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# The long-term outcomes in perimenopausal patients treated for cervical cancer

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## ABSTRACT

**Introduction.** In the coming decades, the population of adults 65 years of age and older will increase significantly. Younger patients between 30 and 40 years of age, who are diagnosed with cervical cancer, have a better prognosis than the older group. The second peak of incidence, involving patients between 60 and 70 years of age, correlates with a poorer prognosis.

**Material and methods.** In our study, we included 360 patients between 40 and 60 years old operated on due to cervical cancer followed by radiochemotherapy. We divided these patients into two groups according to age. The first group was composed of premenopausal patients (aged between 40 and 50 years) and the second of postmenopausal patients (aged between 50 and 60 years), and long-term outcomes (overall survival rates OS) were analysed in both groups of patients.

**Results.** We observed statistically significant differences in the long-term outcomes between the subgroups of patients treated surgically for cervical cancer, and it was better in the premenopausal group of patients. No statistically significant relationship between these two groups of patients as far as clinical features was observed.

**Conclusion.** We found that postmenopausal patients may actually benefit more from having radical surgery. Proving this supports the case for distinguishing geriatric oncology from gynaecological oncology.

**Key words:** cervical cancer, geriatric oncology

Medical Research Journal 2017;  
Volume 2, Number 3, 111–114  
10.5603/MRJ.2017.0014  
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ISSN 2451–2591

Med Res J 2017; 2 (3): 111–114

## Introduction

In the coming decades, the population of adults 65 years of age and older will increase significantly [1]. As the number of elderly patients (and along with it, the number of postmenopausal patients) is increasing from day to day, the current model of medical care will have to change to adapt to the aging population. In clinical practice, two groups of patients with cervical cancer are observed [2]. First, are the women under 40 years old who are sexually active with high exposure to cervical cancer risk factors, such as a high number of partners, cigarette smoking, and lower socioeconomic conditions. The second group comprises an older group of patients, the majority of whom are postmenopausal. Usually these patients have had previous surgical in-

tervention, such as conisation or some of the ablation methods (cryotherapy, laser therapy, or other types of therapies), due to intraepithelial neoplasm. Among patients with cervical cancer, the different peaks of incidence correlate with differences in prognosis. Younger patients between 30 and 40 years of age who are diagnosed with cervical cancer have a better prognosis than the older group. The second peak of incidence, involving patients between 60 and 70 years of age, correlates with a poorer prognosis [3].

The long-term outcome of cervical cancer treatment is still insufficient. Nogueira-Rodrigues et al. presented the results of treatment for a large group of patients, including 1339 younger patients and 143 elderly patients, treated for cervical cancer. The overall five-year survival rate among the younger patients was 58.2%, and 48.5%

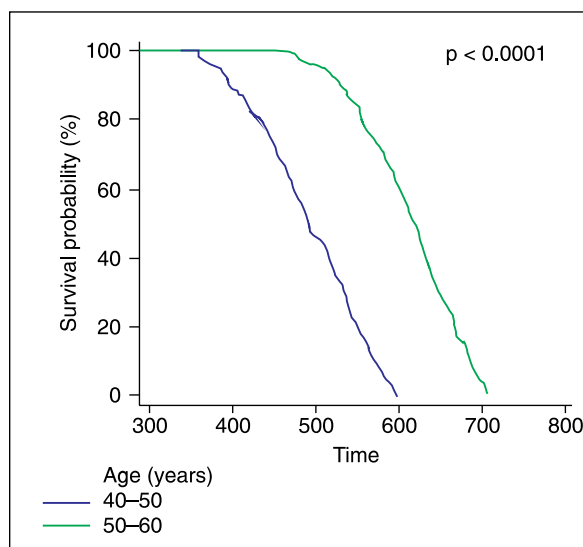
among the older patients (including all stages from FIGO I to IV) [3]. Nevertheless, most of our patients are diagnosed as LACC. In particular, the poorer prognosis found in older as compared to younger women seems to be related to a more advanced stage of the disease at the time of diagnosis [3]. Unfortunately, a widespread mass screening program for cervical cancer has not yet been instituted in all countries, and this fact may impact the long-term outcomes in postmenopausal and elderly women. Another factor, which may also influence the long-term outcome in older patients, is the method of treatment. Postmenopausal and elderly patients with cervical cancer are more often treated using radiotherapy than surgery or radio-chemotherapy [3]. Generally, it is thought that surgery in elderly patients is linked with a greater number of subsequent complications. Although elderly patients with uterine cervical cancer reportedly have a poorer prognosis than younger patients, the group of postmenopausal patients in whom the poorer prognosis is related to comorbidity secondary to the age of the patient needs to be more precisely distinguished from the group of women who may benefit from radical surgery followed by radiotherapy. Although cervical cancer is more common in young women, it is certainly present in postmenopausal and elderly women [4]. Furthermore, while the incidence of cervical cancer among younger patients has decreased, the proportion of patients diagnosed who are over 70 years of age has remained stable (near 18%) [2].

The aim of our study was to investigate whether postmenopausal patients benefit more from radical surgery.

## Material and methods

In our study, we included 360 patients between 40 and 60 years old operated on due to cervical cancer. We divided these patients into two groups according to age. The first group was composed of premenopausal patients (aged between 40 and 50 years), and the second group was composed of postmenopausal patients (aged between 50 and 60 years); long-term outcomes (overall survival rates OS) in both groups of patients were analysed.

Most of these patients (95%) were operated on at the beginning of therapy prior to adjuvant radiochemotherapy. These patients were treated at the Lukaszczyk Oncological Center in Bydgoszcz between 2008 and 2012. We retrospectively evaluated the series of women. The surgical procedure performed consisted of radical hysterectomy with lymphadenectomy. The database of the Kujawsko-Pomorski regional office of the National Health System of Poland provided the data on overall survival rates.



**Figure 1.** Statistically significant differences in the long-term outcomes between the subgroups of patients treated surgically for cervical cancer ( $p < 0.0001$ ) depending on age, older or younger than 50 years

Adjuvant radiochemotherapy was used for cases with high-risk prognostic factors, including tumour size ( $> 4$  cm), parametrial invasion, and lymph node metastasis. Radiotherapy was performed using whole pelvis external beam radiation (59.4 Gy in 28 fractions), and chemotherapy consisted of a platinum-based regimen administered for four to six cycles.

## Results

We observed statistically significant differences in the long-term outcomes between the subgroups of patients treated surgically for cervical cancer. Specifically, we observed a poorer prognosis in the patients between 40 and 50 years of age and a better prognosis in the patients between 50 and 60 years of age (Fig. 1).

No statistically significant relationship between these two groups of patients as far as clinical features, such as initial stage of the disease, grading, or histological type, was observed. Similarly, the proportion of patients treated by surgery alone or surgery followed by radiotherapy did not differ in the examined patients (Tab. 1).

## Discussion

We found that the postmenopausal patients treated for gynaecological cancer have a better prognosis than premenopausal patients.

Generally, gynaecological malignancy correlates with survival rate. Mortality rates depend upon age, and

**Table 1.** Clinical features, such as initial stage of the disease (FIGO), grading, or histological type depending on age of the patients: older or younger than 50 years

Clinical feature	Age			
	40–50 years n = 151		50–60 years n = 209	
IA	11	7	12	6
IB	120	79	180	86
IIA	20	16	17	8
Carcinoma planoepitheliale	140	92	198	94
Adenocarcinoma	10	6	8	4
Carcinoma adenosquamous	1	2	1	0.5
Sarcoma	0	0	2	1.5
G1	15	10	16	7.5
G2	100	66	149	71
G3	36	24	44	21.5

a poorer prognosis is observed in elderly patients. The majority of studies compare the long-term outcomes between elderly and young patients. The mortality rates of patients treated for cervical cancer who are more than 70 years old are typically 2–3-fold higher in comparison to younger women [2]. A few studies distinguished the group of women treated for cervical cancer more precisely. For instance, Sharma et al. assessed a large group of patients with FIGO stage IB1–IIA (28 902), who were stratified by age: < 50, 50 to 59, 60 to 69, 70 to 79, and  $\geq$  80 years. They observed differences in applied therapy relative to the age of the patient. Surgery was most preferably used in patients who were under 50 years of age. More specifically, lymphadenectomy was performed in 66.8% of women < 50 years old versus 9.1% of patients  $\geq$  80 years old, who instead underwent an analogically radical hysterectomy. In advanced stages, the usage of brachytherapy decreased according to age. Elderly women with cervical cancer are not treated as radically as younger patients. The differences start to be measurable at about 50 years of age (surgery is less radical, followed by adjuvant radiation or application of brachytherapy) [4]. The authors suggested that the cancer-specific mortality rate is higher in older women, even when the influence on overall survival rate related to the applied treatment is not taken into consideration [4]. However, in analysing patients who were younger or older than 70 years of age, the authors observed the following relationship: elderly patients have more advanced disease at the time of diagnosis, and this is the factor most indicative of a poorer prognosis. On the other hand, age is an important factor in the allocation of treatment, which also influences overall survival [3]. The classification of the patient for adequate radical therapy is crucial for improving survival.

Nosaka et al. reported that concurrent chemoradiotherapy may be useful in the treatment of cervical cancer patients and is well tolerated in the elderly. The authors examined two groups of patients. The first group included women from 70 to 77 years of age, and the second included those from 70 to 89. The median overall survival rates were comparable between the two groups (66.9 and 60.1 months, retrospectively). However, the profile of toxicities related to the applied therapy differed between older and younger cervical cancer patients. The most common was hyponatraemia, followed by neutropaenia and diarrhoea [5]. Furthermore, it was suggested that geriatric patients with stage I or II cervical carcinoma may benefit from radical surgery followed by radiotherapy [6]. Similarly, Lin et al. demonstrated that patients older than 75 years may be treated curatively with radiotherapy [7]. In our group of patients, we found that patients just beyond menopause, between 50 and 60 years of age, may also benefit from radical surgery and have even better long-term outcomes than patients between 40 and 50 years of age.

Since the poorer prognosis in elderly patients is a result, as was mentioned above, of a more advanced stage of the disease at the time of diagnosis, the screening program must also be used in these patients. Cakmak et al. presented their results from a study of 661 women participating in cervical cancer screening. The patients were divided into two groups. The first comprised postmenopausal patients between 45 and 64 years of age, and the second consisted of elderly patients over 65 years old. Cytological abnormalities have often been found to be statistically significantly in elderly patients. Although the cervical screening program is not usually continuous in elderly patients, squamous intraepithelial lesions can still be encountered in this group, which definitely requires greater attention when it comes to gynaecological care [8]. A cancer screening program is an important tool for decreasing morbidity and mortality rates even among the elderly [9].

It is understood that the number of deaths is related to the total number of patients, and that the number of these patients who are postmenopausal is greater than those who are premenopausal. The two groups therefore differ when it comes to overall survival rates. This fact supports the hypothesis that we should correlate the type of therapy we apply with the age of the patient, not only because of organ efficiency or haemostatic condition, but also because of the biology of the neoplasm itself. Older patients need different standards of treatment beyond just a reduction in dose relative to age. Based on the outcomes obtained, we also need to start to distinguish geriatric oncology from gynaecological oncology.

In summary, we chose cervical cancer patients for our analysis of the potential influences of the range of surgery on treatment outcomes according to age. We

found that postmenopausal patients may benefit more from having radical surgery. Proving this supports the case for distinguishing geriatric oncology from gynaecological oncology.

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