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A study of treatments and outcomes in elderly women with cervical cancer

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ABSTRACT

Objective: With the population aging, development of safe and effective treatments for elderly patients with cancer is needed. Although old age is considered a poor prognostic factor, this is not only because of the patient's disease condition or response to treatment, but also because of treatment strategy and intensity. The purpose of this study was to clarify the influence of age on treatment and prognosis in patients with cervical cancer.

Methods: Women with stage Ib–IV cervical cancer treated at our institution between 1997 and 2014 were retrospectively analyzed. Patients were stratified by age into groups for analysis, <65 years and ≥65 years. Categorical variables were compared using chi-squared and Fisher's exact tests. Survival analyses were performed using the Kaplan–Meier method, and comparisons were made using the log-rank test. Subsequently, Cox proportional hazards models were developed to find independent prognostic factors.

Results: Of 959 patients included in our study, 247 were ≥65 and 712 were <65 years of age. Elderly patients tended to be at a more advanced stage than younger patients ($p < 0.001$). Elderly patients more commonly had comorbidities. More received standard treatment in the younger patient group at any disease stage than in the elderly patient group ($p < 0.001$). Similar rates of adverse effects caused by surgery or radiotherapy were seen in patients from both groups. Although overall survival was statistically shorter in elderly patients (74.7 vs. 57.1%, $p < 0.001$), there was no significant difference in disease-specific survival for patients treated only with standard treatment. In multivariate analyses, clinical stage, histological type, treatment intensity, and primary surgery remained independent prognostic factors. Age was not an independent prognostic factor.

Conclusions: The influence of age on prognosis in patients with cervical cancer was less than we expected. Elderly patients might have better outcomes depending on the type of standard treatment they receive. The appropriate modality and intensity of treatment should be based on the patient's general condition and background.

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Introduction

The proportion of elderly people has increased at a rapid pace, and the percentage of the population over 65 years of age in 2015 was estimated to be 26.7% and will increase to 39.9% by 2060 in Japan [1]. In association with an aging society, the number of cancer patients has increased, with elderly patients making up an estimated 70% of cancer cases in 2012 [2]. Because this trend is predicted to continue, safe and effective management of elderly patients with cancer is needed.

We seem to have had a less positive attitude regarding medical treatment for elderly patients than that for younger patients because of their physical and social background. These days, treatment for geriatric patients with malignancies has become more focused and has been treated as one major field in the National Comprehensive Cancer Network (NCCN) guidelines in the last few years [3].

The proportion of elderly people has also increased yearly in the area of gynecologic treatment. According to studies for elderly women with ovarian cancer, although old age is considered a poor prognostic factor, it appears that the reason for this is related not only to the elderly patient's disease condition or responsiveness to treatment but also to the treatment strategy and intensity [4,5]. The NCCN guidelines describe treatment for elderly patients with

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ovarian cancer only because of a lack of prospective studies of other gynecologic cancers in elderly women.

The purpose of this study was to clarify the following questions. Is the prognosis of cervical cancer poorer in elderly women than in younger women? If the prognosis is poorer in elderly women, is it due to the intensity of treatment? Do age and treatment strategies affect prognosis differently according to clinical stage? In this study, we did a survey of treatment and outcome of elderly patients with cervical cancer.

Materials and methods

We obtained data of women diagnosed with stage Ib–IVb cervical cancer between 1997 and 2014 at the National Hospital Organization Kyushu-Cancer Center. We reviewed clinical records and obtained data including age at diagnosis, FIGO (International Federation of Obstetricians and Gynecologists) stage, histological type, body mass index (BMI), smoking history, comorbidities, history of pap smear screening, methods of treatment, date of diagnosis, last date of patient follow-up, and time of death.

Patients were stratified by age into groups for analysis, <65 years and ≥65 years. Each patient's stage was determined using the staging FIGO criteria from 1997. Primary treatment was categorized as standard treatment, nonstandard treatment, or palliative treatment. The standard treatment group was defined as patients treated along treatment guidelines for cervical cancer, as edited by the Japanese Gynecologic Oncology Group (2015), including patients with stage Ib1 who had a radical hysterectomy (RAH) or radiation therapy (RT), and stage Ib2–IIb who had an RAH or concurrent chemoradiotherapy (CCRT) [6].

Patients who had an RAH also had their pelvic lymph nodes dissected and had a biopsy of their paraaortic lymph nodes. In addition, patients with high risk factors such as metastatic lymph nodes or invasion of the whole myometrium received radiotherapy or chemotherapy in the standard treatment group. External beam radiation therapy (EBRT) consisted of 45–50.4 Gy delivered to the pelvis with 12–30 Gy brachytherapy (BT). Patients were also administered cisplatin (30–40 mg/m^2) every week during the term of EBRT. Reduction in radiation or chemotherapy dose, or termination of therapy because of adverse effects was permitted.

We classified patients with stage III–IV who had aggressive treatment such as the combination of RT or CCRT and systematic chemotherapy as the standard treatment group. Patients who received radiotherapy or medication only for symptomatic relief were regarded as the palliative treatment group. The other patients were classified as the nonstandard treatment group. We excluded eight patients, on whom only conization or radical trachelectomy was performed, from the survival analysis.

Mortality and survival rates at 5 years from diagnosis were calculated in both the younger and elderly groups. Patients who were alive but observed within 5 years were defined as censored. Overall survival (OS) and disease-specific survival (DSS) were compared between the standard and nonstandard treatment groups, and between the <65 and ≥65 year groups.

OS was calculated from the date of diagnosis to the last date of patient contact or death from any cause. DSS was calculated from the date of diagnosis to the last date of patient contact or death from cervical cancer.

Categorical variables were compared using chi-squared and Fisher's exact tests. Survival analyses were performed using the Kaplan–Meier method, and compared using the log-rank test. Univariate analyses were performed to confirm whether clinical factors influence prognosis. Subsequently, Cox proportional hazards models were developed to determine independent prognostic factors. Only a $p < 0.05$ using the two-tailed analysis was regarded as statistically significant. Statistical analysis was performed using SPSS software, version 24 (IBM, Inc.).

This study was approved by the institutional review board, May 22, 2013. The number of the certification is 2013-43. Written consent was obtained from the women.

Results

Of 959 patients with stages Ib–IVb cervical cancer included in our study, 247 were aged ≥65 (range 65–93 years) and 712 were <65 years (range 22–64 years). Table 1 shows patient characteristics classified by age. There were disparities between the elderly patient group and the younger patient group in distribution of stage, histological type, comorbidities, BMI, smoking, and history of pap smear screening for cervical cancer. Elderly patients tended to be at a more advanced stage than younger patients ($p < 0.001$). Elderly patients more commonly had comorbidities, and had either hypertension, diabetes, a malignant tumor, and/or other medical diseases. Although there was no disparity in pap smear experience, elderly patients tended to wait longer between screenings, at least 5 years or more.

In the younger patient group, 555 (96.5%) patients with stages Ib–IIb received standard treatment while 123 (78.3%) in the elderly patients group were treated with standard therapy. Furthermore, the number of patients that received primary surgery was lower in elderly than in younger patients (30.9% vs. 80.2%). Among elderly patients with advanced disease (stages III–IV), standard treatment was administered in 44.9% of them, and 2.2% received only palliative treatment. In contrast, 106 (81.5%) patients in the younger patient group received standard treatment and one (0.8%) patient was treated palliatively. In all advanced patients from both groups, most received radiotherapy (90.8% vs. 95.5%), while CCRT was administered less in elderly patients (60.0% vs. 37.1%). Furthermore, there was a significant difference in the administration of systemic chemotherapy between younger and elderly patients (31.5% vs. 13.5%, Table 2). Similar rates of adverse effects caused by surgery or radiotherapy were seen in patients from both groups.

The real survival rate of patients after 5 years since beginning treatment was higher in the <65 years group than in the ≥65 years

Table 1
Demographic characteristics of the population.

	<65 (n = 713)	≥65 (n = 246)	P-value
stage			<0.001
1	410 (57.5)	84 (34.1)	
2	173 (24.3)	73 (30.0)	
3	73 (10.2)	55 (22.4)	
4	57 (8.0)	34 (13.8)	
Histological type			<0.001
SCC	533 (74.8)	215 (87.4)	
non-SCC	179 (25.1)	31 (12.5)	
unknown	1 (0.1)		
Comorbidity, past history			
hypertension	69 (9.8)	98 (40.3)	<0.001
diabetes	16 (2.3)	25 (10.3)	<0.001
malignant disease	37 (5.3)	24 (9.9)	0.015
other medical disease	98 (13.9)	87 (35.8)	<0.001
BMI (median)	22.1	22.3	0.048
smoking	261 (33.7)	25 (24.0)	<0.001
Pap smear screening			<0.001
none	326 (59.5)	115 (54.2)	
<1 yr	80 (14.6)	23 (10.8)	
1–5 yr	121 (22.1)	20 (8.0)	
>5 yr	21 (3.8)	54 (25.5)	

SCC: squamous cell carcinoma, BMI: body mass index, Pap: Papanicolaou.

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