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Variation in care in concurrent chemotherapy administration during radiation for locally advanced cervical cancer

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HIGHLIGHTS

- Low volume hospitals have a greater variation in concurrent chemotherapy administration
- Significant health disparities exist in the administration of concurrent chemotherapy.
- Quality improvement efforts in cervical cancer should focus on adherence to guideline based care

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ABSTRACT

Background. To evaluate the usage of concurrent chemo-radiotherapy (C-CRT) for the treatment of locally advanced cervical cancer.

Methods. Patients with locally invasive cervical carcinoma diagnosed between January 1, 2004 and December 31, 2012 from the National Cancer Database (NCDB) were included. Outcomes for patients undergoing radiation therapy only, 'RT alone' group were compared to those receiving chemotherapy concurrent with radiation 'C-CRT group'. Trends in utilization of C-CRT and factors associated with the deviation from standard of care were explored. Lastly, the effect of hospital volume on utilization of C-CRT was investigated.

Results. A total of 18,164 patients undergoing definitive radiation therapy were available for analysis. Utilization of C-CRT increased from 72.4% in 2004 to 84.3% in 2012 (p-trend < 0.001). After adjusting for patient, tumor, and treatment factors, a multivariable logistic regression model revealed increasing age, African-American race, Charlson-comorbidity index of ≥2, Medicaid insurance status, uninsured status, and Stage I disease were each independently associated with the lack of C-CRT. After adjusting for patient characteristics, low volume hospitals were noted to have overall significantly lower rates and greater variation in C-CRT administration. Patients in 'RT alone' group had an overall worse survival rate (adjusted-HR 1.47, 95%CI 1.4–1.56).

Conclusion. Rates of C-CRT administration varied significantly across hospitals in the United States. Hospitals with a high case volume had higher rates and more consistent patterns of C-CRT administration. Furthermore, we identified independent factors, all of which represent noteworthy health disparities, associated with lower rates of C-CRT administration.

1. Introduction

In 1999, following the completion of 5 clinical trials, the National Cancer Institute (NCI) released a "Clinical Announcement" citing the benefit of platinum-based concurrent chemo-radiotherapy (C-CRT) for the treatment of locally advanced cervical cancer. [1] Subsequently, a systematic review [2] and a meta-analysis of individual patient-level data [3] have confirmed the benefit of C-CRT. As a result, C-CRT is now the standard of care for the treatment of locally advanced cervical cancer. [4]

Following the NCI statement, a population-based analysis demonstrated an increased usage of C-CRT from 10% between 1992 and 1998 to 60% between 1999 and 2001. [5] This analysis confirmed the magnitude of the survival benefit of C-CRT in the general population to be

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consistent with the results of the clinical trials. However, the extent and patterns of C-CRT usage in the United States have not been studied.

In this context, the objective of this study is to evaluate the variation in the usage of C-CRT in the United States over the last decade utilizing the National Cancer Database (NCDB). In addition, for patients not receiving C-CRT, we sought to determine the factors associated with the deviation from this established standard of care.

2. Methods

2.1. National cancer database

The NCDB is a nationwide, facility-based, comprehensive data set that captures >70% of newly diagnosed malignancies in the United States. This dataset contains >29 million cancer cases from >1500 Commission on Cancer (CoC)–accredited cancer programs across the United States. The NCDB utilizes a hospital-based registry, and CoC requires approved programs to abstract and follow all malignant tumors diagnosed and/or treated at the hospital. [6] Currently, 95.6% of the cervical cancer cases in the United States are reported to the NCDB and it is estimated that >90% of these cases have follow up data [7] Data reported to the NCDB are retrospective and de-identified, ensuring confidentiality. Since all the information from the NCDB is de-identified, this study is exempt from obtaining informed consent by the study participants and approval of an ethics committee.

2.2. Study population

All NCDB cases with invasive cervical carcinoma diagnosed between January 1, 2004 and December 31, 2012 were selected for the analysis using topographic code C53.9. Patients with locally advanced squamous or adenocarcinoma of the cervix (Stages IB1-IIIB) undergoing primary radiation therapy as definitive treatment were the focus of this study (N = 22.995). Patients undergoing surgery prior to radiation were not included in the analysis. We then excluded patients receiving multiagent chemotherapy for >2 weeks prior to the initiation of radiation therapy, as this patient subpopulation represented treatment with neoadjuvant chemotherapy (n = 673; 2.9.%). Additionally, we excluded cases where details of therapies administered (i.e., date of chemotherapy initiation) were not available (n = 1358; 5.9%). Patients with a significant delay in starting radiation therapy (>6 months from the date of diagnosis) were also excluded from the analysis because of concerns surrounding miscoding and potential bias introduced by other factors causing delay of treatment initiation (n = 2735; 11.9%). Finally, patients treated with palliative intent (information on palliative intent is available in the NCDB database) (n = 65; 0.3%) were excluded from the analysis, resulting in a final study population of 18,164 women.

2.3. Variable definitions

Variables were coded according to NCDB Program criteria. Race was categorized as White, African American, or other. Tumor stage was determined using the revised 2009 staging criteria of the International Federation of Gynecologists and Obstetricians (FIGO). Insurance status was categorized as none/unknown, private, Medicare or Medicaid. Tumor histology was categorized as squamous or adenocarcinoma. Tumor grade was categorized as grade 1/2, grade 3/undifferentiated, or unknown. Median household income from zip code of residence was derived from the 2012 American Community Survey data, categorized into quartiles, and used as a proxy for socioeconomic status. Data regarding hospital setting were analyzed using NCDB definitions for teaching and research hospitals; community cancer; and comprehensive community cancer centers. To assess the prevalence of comorbid disease in our cohort, we used the Charlson comorbidity index. Patients were assigned a score of 0, 1, or 2 or greater. Details of the Charlson comorbidity index have been previously published. [8] The mean hospital volume was calculated by dividing total number of cases reported by the hospital for the time period the hospital reported the cases to the National Cancer Database. The mean hospital volume was then ranked into quartiles. Hospitals in the lowest quartile were labelled as 'Low volume,' the second and third quartiles were labelled as 'Intermediate volume,' and those in the fourth quartile were labelled as 'High volume.' Receipt of brachytherapy as a part of primary chemo-radiation in patients with cervical cancer has been shown to significantly improve survival; [9] therefore, information regarding brachytherapy use was abstracted from the radiation therapy details and patients were categorized as either having undergone brachytherapy or not.

Table 1
Demographics and clinical percentage distribution of cervical cases during 2004–2012.

Variable	
Patient factors	
Age (years), mean (sd)	54.1 (14.8)
Race, N (%)	
White	13,410 (74%)
African American	3598 (20%)
Other	1156 (6%)
Insurance status, N (%)	
Private	6682 (37%)
Uninsured	2109 (12%)
Medicaid	4392 (24%)
Medicare	4319 (24%)
Other/unknown	662 (4%)
Income, N (%)	
<$30,000	3952 (23%)
$30,000–$35,999	3902 (22%)
$36,000–$45,999	5014 (29%)
≥$46,000	4665 (27%)
Charlson score, N (%)	
0	15,547 (86%)
1	2028 (11%)
2 or more	589 (3%)
Tumor factors	
Stage, N (%)	
I B1	583 (3%)
I B2	2882 (16%)
II A	1599 (9%)
II B	5539 (30%)
III A	827 (5%)
III B	6734 (37%)
Histology, N (%)	
Squamous carcinoma	16,305 (90%)
Adenocarcinoma	1859 (10%)
Grade, N (%)	
1–2	6709 (37%)
3/undifferentiated	5870 (32%)
Unknown	5585 (31%)
Treatment factors	
Facility type, N (%)	
Community	1158 (8%)
Comprehensive Community Cancer Center	6011 (40%)
Academic/research	7005 (46%)
Integrated network	1003 (7%)
Year of diagnosis, N (%)	
2004	1977 (11%)
2005	1894 (10%)
2006	1942 (11%)
2007	2030 (11%)
2008	2023 (11%)
2009	1996 (11%)
2010	2040 (11%)
2011	2116 (12%)
2012	2146 (12%)
Hospital volume, N (%)	
Low	4634 (26%)
Intermediate	9115 (50%)
High	4224 (24%)