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Original Article

Effect of Age on Survival in Patients with Cervical Cancer

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ABSTRACT

Cervical cancer survival rates depend on several factors, such as the stage of the cancer, age of the patient, and overall health status. However, early detection through regular screening and prompt treatment can significantly increase the chances of survival. **Objectives:** To determine the effects of age and other prognostic factors on survival in patients with cervical cancer. **Methods:** The medical records of 142 patients with cervical cancer were retrospectively reviewed. All patients were diagnosed by biopsy between January 2000 and December 2012 at the Princess Norah Oncology Center of King Abdul Aziz Medical City (Jeddah, Saudi Arabia). Kaplan-Meier survival curves and log-rank tests were used to compare groups. **Results:** The mean age at diagnosis was 51.77 ± 13.36 years (range, 28–96 years). The 1-year survival rates for each age group were as follows: < 30 years, 100%; 30–54 years, 83.9%; 55–65 years, 72.2%; and > 65 years, 73.3%. By contrast, the 5-year survival rates (0%, 38.5%, 30.8%, and 33%, respectively) were much lower. No significant differences in survival outcomes were identified among the age groups. Low mean hemoglobin levels during treatment were associated with poor survival rates. The mean hemoglobin level for all patients was 14.22 ± 16.28 mg/dL. **Conclusions:** Survival outcomes in patients with cervical cancer were not influenced by age at diagnosis. It will be necessary to perform systematic reviews of multiple studies on this topic to come to a more definitive conclusion.

INTRODUCTION

The third most frequent malignancy and the fourth most frequent cause of cancer-related fatalities globally is cervical cancer. In 2008, 275,100 cervical cancer patients passed away and an estimated 529,800 patients received a diagnosis. Importantly, less affluent nations account for more than 85% of cervical cancer instances and fatalities. This can be explained by the poor implementation of effective screening programs to detect precancerous and early malignant lesions [1]. Since the early 1970s, numerous studies have focused on the predictive importance of age in cervical cancer. Age at diagnosis has not always been studied as a prognostic indicator in the same manner. The main topic of discussion was frequently whether youthful patients have worse prognoses than elderly patients [2, 3]. It was assumed that cancer is physically more aggressive in people who are younger. Other studies have associated an older age with a poorer outlook, presuming that elderly patients receive less aggressive, and hence unsuitable, therapy, thereby affecting their longevity [4]. Several other mortality studies on cervical cancer in general or assessment studies on screening programs [5,6] have included age as a prognostic component in the survival analysis. Nevertheless, it is still not obvious whether age is a distinct prognostic factor in cervical cancer. There haven't been many population-based research released up to this point. In fact, the prevalence and mortality of cervical cancer have declined in industrialized nations as a result of the adoption of efficient screening programs [7]. In Saudi Arabia, according to the Saudi Cancer Registry, the number of newly diagnosed patients per year remained

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stable from 1994 to 2009 (97 new cases diagnosed in 1994; 101 new cases diagnosed in 2009)[8] likely due to the lack of effective screening programs for this disease in Saudi Arabia. Various studies have examined the prognostic factors that affect the survival and outcomes of patients with cervical cancer. Advanced stage, Tumor bulk, number of tumors, number of sites of involvement, and incomplete treatment courses are well-known factors associated with poor survival [9]. Other factors such as low hemoglobin level and tumor size usually greater than 4 cm have also been reported to be associated with poor survival and outcomes [10, 11]. Although some studies have examined the effect of age at diagnosis on patient survival, the results have been inconsistent. For example, some studies have shown that patients aged 65 years and older have poorer survival rates than younger patients [12, 13]. Brune *et al.*, demonstrated that women with invasive cervical cancer have increased mortality rates than normal women until the age of 75 after which this factor does not contribute much [14]. By contrast, some studies have shown that younger patients (defined by cut-off ages of 45, 35, or 40 years, respectively) have worse survival outcomes than older patients [14-16]. Other studies have shown that age does not affect the prognosis or final survival outcomes of patients with cervical cancer [17, 18]. Furthermore, no studies on the relationship between age and survival in patients with cervical cancer have been performed in Saudi Arabia. Therefore, in this study, we aimed to determine whether survival rates differed among patients diagnosed with cervical cancer at different ages, based on data collected from "Princess Norah Oncology Center, King Abdul Aziz Medical City-Jeddah in Saudi Arabia". Our study was expected to help national awareness programs for cervical cancer screenings target messages to high-risk patients.

METHODS

This was a retrospective study analyzing the medical records of women with cervical cancer diagnosed by histological biopsy specimens between January 2000 and December 2012 and treated at Princess Norah Oncology Center, King Abdul Aziz Medical City (Jeddah, Saudi Arabia). Using the International Classification of Diseases (ICD) 9 and 10 codes for cervical cancer, the records of 193 patients were retrieved. Of these, 142 patients were considered appropriate for review. Fourteen patients did not fit our inclusion criteria because they were diagnosed with a disease other than cervical cancer, and 37 had records with missing information that would have affected the analysis. We collected information on variables including demographic data, smoking history, Pap smear screening history, FIGO staging, histological type, and grading, tumor size (cm), hemoglobin level (g/dl), lymph node involvement, and treatment modality. We analyzed survival based on 1- and 5-year survival rates, irrespective of disease status. The treatment modalities for patients with cervical cancer included radiotherapy, simple or radical surgical hysterectomy, chemotherapy, or a combination of radiotherapy and surgery or concurrent chemoradiotherapy. The treatment modality was chosen according to the International Federation of Gynecology and Obstetrics (FIGO) staging at diagnosis. All data analyses were conducted using SPSS version 21. The variables were summarized using descriptive statistics. The 1- and 5-year survival rates were estimated using Kaplan-Meier survival curves. Significance was analyzed using log-rank tests, and differences with *p-values* less than 0.05 were considered statistically significant. Different prognostic factors were adjusted according to age groups using multivariate analysis. Ethical approval for our study was obtained from the ethical committee of King Abdul Aziz Medical City-Jeddah.

RESULTS

For the 142 patients reviewed, the mean age (± standard deviation) at diagnosis was 51.77 ± 13.36 years (range, 28–96 years). By age group, 3.5% of patients were younger than 30 years, 59.2% were aged 30–54 years, 17.6% were aged 55–65 years, and 19.7% were older than 65 years. Regarding smoking status, 8.45% of patients were smokers, 38.73% were nonsmokers, and the remaining 52.82% had an unknown smoking status (Table 1). The most common histopathological type was squamous cell carcinoma (78.2%), and high-grade cancers were the most common 62 (43.66%) (Table 1). Concerning lymph node involvement, 35.92% of patients had negative lymph nodes, 2.11% had positive lymph nodes as diagnosed during surgery, 30.99% had positive lymph nodes as diagnosed by imaging (e.g., computed tomography and magnetic resonance imaging), and 30.99% had unknown lymph node status (Table 1). Lymph node involvement was not associated with survival (p = 0.170). However, the size of the primary tumor was significantly associated with survival ($p < 0.001$).

Characteristics	Total (n)	Age groups (years)			
		>65	55–64	30–54	<30
Histopathologic type					
Squamous	111	23	21	63	4
Adenocarcinoma	20	4	2	14	0
Other	11	1	2	7	1
Grade					
Low		2	2	9	1
Moderate		7	8	26	1
High		12	12	35	3
Not reported		7	3	14	0

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History of smoking					
Smoker		3	2	6	1
Nonsmoker		10	11	32	2
Not reported		15	12	46	2
Lymph node involvement					
None		5	8	35	3
Surgical		0	1	2	0
Imaging		11	5	26	2
Not reported		12	11	21	0

Table 1: Patient clinicopathological characteristics by age group.

No significant differences in local recurrence were found among age groups (<30 years, 0%; 30–54 years, 17%; 55–65 years, 3%; and >65 years, 4%). Overall, stage 2B was the most common stage at diagnosis, accounting for 46.48% of all cases (Table 2). A significant association between the advanced stage at diagnosis and poor survival outcome was identified ($p < 0.001$). None of the patients had any record of a Pap smear screening before diagnosis.

Stage	Total (n)	Age groups (years)			
		>65	55–64	30–54	<30
1A	1	0	0	1	0
1B	17	1	1	14	1
1C	1	0	0	1	0
2A	9	3	2	3	1
2B	66	12	11	41	2
3A	5	0	1	4	0
3B	16	3	5	8	0
3C	1	0	0	0	1
4A	10	4	2	4	0
4B	6	2	2	2	0
Not reported	10	3	1	6	0
Total	142	28	25	84	5

Table 2: Analysis of cancer stage in different age groups

The 1-year survival rate for the overall study population was 78%. By age group, the 1-year survival rates were 100% for patients younger than 30 years, 83.9% for those aged 30–54 years, 72.2% for those aged 55–64 years, and 73.3% for those than 65 years (Figure 1). By contrast, only 22% of the study population survived for 5 years or more, with 5-year survival rates of 0%, 38.5%, 30.8%, and 33.3%, respectively, for the four age groups. No significant differences were observed among groups using the log-rank test ($p = 0.934$).

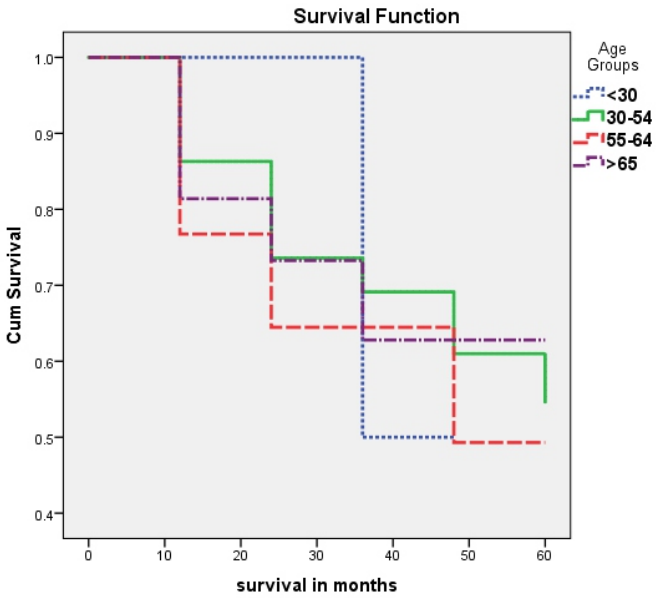

Figure 1: Overall survival according to age groups

Concerning treatment modalities, 76% of patients did not undergo surgical intervention, 9.859% underwent a simple hysterectomy, 8.451% underwent a radical hysterectomy, and 4.22% underwent other surgical treatments. Moreover, 62% received concurrent chemotherapy, and 26.65% received radiotherapy. Of all patients, 80.81% received an entire course of cisplatin therapy, and 88.64% completed radiotherapy. As expected, completion of treatment was positively associated with overall survival (cisplatin chemotherapy, $p = 0.004$; radiotherapy, $p = 0.000$). For patients completing treatment on concurrent chemoradiation, no significant difference was found. Patients who started palliative therapy (11.76%) had poor survival rates ($p = 0.005$) due to the advanced stage of cancer at the time of diagnosis. Only 8% of patients underwent pelvic boost radiotherapy. Interestingly, low mean hemoglobin levels (less than 10 mg/dL) during treatment were negatively associated with survival rates ($p = 0.002$). The mean hemoglobin level for all patients was 14.22 ± 16.28 mg/dL.

DISCUSSION

In this study, we aimed to determine the effect of age at diagnosis on the prognosis of patients with cervical cancer. Our results showed that age at diagnosis is not associated with survival rates and no significant difference in survival rate was found among age groups. Moreover, other well-established prognostic factors for cervical cancer did not differ among age groups. These results are important for the implementation of screening and vaccination programs in less-developed countries, such as Saudi Arabia. Our results showed no significant differences in survival or prognostic factors among age groups. These

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results are consistent with those of other studies that used different age cut-offs, including a population-based study with 2,000 cases of cervical cancer (age groups, <30 years and 40–60 years) [16, 17]. By contrast, in our study, we divided the study population into four groups (<30 years, 30–54 years, 55–64 years, and >65 years) to identify more detailed relationships between 1- and 5-year survival rates and age. We also found that low hemoglobin level (below 10 mg/dL) during treatment is associated with a lower survival rate. This result was consistent with that of other studies investigating the effects of anemia on survival rates [10]. Notably, the mean hemoglobin level in our population was in the normal range. Increased tumor size was negatively associated with survival outcomes, which was consistent with the results of other studies [19]. Moreover, our results confirmed the well-known effects of cervical cancer staging on patient survival: the advanced FIGO stage was significantly associated with low survival rates. Additionally, patients who received palliative therapy had lower survival rates, which could be explained by the advanced stage at diagnosis. Completion of chemotherapy or radiotherapy was significantly associated with higher survival rates. However, in patients receiving chemoradiotherapy, completion of treatment was not associated with better survival, similar to the results of Tharavichitku *et al.*, [20]. Importantly, none of the patients in our study reported to have undergone screening for cervical cancer using Pap smears. Screening for cervical cancer has decreased both the incidence of and mortality from this malignancy worldwide [7]. However, the number of newly diagnosed cases of cervical cancer per year has remained stable in Saudi Arabia, which could be explained by the country's lack of appropriate screening programs [8]. One limitation of this study was that a small number of patients were involved in the different categories. For example, only five patients younger than 30 years of age were included. This resulted in the exaggeration of the 1- and 5-year survival rates (100% and 0%, respectively). Therefore, further studies with a big sample pool and more categorizations of ages are needed to confirm our results.

CONCLUSIONS

In conclusion, in our population, age at diagnosis did not affect the survival outcomes of patients with cervical cancer. However, systematic reviews of multiple studies on this topic should be conducted to obtain a more definitive conclusion. Based on our results, we recommend the establishment of screening and awareness programs to emphasize the importance of cervical cancer screening for all age groups equally rather than targeting a specific age group.

Conflicts of Interest

The authors declare no conflict of interest.

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