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Assessment of treatment factors and clinical outcomes in cervical cancer in older women compared to women under 65 years old

Elisabeth J. Diver [a,1], Emily M. Hinchcliff [a,b,2], Allison A. Gockley [a,b], Alexander Melamed [a,b], Leah Contrino [b], Sarah Feldman [b], Whitfield B. Growdon [a,*]

[a] Massachusetts General Hospital, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Harvard Medical School, 55 Fruit Street, Yawkey 9-E, Boston, MA 02114, USA
[b] Brigham and Women's Hospital, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Harvard Medical School, 75 Francis Street, Boston, MA, 02115, USA

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ABSTRACT

Objective: This study aims to understand the treatment patterns and clinical outcomes of older women with cervical cancer compared to younger women.
Methods: Women undergoing care for cervical cancer between 2000 and 2013 at two academic institutions were identified. The cohort of older patients was defined as >65 years old at diagnosis. Patient charts were retrospectively reviewed, and clinical variables were extracted. Fisher's exact tests, logistic regression, and Kaplan-Meier analyses were performed.
Results: From 2000 to 2013 1119 women with cervical cancer were identified. Of these, 191 (17.0%) were >65 years old at the time of diagnosis. Older women were more likely to present with higher stage disease ($p < 0.001$). Controlling for stage, older women were less likely to undergo surgery during their treatment course (38% versus 70%, $p < 0.001$) and more likely to undergo radiation (77% versus 52%, $p < 0.001$), but no more likely to receive chemotherapy ($p = 0.34$). If they did undergo surgery, older women were less likely to have a pelvic lymph node dissection performed (41% versus 61%, $p = 0.04$), though the rate of positive pelvic lymph nodes was not different ($p = 0.80$). Overall survival was decreased in the older cohort ($p < 0.001$). A multivariate model identified age > 65 (HR 1.76, 95%CI 1.30–2.40), stage (HR 2.77, 95%CI 2.40–3.21), and ever undergoing surgery (HR 0.60, 95%CI 0.44–0.82) as independently associated with overall survival.
Conclusions: Women over age 65 with cervical cancer are less likely to undergo surgical management and were observed to have a decreased overall survival, even when controlling for use of surgery and stage of disease.

1. Introduction

In the United States, cervical cancer is the third most common gynecologic malignancy, with an estimated 12,820 cases and 4210 deaths in 2017 [1]. Numerous epidemiologic data have identified age as a clear risk factor for invasive disease with spikes in incidence for women in their third and sixth decades of life [2]. Widespread human papilloma virus (HPV) vaccination programs are likely to shift these age-related patterns as a younger cohort of women become less likely to manifest high grade intraepithelial and invasive lesions [3] leaving older populations with an unchanged baseline risk. As life expectancy in the United States increases, it will be increasingly important to understand the treatment and outcomes of older women with gynecologic cancers [4].

Population differences in the management of older patients may be related to systems factors or individual factors. Currently, cervical cancer screening is not routinely performed in women over 65 years of age, based on the American Society for Colposcopy and Cervical Dysplasia (ASCCP) recommendation to stop all screening over the age of 65 in patients with adequate prior screening. Unfortunately, this population has been shown to be more likely to present with advanced stage disease should these women develop cervical cancer [5]. Public health efforts to reduce invasive cervical cancer also do not affect older women. Because the first HPV vaccine was approved by the Food and Drug Administration in the United States in 2006 for women ages 9–26, women currently over age 65 were not eligible to have received it [6].

Additionally, there are many individual factors that contribute to cancer management of each patient by each provider. As a result, older women, who are more likely to have other medical co-morbidities or a

* Corresponding author at: 55 Fruit St., Yawkey 9E, Boston, MA 02114, USA
E-mail addresses: Elisabeth.diver@stanford.edu (E.J. Diver), emhinchcliff@mdanderson.org (E.M. Hinchcliff), agockley@partners.org (A.A. Gockley), amelamed@partners.org (A. Melamed), lcontrino1@partners.org (L. Contrino), sfeldman@partners.org (S. Feldman), wgrowdon@mgh.harvard.edu (W.B. Growdon).
[1] Present address: Stanford Hospital, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Stanford University Medical School, 875 Blake Wilbur Drive, Stanford, CA 94305, USA.
[2] Present address: Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, 7900 Fannin Street, Houston, TX 77054, USA.

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lower performance status, may receive different care than their younger counterparts. Numerous studies have described altered care patterns and characterized disparities in care for older patients that can lead to differences in patient outcome [7–12]. Both minimally invasive and open radical hysterectomy have been demonstrated to be feasible in older women [13]. Additionally, chemoradiation has been shown to be feasible in older women with cervical cancer, however it may present some unique challenges [14–16]. The Gynecologic Oncology Group demonstrated that weekly cisplatin with radiation therapy was tolerated well with similar treatment outcomes in women over age 55 years, however excess hematologic toxicity was noted in this population [17]. Women over 65 with cervical cancer as a population can pose a clinical challenge, as they may be unable to participate in the standard therapies administered to younger women. The aim of this investigation is to examine the patterns of care for women with cervical cancer over age 65 compared with their younger counterparts and understand, if treatment alterations exist, how they may contribute to clinical outcome.

2. Materials and methods

With Internal Review Board approval at both institutions, the cancer center databases of the Massachusetts General Hospital (MGH) and Brigham and Women's Hospital (BWH) were queried to identify all women treated at either institution for cervical cancer between January 2000 and December 2013. In total 1119 women were identified. The cohort of older women was defined as age >65.0 years old at the time of diagnosis. These women were compared with the cohort of younger patients, <65 years at the date of diagnosis of cervical cancer. Eligibility for Medicare in the United States begins at 65 years, and additionally this is the age when the ASCCP recommends to stop cervical cancer screening with adequate negative screening history, therefore this this age cutoff was chosen prior to data collection and analysis. All patients had pathologic confirmation of cervical cancer diagnosis of any histology.

Patient charts were retrospectively reviewed, and relevant clinical and pathologic variables were extracted and recorded. Data included patient variables such as age, body mass index (BMI), and smoking history, clinical outcomes including stage, progression free and overall survival and the need for adjuvant therapy, and pathologic variables such as histology and grade. Data could be collected from the primary source, such as a pathology report, or recorded by a physician in a documented history and physical without the pathologic report required. Additional patient data, such as co-morbidity data, was not collected as it was not uniformly reported. *t*-tests, Fisher's exact tests, and Kaplan-Meier analyses were performed. Multivariable survival analysis was performed utilizing age adjusted cox proportional hazard modeling. Statistical significance was set prior to data collection at $p < 0.05$. Overall survival was defined as date of cervical cancer diagnosis to date of death. Stata (version 14.2; Stata Corp, College Station, TX) was used to conduct all statistical analysis.

3. Results

The cohort consisted of 1119 women with cervical cancer at BWH and MGH over a fourteen-year period. Of these, 191 women (17.1%) formed the older patient cohort, defined as equal to or older than 65.0 years at the time of diagnosis. The remaining 928 women (82.9%) were younger than 65.0 years at diagnosis and were included as the referent population. Table 1 compares patient and clinical variables by patient age at diagnosis. Older women were more likely to present with advanced International Federation of Gynecology and Obstetrics (FIGO) stage disease ($p < 0.001$). Squamous cell carcinoma was a more common histology in the older cohort ($p < 0.001$) compared with adenocarcinoma and other histologies. This cohort was also more likely to have a current or past history of tobacco use ($p = 0.04$). Older women were less likely to have a reported history of Papanicolaou (pap) testing ($p < 0.001$). Hypertension and diabetes were both more likely to be reported in the medical histories of women over 65 ($p < 0.001$ and $p = 0.007$ respectively).

Table 1
Patient characteristics by patient age cohort.

	Younger cohort (<65 yo)	Older cohort (≥65 yo)	p-Value (univariate)
Number patients (n)	928 (83%)	191 (17%)	
Stage[a]			<.001
1	523 (58%)	54 (30%)	
2	148 (16%)	60 (33%)	
3	153 (17%)	42 (23%)	
4	82 (9%)	26 (14%)	
Histology			<.001
Squamous cell	519 (56%)	142 (74%)	
Adenocarcinoma	325 (35%)	28 (15%)	
Other	84 (9%)	21 (11%)	
Current/past tobacco			.04
Yes	365 (39%)	89 (47%)	
No	515 (55%)	88 (46%)	
Unknown	48 (5%)	14 (7%)	
Reported history of Papanicolaou testing			
Yes	660 (71%)	94 (49%)	<.001
No	29 (3%)	12 (6%)	
Unknown	239 (26%)	85 (45%)	
Hypertension			<.001
Yes	164 (18%)	97 (51%)	
No	731 (79%)	86 (45%)	
Unknown	33 (4%)	8 (4%)	
Diabetes			.007
Yes	60 (6%)	23 (12%)	
No	836 (90%)	160 (84%)	
Unknown	32 (3%)	8 (4%)	

[a] Stage information missing for 22 (2%) women in younger cohort, 9 (5%) women in older cohort.

Overall, older women received different modalities of therapy for cervical cancer treatment when controlling for FIGO stage (Table 2). Older women were less likely to undergo surgery (38% versus 70%, $p < 0.001$) and more likely to undergo radiation (77%% versus 52%, $p < 0.001$). Univariate analysis revealed that older women were more likely to receive chemotherapy (59% versus 49%, $p = 0.004$), however when controlling for stage there was no difference in the rate of administration of chemotherapy ($p = 0.34$). Older women who did undergo surgery did not receive the same surgical management as their younger counterparts, as they were less likely to have a pelvic lymph node dissection performed (41% versus 61%, $p = 0.04$). The rate of positive

Table 2
Treatment characteristics by patient age cohort.

	Younger cohort (<65 yo)	Older cohort (≥65 yo)	p-Value (univariate)
Number patients (n)	928 (83%)	191 (17%)	
Surgery[a]			<.001
Yes	649 (70%)	73 (38%)	
No	277 (30%)	118 (62%)	
Pelvic Lymphadenectomy			.04
Yes	394 (61%)	30 (41%)	
No	227 (33%)	31 (42%)	
Unknown	28 (4%)	12 (16%)	
Radiation			<.001
Yes	482 (52%)	148 (77%)	
No	420 (45%)	32 (17%)	
Unknown	26 (3%)	11 (6%)	
Chemotherapy			.004
Yes	456 (49%)	112 (59%)	
No	454 (49%)	69 (36%)	
Unknown	18 (2%)	10 (5%)	

[a] Surgery information missing for 2 (0.2%) women in the younger cohort.

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