI 0.64-0.92), and Charlson-Deyo comorbidity score ≥1 (aOR 0.78, 95% CI 0.69-0.89) were patient characteristics associated with receipt of nonguideline

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Presented at the 2017 Society of Gynecologic Oncology Annual Meeting on Women's Cancer Scientific Plenary III, March 13, 2017, National Harbor, MD.

Financial Disclosure
The authors did not report any potential conflicts of interest.

Each author has indicated that he or she has met the journal's requirements for authorship.

care. Receiving adherent care was less common in low-volume centers (45.9%) than in high-volume centers (50.9%) (effect size=0.90, 95% CI 0.84-0.96). Death from cervical cancer was more common in the non-adherent group (13.3%) than in the adherent group (8.6%) (effect size=1.55, 95% CI 1.34-1.80). Black race (aHR 1.56, 95% CI 1.08-2.27), Medicaid payer status (aHR 1.47, 95% CI 1.15-1.87), and Charlson-Deyo comorbidity score ≥1 (aHR 2.07, 95% CI 1.68-2.56) were all associated with increased risk of dying from cervical cancer.

Conclusion—Among patients with early-stage cervical cancer, NCCN guideline nonadherent care was independently associated with increased cervical cancer-specific mortality, along with Black race, and Medicaid payer status. Nonadherence was more prevalent in patients with older age, lower socioeconomic status, and receipt of care in low-volume centers. Attention should be paid to increase guideline adherence.

Introduction

While predominantly a disease of women in low and middle-income countries where cervical cancer screening is not widely available,[1] 13,240 new cases and 4,170 cervical cancer-related deaths are expected in the United States in 2018.[2] Five-year relative survival rates in the United States for cervical cancer have remained stagnant over the last 35 years (69.1% in 1975-1977, 68.8% in 2007-2013), while rates for breast cancer (74.8% in 1975-1977, 91.1% in 2007-2013) and ovarian cancer (36.0% in 1975-1977, 46.7% 2007-2013) have improved.[3]

Women from minority and socioeconomically disadvantaged groups have decreased access to screening, increased incidence, later stage at diagnosis, and higher mortality from cervical cancer; these issues, along with decreased receipt of guideline-adherent care, are thought to explain poorer cervical cancer survival for this population.[3–21]

Receipt of guideline-adherent treatment is associated with improved survival for locally advanced cervix cancer[22] and other cancers, including ovarian cancer.[23] However, there are limited data regarding association of guideline-adherent treatment to survival for early stage cervical cancer patients; in fact, there are no papers of this subject in English language literature in recent years. We hypothesized that 5-year survival for early stage cervical cancer patients would be higher for those receiving NCCN guideline-adherent care. Thus, studying women with stage IB-IIA cervical cancer in California, our primary objective was to determine whether National Comprehensive Cancer Network (NCCN) guideline adherence was associated with improved survival. Our secondary objective was to evaluate the association of sociodemographic and hospital characteristics with adherence to NCCN treatment guidelines.

Materials and Methods

This was a retrospective population-based cohort study of new cervical cancer cases diagnosed and reported to the California Cancer Registry (CCR) from January 1, 1995, through December 31, 2009. Incident cases from 1995 through 2009 were requested to ensure an adequate sample size within a time of relatively unchanged treatment paradigm, and to enable the evaluation of 5-year survival, with initial data analysis performed in 2016.

Since 1988, standardized data collection and quality control measures have been in place and it has been legally mandated that every cancer diagnosis in California is reported to the CCR. Within 18 months of the end of a calendar year, completeness of case reporting exceeds 95% in the CCR.[24] This statewide population-based cancer surveillance system provided the opportunity for data linkage to Office of Statewide Health Planning and Development (OSHPD) hospital discharge data for our cohort. The OSHPD database contains International Classification of Disease (ICD) diagnosis information and inpatient discharge data for each admission to a licensed hospital in California. The Surveillance, Epidemiology, and End Results (SEER) primary site codes for cervical cancer (C530-C539) were used to identify incident cervical cancer cases for inclusion in our study cohort. The study was approved by the institutional review board of the University of California, Irvine (HS#2014-1527) and the State of California Health and Human Services Agency Committee for the Protection of Human Subjects (15-02-1867).

The study included women 18 years of age or older in whom invasive cervical cancer was the first or only cancer diagnosis using the ICD-9 before 1999 and ICD-10 for 1999 and later. A total of 22,975 incident cases of cervical cancer were identified with follow up through May 2015. Among these, a total of 6,063 cases of stage IB-IIA cervical cancer were identified after excluding pre-invasive disease, stage IA, stage IIB or greater, unknown stage, incomplete stage information and diagnosis at autopsy (Figure 1). Stage IA cases were excluded due to inability of the database to differentiate between stage IA1 and IA2, which have different NCCN guideline treatment recommendations. The database did not differentiate between stage IB1 and IB2, however overlap in guideline care was deemed sufficient to group these patients together.

Explanatory variables included patient, tumor and hospital characteristics. Patient variables included age at diagnosis, year of diagnosis, race, ethnicity, insurance payer, socioeconomic status, marital status, and health status (Charlson-Deyo comorbidity score). Age at diagnoses was used both as a continuous variable and as a categorical variable with three groups: 18 to 39 years of age, 40 to 64 years of age, and 65 years of age and older. Race and ethnicity of the patient was categorized into five groups: non-Hispanic white, non-Hispanic black, Hispanic, Asian or Pacific Islander, and other. Insurance type was categorized into 5 groups: Managed care (managed care, HMO, PPO or private insurance), Medicaid, Medicare, other insurance type, and uninsured or unknown. Socioeconomic status (SES) was classified into quintiles based on the Yost or Yang score. The Yost score, utilized for patients who were diagnosed before 2006, is a composite index of socioeconomic status contained in the CCR that is based on principal component analysis of block group level census variables such as education, income and occupation.[25] The Yang scale, which was used for patients who were diagnosed after 2006, is a similar index based on American Community Survey variables at the block group level.[26] Patient comorbidity was measured by the Deyo adaptation of the Charlson Comorbidity Index.[27] Comorbidity scores were calculated by using diagnosis codes for comorbidities included in OSHPD hospital discharge data at the time of the cancer diagnosis. Charlson-Deyo comorbidity score was categorized into 3 groups: 0, ≥1, and unknown; scores of 1 and higher were grouped together because only 5% of our study population had a score of 2 and only 6% had a score of 3 or higher. Tumor variables included clinical stage, histopathologic grade, tumor size, and histology. Hospital characteristics included American College of Surgeons (ACoS) Commission on Cancer (CoC) accreditation and hospital volume. The ACoS CoC accredits programs that have data-driven performance measures for comprehensive, high-quality and multidisciplinary patient-centered care. Distribution of hospital volume was examined. Cutoffs for quartiles of hospital annual cases in the data were 4.4, 8.1 and 17.0 cervical cancer cases of all stages per year. Cutoffs for quintiles were 3.9, 6.4, 10.7 and 19.5 cases per year. To minimize the number of the categories of hospital volume and maximize the effect of hospital volume, the optimal cutoff was 20 cervical cancer cases of all stages per year, dividing the cohort such that just over 80% of patients were treated in low-volume centers and nearly 20% of patients were treated in high-volume centers. Further, previous ovarian cancer literature uses the same cutoff of 20 cases per year.[23] Using this cutoff, we categorized 8 hospitals as high-volume and 358 hospitals as low-volume.

The first main outcome variable was adherence to NCCN treatment guidelines, accounting for guideline changes that occurred during the study time period. The NCCN Clinical Practice Guidelines represent consensus statements of evidence regarding currently accepted standard of care approaches to cancer treatment. Guideline change requests can be submitted when practice changing data are published, after which the expert panel discusses the request and associated references and decides when changes to the NCCN guidelines are appropriate. For stages IB-IIA, NCCN adherence included surgical or primary radiation approaches. Guideline-adherent surgery was defined as radical hysterectomy with pelvic lymphadenectomy. If pelvic lymph nodes were negative, either radiation or no radiation was considered adherent care due to absence of information regarding other risk factors that are not included in the CCR database. If pelvic lymph nodes were known to be positive, this had to be followed by pelvic radiation with or without brachytherapy. For patients diagnosed after 1/1/2000 with positive pelvic lymph nodes, adherence required concurrent chemotherapy with pelvic radiation; if treatment was on or before 12/31/1999, chemotherapy administration was not required for treatment to be considered adherent care. For stages IB-IIA, adherent non-surgical management required both pelvic radiation and brachytherapy; concordant chemotherapy was included for guideline adherence on or after 1/1/2000.

The second main outcome variable was cervical cancer-specific 5-year survival. Cause of death was recorded according to ICD criteria in effect at the time of death. The last date of follow-up was either the date of death or the last date of contact. Cervical cancer-specific death was defined as death caused by cervical cancer alone. Patients who died from other causes were treated as censored cases at the time of the event. Given the sample sizes of 2,831 patients receiving guideline-adherent care compared to 3,232 patients receiving non-NCCN guideline adherent care, the study was powered to detect odds ratios of at least 1.15 for a prevalence of exposure of 25%. Similarly, with 674 deaths from cervical cancer, the study was powered to detect hazard ratios as small as 1.25 for a characteristic with 25% prevalence.

Descriptive statistics for demographic, clinical and hospital characteristics by patients' status of receiving NCCN adherent care were analyzed with^2 test for categorical variables. Multivariate logistic regression analysis was performed to estimate the probability of adherence to NCCN guidelines, generating adjusted odds ratios and 95% confidence intervals. Survival analysis was performed using the Kaplan-Meier estimate of survival probability and log rank test. After verifying the proportionality assumption, a Cox-proportional hazards model was fitted to evaluate the independent effect on survival of each predictor. Possible interaction terms of main effects were tested. Adjusted hazard ratios and 95% confidence intervals (CI) were generated. All *P* values are two sided. All statistical analysis was performed on SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

A total of 6,063 patients were identified for study inclusion. The median follow-up time was 8.7 years with a range of 0-20.2 years. Age at diagnosis ranged from 18 to 98 with most women being reproductive age and only 13.7% were 65 years of age or older (Table 1). The majority presented with stage I disease (88.1%) and 26.2% had a Charlson-Deyo comorbidity score of ≥1. The largest racial and ethnic group was non-Hispanic white (41.8%) women, followed in frequency by Hispanic women (38.3%) and Asian or Pacific Islander (13.8%) women. Only 5% of the population was identified as non-Hispanic black women. Just over half (51.5%) of the study population was treated in a hospital with ACoS CoC accreditation and only 18.8% of patients were treated in high-volume hospitals. Overall, 46.7% of patients received NCCN guideline-adherent care. Details regarding the treatment provided to patients receiving non-adherent care are delineated in Appendix 1, available online at http://links.lww.com/xxx.

The multivariate logistic regression model for adherence to NCCN treatment guidelines revealed statistically significant decreased odds of receiving guideline-adherent care with increasing age, lower SES, higher Charlson-Deyo comorbidity score, larger tumor size, higher stage of disease, and treatment in a low-volume center (Table 2). Compared with those in the highest SES quintile, women in the lowest SES quintile were 32% less likely to receive guideline-adherent care (aOR 0.69, 95% CI 0.57-0.84, $P<.001$). Women with a Charlson-Deyo comorbidity score ≥1 had a similarly decreased likelihood of receiving guideline-adherent care (aOR 0.78, 95% CI 0.69-0.89, $P<.001$). In low-volume centers, 45.9% of patients received adherent care compared to 50.9% in high-volume centers (effect size=0.90, 95% CI 0.84-0.96; aOR 0.74, 95% CI 0.64-0.85, $P<.001$).

The Cox proportional hazards model demonstrated that the risk of death from cervical cancer was increased in subjects who failed to receive NCCN guideline-adherent care (aHR 1.43, 95% CI 1.19-1.73, $P<.001$) compared to those who received NCCN guideline-adherent care (Table 3). Specifically, 13.3% of patients receiving non-NCCN guideline-adherent care died from cervical cancer compared to 8.6% of those patients receiving NCCN guideline-adherent care (effect size=1.55, 95% CI 1.34-1.80). Patients who received care in a low-volume hospital (<20 cases treated per year) were not found to have a statistically significant increased risk of death from cervical cancer (aHR 1.29, 95% CI 0.99-1.67, $P=.057$). Black race, Medicaid payer status, Charlson-Deyo score, larger tumor size, higher tumor grade, and higher stage at diagnosis were each statistically significantly associated with increased probability of dying from cervical cancer. After adjusting for other variables, socioeconomic status was not a significant predictor of cervical cancer-specific survival.

The cervical cancer-specific 5-year survival of the study population was 90.4% (Standard Error SE=0.4%). For patients receiving NCCN guideline-adherent care, the cervical cancer-specific 5-year survival was 93.0% (SE=0.5%) compared with 88.1% (SE=0.6%) among those receiving non-adherent care (Log rank test P<.001) (Figure 2).

Discussion

In this large population-based cohort study of early cervical cancer patients in California, we found a significant association between adherence to NCCN guidelines and 5-year survival. Patients with increasing age, lower SES, higher comorbidities, and receipt of care in a low-volume hospital were more likely to receive non-NCCN guideline-adherent care. The survival difference associated with adherence persisted after multivariate analysis controlling for factors known to impact survival. Black race, Medicaid payer status, higher comorbidities, stage II disease, grade 2 or higher histology, and larger tumor size were also associated with an increased risk of death from cervical cancer. Our study reinforces that improvements in cervical cancer screening, early detection, and treatment have not been evenly distributed among women of all racial, ethnic, and socioeconomic backgrounds.[20]

Cervical cancer in the United States has persistently and disproportionately burdened the socioeconomically disadvantaged and racial and ethnic minorities, resulting in a higher rate of disease and mortality for these groups.[3–21] Previous work has established that differences in cervical cancer-specific survival are intimately tied to advanced stage at diagnosis,[13,16,18] race,[14,16] insurance status,[7] and socioeconomic status.[16,18] Recent research demonstrated that hysterectomy-corrected age-standardized cervical cancer mortality rates were higher and more disparate between black and white women than previously thought. After correcting for hysterectomy, the mortality rate was 10.1 per 100,000 for black women compared to 4.7 per 100,000 for white women.[28] However, in a study of the United States Military Health Care System, where black and white women had equal access regardless of race, ethnicity, or socioeconomic status, 5- and 10-year survival were comparable, indicating that race was not an independent predictor of survival after controlling for access to equal care.[11] Similarly, in a population of women who all had Medicare fee-for-services insurance, race, ethnicity, and socioeconomic status were not associated with variations in survival.[10] Persistent racial, ethnic and socioeconomic disparities in cervical cancer-specific mortality prompted this investigation to determine whether receipt of NCCN guideline-adherent care, rather than other patient characteristics, may be a driving force behind disparate survival outcomes. Our data add to the existing body of literature regarding cervical cancer disparities by demonstrating that receipt of non-NCCN-guideline-adherent care is an independent predictor of cervical cancer-specific mortality, specifically in early cervical cancer patients.

Strengths of this study include the reliability of statewide reporting to the California Cancer Registry and the large sample size, which is particularly essential for evaluating survival in this patient population, given 5-year survival of 90% for early cervical cancer. Furthermore, the database included a diverse population including women of all ethnicities and socioeconomic backgrounds. Many prior studies compared black and white women only, while more than half of our study population was Hispanic (38.3%) or Asian-American

(13.8%), providing an excellent representation of other minority populations in the United States. The socioeconomic, racial and ethnic makeup of California closely represents the projected makeup of the United States in 40 years according to US Census Bureau data.[29] Therefore, understanding disparities in care and outcomes in the California population now will help physicians, administrators, and policy makers to address similar issues in early cervical cancer patients throughout the United States in the future.

The current study also has limitations that must be considered when interpreting the data presented. Tumor size and lymph node status were not consistently reported and additional information such as lymphovascular space invasion, depth of cervical stromal invasion, margin and parametrial status of surgical specimens were not available in order to determine which subsets of patients with negative pelvic lymph nodes should have received adjuvant radiation in accordance with NCCN guidelines. Additionally, among the 22,975 incident cervical cancer cases from January 1, 1995, through December 31, 2009 there was a sizeable portion (16.6%) with unknown (n=2,775) or incomplete (n=1,033) staging who were excluded from analysis, potentially creating selection bias.

In conclusion, for women in California with early stage cervical cancer, disparities exist in access to NCCN guideline adherent care. Failure to receive adherent care was associated with decreased survival, even in a subpopulation with high 5-year survival. By taking a systematic approach to identify the factors contributing to delivery of non-NCCN guideline care, we can begin to implement health policy and health care delivery systems designed to mitigate the driving forces contributing to variation in delivery of adherent care, including not only patient and hospital characteristics but also provider practices and geographic distribution of care. With the goal to diminish disparities in survival, continued focus is merited on the delivery of NCCN guideline adherent care for women with early stage cervical cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported by the Ruth L. Kirschstein National Research Service Award Institutional Training Grant, NIH T32 CA-060396-11.

The authors thank Elani Streja, PhD, who contributed to data cleaning and approach to data analysis.

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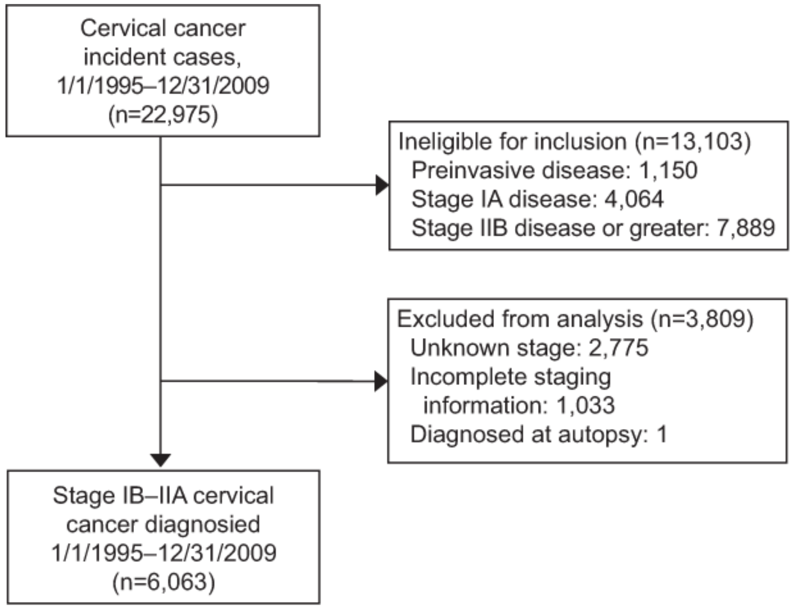

Fig. 1.
Flow diagram illustrating inclusions and exclusions to arrive at the final cohort.

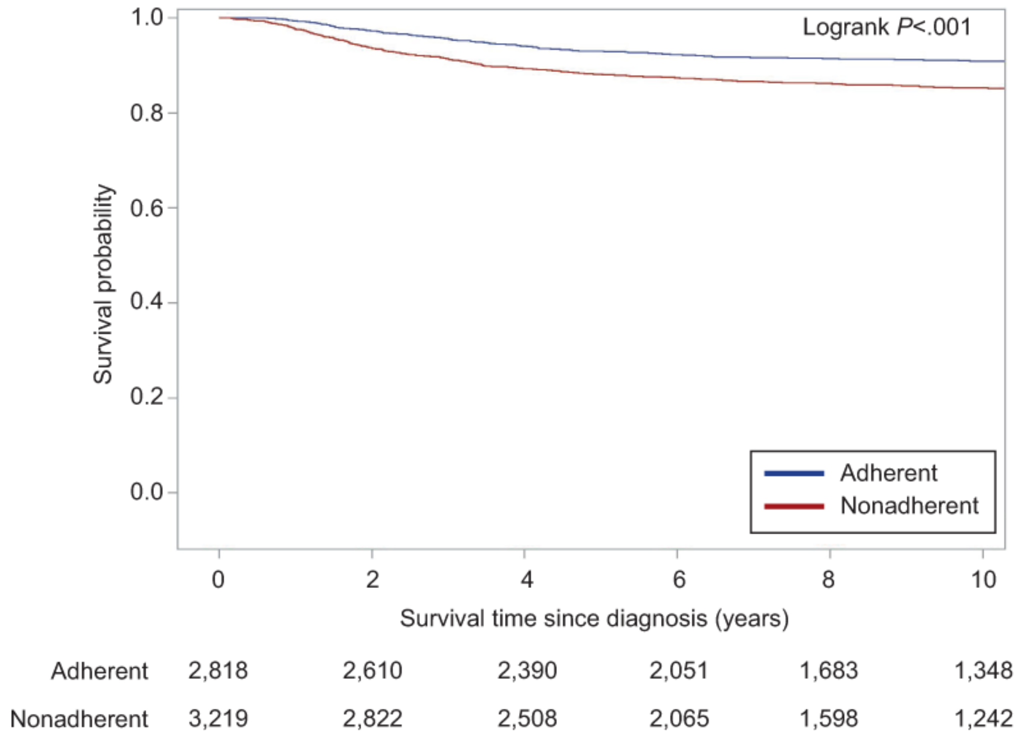

Fig. 2.

Kaplan-Meier survival curve for cervical cancer-specific survival according to National Comprehensive Cancer Network guideline adherence.

Table 1

Patient, tumor and hospital characteristics

	Total n=6,063		Adherent n=2,831 (46.7%)		P^*
	n	%	n	%	
Patient demographics					
Age at diagnosis (years)					<.001
18-39	1,970	32.5	992	35.0	
40-64	3,263	53.8	1,503	53.1	
65+	830	13.7	336	11.9	
Year of diagnosis					<.001
1995-1999	2,055	33.9	1,082	38.2	
2000-2004	1,946	32.1	884	31.2	
2005-2009	2,062	34.0	865	30.6	
Race and ethnicity					.111
Non-Hispanic white	2,532	41.8	1,224	43.2	
Black	306	5.0	131	4.6	
Hispanic	2,322	38.3	1,049	37.1	
Asian or Pacific Islander	835	13.8	398	14.1	
Others/Unknown	68	1.1	29	1.0	
Insurance					<.001
Managed care	2,585	42.6	1,267	44.8	
Medicare	569	9.4	223	7.9	
Medicaid	1,444	23.8	652	23.0	
Other insurance	995	16.4	471	16.6	
Not insured/Unknown	470	7.8	218	7.7	
Socioeconomic Status (SES)					<.001
Highest SES	883	14.6	464	16.4	
Higher-middle SES	1,181	19.5	587	20.7	
Middle SES	1,201	19.8	559	19.7	
Lower-middle SES	1,304	21.5	584	20.6	
Lowest SES	1,494	24.6	637	22.5	

	Total n=6,063		Adherent n=2,831 (46.7%)		P^*
	n	%	n	%	
Marital status at diagnosis					<.001
Not married (Single, divorced, widowed etc.)	2,921	48.2	1,298	45.8	
Married	3,142	51.8	1,533	54.2	
Charlson comorbidity score					<.001
0	3,589	59.2	1,803	63.7	
≥1	1,586	26.2	652	23.0	
Unknown	888	14.6	376	13.3	
Tumor characteristics					
Stage					<.001
I	5,343	88.1	2,563	90.5	
II	720	11.9	268	9.5	
Grade					<.001
Grade I or well-differentiated	777	12.8	370	13.1	
Grade II or moderately well-differentiated	2,074	34.2	1,003	35.4	
Grade III or poorly differentiated	2,023	33.4	985	34.8	
Grade IV or undifferentiated/anaplastic	138	2.3	54	1.9	
Grade and differentiation not stated	1,051	17.3	419	14.8	
Size					<.001
<20mm	1,527	25.2	798	28.2	
≥ 20 mm	2,810	46.3	1,297	45.8	
Unknown	1,726	28.5	736	26.0	
Histology					.477
Squamous	3,709	61.2	1,711	60.4	
Glandular	1,951	32.2	933	33.0	
Others	403	6.6	187	6.6	
Hospital characteristics					
ACoS approved hospital					<.001
Not ACoS approved	2,882	48.5	1,285	45.4	
ACoS approved	3,065	51.5	1,501	53.0	
Hospital volume					.002

	Total n=6,063		Adherent n=2,831 (46.7%)		P^*
	n	**%**	**n**	**%**	
High (≥ 20 cases/year)	1,123	18.8	572	20.2	
Low (< 20 cases/year)	4,856	81.2	2,229	78.7	
ACoS and Hospital Volume					<.001
ACoS approved and High-volume	684	11.6	354	12.5	
Non-ACoS approved and High-volume	432	7.4	213	7.5	
ACoS approved and Low-volume	2,375	40.4	1,145	40.4	
Non-ACoS approved and Low-volume	2,381	40.5	1,047	37.0	

ACoS, American College of Surgeons.

* Chi square test for association between patient's characteristics and adherence status

Table 2

Univariate and multivariate logistic regression on receipt of NCCN guideline-adherent care

	Unadjusted OR (95% CI)	Adjusted OR (95% CI) *
Patient demographics		
Age at diagnosis (years, continuous)	0.988 (0.985-0.992)†	0.993 (0.988-0.997)‡
Year of diagnosis (continuous)	0.96 (0.94-0.97)†	0.95 (0.94-0.96)†
Race and ethnicity		
Non-Hispanic white	1.00 (reference)	1.00 (reference)
Black	0.80 (0.63-1.02)	0.91 (0.71-1.17)
Hispanic	0.88 (0.79-0.99)§	0.99 (0.87-1.13)
Asian or Pacific Islander	0.97 (0.83-1.14)	1.03 (0.88-1.22)
Others and Unknown	0.80 (0.49-1.29)	0.85 (0.52-1.40)
Insurance		
Managed care	1.00 (reference)	1.00 (reference)
Medicare	0.67 (0.56-0.81)†	0.99 (0.80-1.24)
Medicaid	0.86 (0.75-0.97)§	0.99 (0.86-1.15)
Other insurance	0.94 (0.81-1.08)	0.91 (0.78-1.06)
Not insured or Unknown insurance	0.90 (0.74-1.10)	0.82 (0.67-1.02)
Socioeconomic Status		
Highest SES	1.00 (reference)	1.00 (reference)
Higher-middle SES	0.89 (0.75-1.06)	0.92 (0.77-1.11)
Middle SES	0.79 (0.66-0.94)‡	0.82 (0.68-0.98)§
Lower-middle SES	0.73 (0.62-0.87)†	0.76 (0.64-0.92)‡
Lowest SES	0.67 (0.57-0.79)†	0.69 (0.57-0.84)†
Marital status at diagnosis		
Not married (Single, divorced, widowed etc.)	1.00 (reference)	1.00 (reference)
Married	1.19 (1.08-1.32)†	1.08 (0.97-1.20)
Charlson comorbidity score		
0	1.00 (reference)	1.00 (reference)
≥1	0.69 (0.61-0.78)†	0.78 (0.69-0.89)†
Unknown	0.73 (0.63-0.84)†	0.83 (0.70-0.97)§
Tumor characteristics		
Stage		
I	1.00 (reference)	1.00 (reference)
II	0.64 (0.55-0.76)†	0.76 (0.64-0.90)‡
Grade		
Grade I or well differentiated	1.00 (reference)	1.00 (reference)
Grade II or moderately well differentiated	1.03 (0.87-1.22)	1.11 (0.93-1.32)
Grade III or poorly differentiated	1.04 (0.89-1.23)	1.17 (0.98-1.40)
Grade IV or undifferentiated/anaplastic	0.71 (0.49-1.02)	0.80 (0.55-1.18)

	Unadjusted OR (95% CI)	Adjusted OR (95% CI) *
Grade and differentiation not stated	0.73 (0.61-0.88)‡	0.84 (0.69-1.02)
Size		
<20mm	1.00 (reference)	1.00 (reference)
≥20mm	0.78 (0.69-0.89)†	0.81 (0.71-0.92)‡
Unknown	0.68 (0.59-0.78)†	0.69 (0.59-0.80)†
Histology		
Squamous	1.00 (reference)	1.00 (reference)
Glandular	1.07 (0.96-1.20)	1.01 (0.89-1.14)
Others	1.01 (0.82-1.24)	1.03 (0.83-1.28)
Hospital characteristics		
Hospital volume		
High (≥ 20 cases/year)	1.00 (reference)	1.00 (reference)
Low (< 20 cases/year)	0.82 (0.72-0.93)‡	0.74 (0.64-0.85)†

OR, odds radio; CI, confidence interval; SES, socioeconomic status.

*The final multivariate logistic model included all factors listed in the table.

†P<.001

‡P<.01

§P<.05

Table 3

Predictors of cervical cancer-specific mortality analyzed using Cox proportional hazards model

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*
Patient demographics		
Race and ethnicity		
Non-Hispanic white	1.00 (reference)	1.00 (reference)
Black	1.64 (1.23-2.20)†	1.56 (1.08 -2.27)‡
Hispanic	0.99 (0.83-1.18)	0.95 (0.76-1.20)
Asian or Pacific Islander	0.94 (0.74-1.20)	1.00 (0.75-1.33)
Others and Unknown	0.92 (0.44-1.95)	1.34 (0.58-3.10)
Insurance		
Managed care	1.00 (reference)	1.00 (reference)
Medicare	2.11 (1.66-2.67)†	1.24 (0.82-1.86)
Medicaid	1.59 (1.32-1.93)†	1.47 (1.15-1.87)§
Other insurance	1.11 (0.88-1.40)	1.25 (0.95-1.64)
Not insured or Unknown insurance	1.05 (0.76-1.44)	1.35 (0.90-2.01)
Socioeconomic Status (SES)		
Highest SES	1.00 (reference)	1.00 (reference)
Higher-middle SES	1.08 (0.82-1.41)	0.99 (0.71-1.37)
Middle SES	1.10 (0.84-1.44)	0.88 (0.64-1.22)
Lower-middle SES	1.20 (0.92-1.56)	0.90 (0.65-1.25)
Lowest SES	1.29 (1.00-1.67)‡	0.87 (0.62-1.21)
Marital status at diagnosis		
Not married (Single, divorced, widowed etc.)	1.00 (reference)	1.00 (reference)
Married	0.76 (0.65-0.88)†	0.93 (0.77-1.13)
Charlson comorbidity score		
0	1.00 (reference)	1.00 (reference)
≥1	2.13 (1.82-2.50)†	2.07 (1.68-2.56)†
Unknown	0.93 (0.70-1.23)	0.79 (0.56-1.10)
Tumor characteristics		
Stage		
I	1.00 (reference)	1.00 (reference)
II	3.27 (2.76-3.89)†	2.52 (1.99-3.19)†
Grade		
Grade I or well differentiated	1.00 (reference)	1.00 (reference)
Grade II or moderately well differentiated	1.56 (1.15-2.13)§	1.51 (1.05-2.16)‡
Grade III or poorly differentiated	2.41 (1.78-3.25)†	2.21 (1.55-3.16)†
Grade IV or undifferentiated/anaplastic	3.57 (2.22-5.73)†	3.70 (2.06-6.68)†
Grade and differentiation not stated	1.68 (1.20-2.35)§	1.37 (0.92-2.03)
Size		

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[*]
<20mm	1.00 (reference)	1.00 (reference)
≥20mm	3.85 (2.96-5.01)[†]	3.01 (2.25-4.05)[†]
Unknown	2.80 (2.11-3.71)[†]	2.28 (1.65-3.16)[†]
Histology		
Squamous	1.00 (reference)	1.00 (reference)
Glandular	0.79 (0.67-0.94)[§]	1.13 (0.91-1.41)
Others	0.96 (0.70-1.30)	1.48 (1.03-2.15)[‡]
Hospital characteristics		
Hospital volume		
High (≥ 20 cases/year)	1.00 (reference)	1.00 (reference)
Low (< 20 cases/year)	1.19 (0.97-1.46)	1.29 (0.99-1.67)
Treatment		
Adherence		
Adherent	1.00 (reference)	1.00 (reference)
Not adherent	1.67 (1.43-1.96)[†]	1.43 (1.19-1.73)[†]

HR, hazards ratio; CI, confidence interval; SES, socioeconomic status.

[*] Age at diagnosis and year of diagnosis were included in the multivariate Cox model as strata. The final model also included all factors listed in the table.

[†] *P*<.001

[‡] *P*<.05

[§] *P*<.01