Original Research

Cervical Cancer in Women Aged 35 Years and Younger

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ABSTRACT

Purpose: Age has been evaluated as a prognostic factor in cervical cancer in both hospital- and population-based studies. Results regarding the relation of age and cervical cancer prognosis are conflicting. This study pursued a contemporary assessment of the association of extreme young age at the time of a cervical cancer diagnosis on survival.

Methods: Institutional review board approval was obtained, and retrospective data collection at 2 academic institutions was performed. Inclusion criteria involved women ≤35 years diagnosed with cervical cancer between 1990 and 2012. Data included demographic and prognostic information pertinent to survival and progression. Characteristics of very young (≤25 years) and young (>25–35 years) women were compared. Kaplan-Meier estimates, the log-rank test, and Cox proportional hazards modeling were used to assess the association of age, tumor histology, grade, stage, and parametrial involvement with progression-free survival (PFS) and overall survival (OS).

Findings: Incident cases (n = 126) of cervical cancer in patients ≤35 years of age were identified of which complete clinical information was available for 114 women. Fifteen percent (17 of 114) were ≤25 years, with the remaining 85% (97 of 114) being 26 to 35 years of age. Race, smoking status, and marital status were comparable between the 2 groups. Squamous histology dominated overall (77 of 114; 68%) with adenocarcinoma contributing ~25% (30 of 114; 26%) of cases. The majority (96 of 114, 84%) had either stage 1A (31 of 114, 27%) or 1B (65 of 114, 57%) disease. A log-rank test revealed no evidence to infer a difference in either PFS or OS among the age groups ($P = 0.511$ and $P = 0.340$). In a univariate analysis, grade and stage significantly affected OS ($P < 0.0001$, $P = 0.045$), and stage significantly affected PFS ($P < 0.0001$). In multivariate modeling, presence of parametrial involvement and histologic cancer type significantly affected both PFS ($P = 0.002$, $P = 0.001$) and OS ($P = 0.001$, $P = 0.001$).

Implications: Tumor histology, parametrial involvement, and stage continue to be strong prognosticators for PFS and OS. Progression and survival outcomes are age independent in women with cervical cancer ≤35 years of age. Further study of a larger young cohort may potentially yield different outcomes. (*Clin Ther*. 2016;38:459–466)

Key words: age, cervical cancer, progression, survival, young women.

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INTRODUCTION

Cervical cancer, although largely preventable, is the most common site of gynecologic malignancy in women <35 years of age in the United States. Worldwide, cervical cancer is second only to breast cancer in cancers that affect women.[1] Young patient age has been posited as a risk factor for more aggressive cervical cancers. Alternatively, although no genetic predisposition for cervical cancer has been accepted, researchers have proposed that there is a heritable inability to clear human papillomavirus (HPV) infection because population studies have found an increased incidence of cervical cancer in some families. In a Swedish study of >9000 siblings or half-siblings with cervical cancer or dysplasia, 64% of cases were attributed to genetics and only 36% to environmental exposures.[2] It seems improbable for young women to develop advanced disease, given the classic teaching that the risk of progression from mild dysplastic changes of the cervix to severe dysplasia, let alone cancer, is only 1% per year.[3] Therefore, the development of cancer in young women, especially the very young, has led to the theory that cervical cancer in the very young must be more aggressive.[4] Others blame changes in sexual behavior with an earlier age of first intercourse, greater frequency of multiple partners and HPV infection, and tobacco use for the observations.[5–8] Current estimates put the prevalence of HPV (all types) at 59% in 20- to 24-year-old women and 50% in 25- to 29-year-old women.[9]

Several investigators have examined the relation between age at diagnosis and prognosis with conflicting results. In a study by Rutledge et al,[10] 250 women ≤35 years were matched by stage and treatment to older women. Younger women with advanced stage disease were noted to have worse overall survival (OS), yet they survived longer when diagnosed with early-stage disease. Conversely, Clark et al[11] concluded that cervical cancer behaved more aggressively in their comparison of 41 women ≤35 years old with 96 women aged ≥36 years in that there was a higher incidence of nodal metastases observed in the younger patients despite less-advanced clinical stage of disease. Paradoxically, they simultaneously observed that youth conferred better survival outcomes overall. In other studies, clinical behavior was age independent, but these studies compared women <35 years with older women.[12–14] Our hypothesis is that cervical cancer in the very young (women <25 years) is a more aggressive disease.

We sought to evaluate the relation of very young age to aggressiveness of cancer by comparing the young with the very young. This is a contemporary investigation after changes to practice that followed the 1999 National Cancer Institute alert that all patients with cervical cancer treated with radiation should also receive sensitizing cisplatin.

The primary objective of this study was to assess the effect of age on progression-free survival (PFS) and OS in women with cervical cancer ≤35 years of age. Secondarily, we sought to evaluate the impact of tumor histology, grade, stage, and parametrial involvement on PFS and OS in this cohort.

METHODS

Retrospective data collection was performed after approval from the institutional review boards at 2 tertiary academic medical centers (University of Virginia Health System, Charlottesville, VA; University of North Carolina, Chapel Hill, NC). Data for patients with cervical cancer aged ≤35 years treated between 1990 and 2012 were abstracted.

Chart review included abstraction of demographic information (age, race, smoking status, and marital status), disease characteristics (histology, grade, stage, parametrial involvement), treatment history (surgery, radiation, chemotherapy, combination), and outcome data (OS and time to recurrence).

To assess the primary outcome of the effect of age on PFS and OS, patients were classified according to age at diagnosis. These age groups were defined as very young (≤25 years old) and young (>25–35 years old) women. PFS was defined as the time from date of diagnosis to disease progression or death from any cause. OS was defined as the time from date of diagnosis to death from any cause. Secondary outcomes included assessing the effect of tumor histology, grade, stage, and parametrial involvement on PFS and OS.

Differences in OS and PFS among the age groups were evaluated with Kaplan-Meier survival estimates and the log-rank test. Multivariate Cox proportional hazards modeling was used to perform time-to-event analysis of OS and PFS, including the predictors tumor histology, parametrial involvement, and age. Tumor grade was not stated for >20% of women, and some subgroups of stage were too small and observed no events, so these variables were excluded from our final multivariate model. Significance was