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Delays in definitive cervical cancer treatment: An analysis of disparities and overall survival impact☆,☆☆

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HIGHLIGHTS

- Time to treatment initiation for cervical cancer has increased between 2004 and 2014.
- There are significant disparities in TTI for cervical cancer.
- Hispanic and Non-Hispanic Black women have the longest delays to treatment.
- TTI is not associated with OS.
- Further study into TTI's impact on other endpoints is warranted.

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ABSTRACT

Objective. Delays in time to treatment initiation (TTI) with definitive radiation therapy (RT) or chemotherapy and RT (CRT) for cervical cancer could lead to poorer outcomes. This study investigates disparities in TTI and the impact of TTI on overall survival (OS).

Methods. Adult women with non-metastatic cervical squamous cell carcinoma diagnosed between 2004 and 2014, treated with definitive RT or CRT, and reported to the National Cancer Database were included. TTI was defined as days from diagnosis to start of RT or CRT. The impact of TTI on OS in patients treated with concurrent CRT which included brachytherapy was then assessed.

Results. Overall, 14,924 patients were included (84.7% CRT, 15.3% RT). TTI was significantly longer for Non-Hispanic Black (NHB) (RR, 1.14; 95% CI, 1.11 to 1.18) and Hispanic women (RR, 1.19; 95% CI, 1.15 to 1.24) compared to Non-Hispanic White (NHW) women. Expected TTI (eTTI) for NHW, NHB, and Hispanic women were 38.1, 45.2, and 49.4 days. eTTI rose from 36.2 days in 2004 to 44.3 days by 2014. Intensity-modulated radiation therapy (IMRT) was associated with increased eTTI of 46.5 days versus 40.0 days for non-IMRT. Longer TTI was not associated with inferior OS in patients treated with concurrent CRT.

Conclusions. Delays in starting RT/CRT for cervical cancer increased from 2004 to 2014. Delays disproportionately affect NHB and Hispanic women. However, increased TTI was not associated with increased mortality for women receiving CRT. Further study of TTI's impact on other endpoints is warranted to determine if TTI represents an important quality indicator.

1. Introduction

In the United States, 12,990 women were diagnosed with cervical cancer, and 4120 died from this disease in 2016. Incidence and death rates for cervical cancer were higher among Non-Hispanic Black (NHB) and Hispanic women compared to Non-Hispanic White (NHW) women [1]. Evidence suggests NHB and Hispanic women are also less likely to receive guideline-based treatment nationwide [2,3]. NHB and Hispanic patients also face longer wait times for definitive treatment for a variety of cancer diagnoses [4–8].

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In other disease sites, delayed cancer management has been correlated with increased patient distress, decreased disease control, and lower survival [7,9–11]. Recent national analyses among breast cancer and head and neck cancer patients have shown worse survival when definitive treatment is delayed [7,9–12]. Meta-analyses have also shown increased local recurrence among breast cancer and head and neck cancer patients when therapy is delayed [11,13]. Analyses of treatment delay for women with cervical cancer have been more limited in scope [14–18]. To our knowledge, no previous nationwide study has assessed treatment delay and its impact on survival for women with cervical cancer in the US. Prior to initiating quality improvement efforts to address a specific component of care (such as treatment delay), the importance of that indicator to patient and/or societal outcomes should be established using available evidence [19]. We therefore investigated which factors impact time to definitive radiation therapy (RT) or to chemotherapy and RT (CRT) for patients with cervical cancer and the impact of delays on overall survival (OS). Specifically, we aimed to determine whether racial/ethnic disparities in time to treatment initiation (TTI) exist for women with cervical cancer.

2. Methods

The local Human Subjects Research Office granted institutional review board exemption for this project; the American College of Surgeons granted access to the 2014 National Cancer Database (NCDB) data. The NCDB is a joint project of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. The CoC's NCDB and the hospitals participating in the CoC NCDB are the source of the de-identified data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors. The NCDB receives data from >1500 programs on approximately 70% of new cancer cases in the United States and Puerto Rico [20]. For cervical cancer, NCDB reporting rates are even higher at >90% of cases [21]. Data reported to the NCDB undergoes >600 automated checks to insure internal consistency and reduce missing data. Institutions are subject to regular audits to ensure the accuracy and completeness of data [22,23]. Reporting centers are required to have at least a 90% follow-up rate for patients for 5 years [22].

2.1. Patient selection

Adult patients (ages 18 and above) with non-metastatic squamous cell carcinoma of the uterine cervix diagnosed between 2004 and 2014 and treated with definitive-intent RT or CRT were included. A flow diagram (Fig. 1) demonstrates patients excluded based on each subsequent criteria. Patients with American Joint Committee on Cancer (AJCC) clinical group stage 1 or 1B disease but with unknown tumor size were excluded to allow for more refined staging analyses (i.e., to allow categorization of patients as AJCC stage 1A-1B1 vs. 1B2). Histology was defined based on International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) site codes [24]. Patients treated with surgery, chemotherapy alone, brachytherapy alone, or radiation of unspecified type were excluded. Patients treated with radiation modalities considered non-standard for definitive cervical cancer treatment (e.g., orthovoltage, neutrons, stereotactic radiosurgery, Gamma knife, strontium, etc.) were also excluded. Finally, patients with unknown TTI, a TTI of 0 days, or a TTI > 365 days were excluded (given concern that a TTI of 0 days or longer than 1 year could represent coding error) [9].

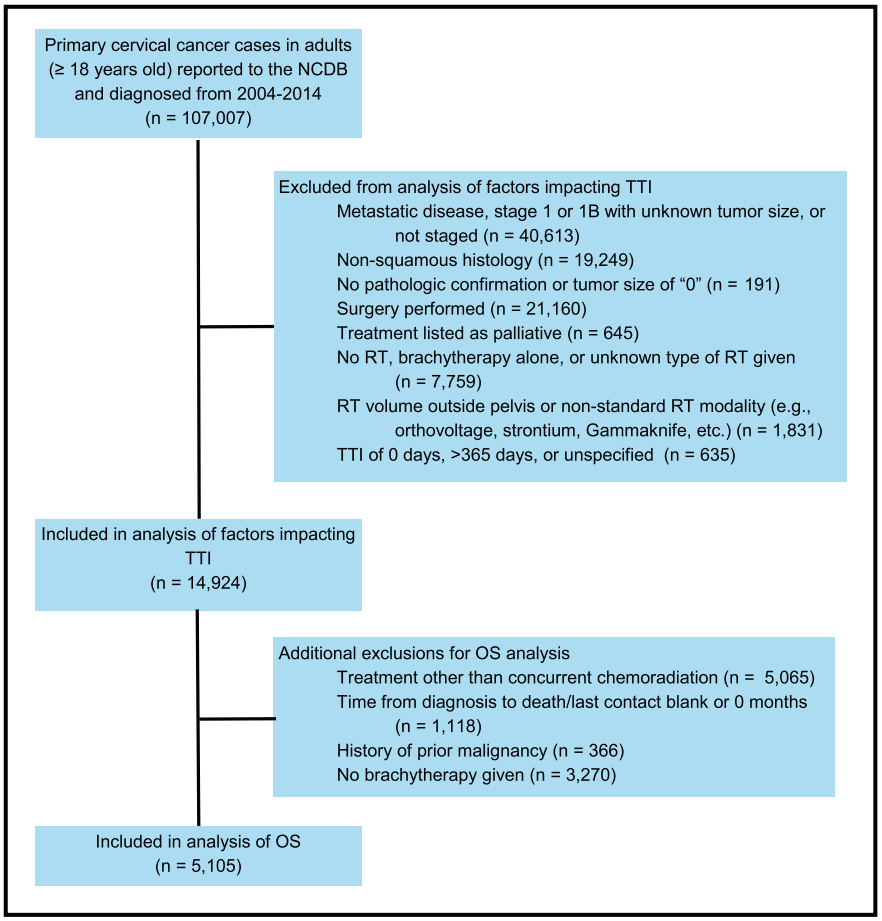

Fig. 1. Diagram of sequential exclusion criteria for analysis of factors impacting time to treatment initiation (TTI) and overall survival (OS).