



Oncological Outcomes in Geriatric Patients with Early Stage Gynecological Cancer who Underwent Surgery and Radiotherapy

Erken Evre Jinekolojik Kanserli Geriatrik Hastalarda Onkolojik Sonuçlar

Necla Gurdal, Berna Akkus Yildirim

Prof. Dr. Cemil Tascioglu City Hospital, Department of Radiation Oncology, Istanbul, Turkey

Abstract

Aim: Evaluation of oncological results obtained with surgery and adjuvant radiotherapy (RT) in geriatric patient group with early stage gynecological cancer.

Material and Method: 31 patients aged 65 years and older who were operated for early stage gynecological cancer and had adjuvant RT were included in the study. All patients were evaluated in terms of general characteristics, local and systemic treatments, and oncological outcomes.

Results: The percentages of patients diagnosed with endometrium cancer and cervix cancer are 80.6% and 19.4%, respectively. The median age of the patients was 69 (range, 65-86). All patients underwent total abdominal hysterectomy and bilateral salpingo oophorectomy, followed by adjuvant pelvic radiotherapy. Intracavitary vaginal brachytherapy was applied to 90.3% of the patients. At a median follow-up of 69 months, 3.2% of patients had local recurrence and 3.2% had distant metastases. The five-year DFS and OS rates were 93% and 80%, respectively

Conclusions: Treatment planning in geriatric patient group should be shaped according to prognostic factors, age group, and comorbidity. Remarkable oncological results can be obtained with multimodality treatments in the selected patient group.

Keywords: Gynecologic cancer, radiotherapy, geriatric patients

Öz

Amaç: Erken evre jinekolojik kanserli geriatrik hasta grubunda cerrahi ve adjuvan radyoterapi ile elde edilen onkolojik sonuçların değerlendirilmesidir.

Gereç ve Yöntem: 65 yaş ve üzeri, erken evre jinekolojik kanser nedeni ile opere edilmiş ve adjuvan radyoterapi uygulanmış 31 hasta çalışmaya dahil edilmiştir. Tüm hastalar genel özellikler, uygulanan lokal ve sistemik tedaviler, ve onkolojik sonuçlar açısından değerlendirilmiştir.

Bulgular: Hastaların tanısına bakıldığında %80,6'sının endometrium kanseri %19,4'ünün serviks kanseri olduğu gözlenmiştir. Hastaların ortanca yaşı 69 (65-86) idi. Tüm hastalara total abdominal histerektomi ve bilateral salpingo ooferektomi uygulandı. Hastaların tamamına eksternal pelvik RT uygulanmıştı. Intrakaviter vaginal brakiterapi hastaların %90,3'sine uygulanmıştı. Hastaların %3,2'sinde lokal rekürrens ve yine %3,2'sinde uzak metastaz gözlenmişti. Beş yıllık hastalısız sağkalım ve genel sağkalım oranları sırasıyla %93 ve %80 idi.

Sonuç: Geriatrik hasta grubunda tedavi planlaması prognostik faktörler, yaş grubu ve komorbiditeye göre uygun olarak şekillendirilmelidir. Seçili hasta grubunda multimodalite tedaviler ile gayet iyi onkolojik sonuçlar elde edilebilmektedir.

Anahtar Kelimeler: Jinekolojik kanser, radyoterapi, geriatri



INTRODUCTION

Although there are different definitions in the literature for the definition of geriatric patients, such as 65, 70, 75 years and older, patients aged 65 and over are considered as the geriatric patient group according to World Health Organization (WHO).^[1] With today's technology and knowledge, we are encountering more and more geriatric patients thanks to early diagnosis in cancer, richer treatment options and multidisciplinary approaches.^[2] It is known that both palliative and curative radiotherapy (RT) is needed at a rate of approximately 50% nowadays, where increasingly older cancer patients are treated on the basis of factors such as the prolongation of the average human lifespan and the aging of the world population.^[3,4] The geriatric patient group needs more physical and social support due to reasons such as increasing burden of comorbidity, decrease in organ function capacities, and difficulty in accessing the hospital, so this group of patients has difficulty in receiving all the planned treatments. This situation may negatively affect the success of oncological outcomes in patients diagnosed at an advanced age compared to those who receive treatment at a young age.^[5] Therefore, it has been reported in many studies that cancer-specific survival rates are lower in geriatric patients than in younger patients.^[6]

When deciding on oncological treatment in geriatric patients, detailed geriatric evaluation including performance, basic care needs, weakening of the immune system, physical and mental health condition, can be used to predict treatment tolerance and predict overall survival.^[7,8] A Norwegian cluster-randomised controlled pilot study was designed to observe the contribution of a specific geriatric assessment and process management to oncogeriatric patients scheduled for RT. The results of the study, which is aimed to evaluate the contribution of special evaluation and treatment planning strategy in making RT decision in geriatric patients aged 65 and over, are awaited.^[9]

MATERIAL AND METHOD

Study Population

Thirty one patients aged 65 and over who were treated with surgery and adjuvant RT for gynecological cancer between 2007 and 2021 were included in the study. All patients were evaluated in terms of general characteristics of the patient, tumor stage and pathological findings, local and systemic treatments applied, disease control, recurrence, distant metastasis and survival results.

Statistical Analysis

The descriptive statistics of the numerical variables obtained in the study are given as the median (range) value. The descriptive statistics of the categorical variables are given as numerical values and percentages. Data distribution was assessed by the Kolmogorov–Smirnov test. In consideration of the sample size, the non-normal distribution of variables was assumed, and nonparametric tests were used for between-group comparisons. So the categorical and numerical variables were

compared using the chi-square test and Mann–Whitney U-test, respectively. Kaplan–Meier curves were generated for overall survival (OS) and disease-free survival (DFS) and significance was assessed using the log-rank test. Statistical analyses were performed using SPSS 25 software (SPSS Inc., Chicago, IL, USA). A probability value of $p < 0.05$ was considered significant.

RESULTS

Patient Characteristics

The diagnosis of 80.6% of the patients included in the study was endometrium ca, and the diagnosis of 19.4% was cervix ca. The median age of the patients was 69 (range, 65-86). Median follow-up was 69 (range, 8 -219) months. 26% of the patients were grade 3, 51.5% were grade 2. 61% of the patients were between 65 and 70 years of age; 39% were 71 years or older. The median tumor size was 4 cm (range: 1,5-9). Lymphovascular space invasion (LVSI) was present in 64.5% of patients. All patients underwent total abdominal hysterectomy and bilateral salpingo oophorectomy (TAH+BSO). Lymphadenectomy was applied to 67.5 % of the patients. All patients underwent external pelvic RT. Intracavitary vaginal brachytherapy (VBT) was applied to 90.3% of the patients. The median dose of RT administered was 46 Gy (45-50 Gy) and median dose of VBT was 18 Gy (15-27.5 Gy). Chemotherapy (CT) was performed in only 4% of patients. Local recurrence was observed in 3.2% of the patients and distant metastasis was observed in 3.2% of the patients. The baseline characteristics of the patients are presented in **Table 1**. When patients aged 71 years and older were compared with patients aged 65-70 years, no difference was observed in terms of LVSI involvement, whether pelvic lymphadenectomy was performed or the number of lymph nodes dissected, disease-free survival, recurrence, and mortality. The five-year DFS and OS rates were 93% and 80%, respectively (**Figure 1-2**).

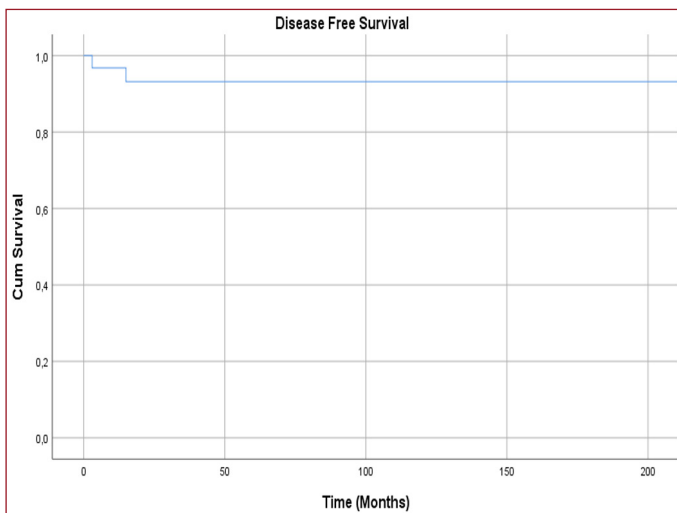
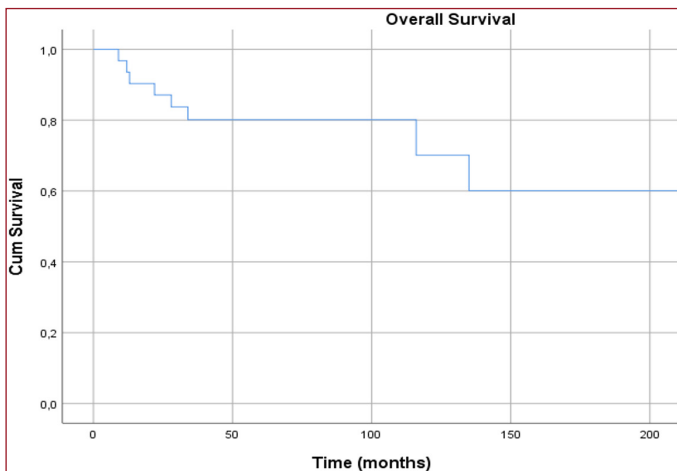
Table 1: Patient and tumor characteristics

	Patients (n:31,%)
Age	Median: 69 (range 65-86)
65-70 yr	19 (61.3%)
≥71 yr	12 (38.7%)
Comorbidity	
Yes	15 (48.4%)
No	16 (51.6%)
Tumor Location	
Endometrium	25 (80.6%)
Uterin cervix	6 (19.4%)
T Stage	
T1	5 (16.1%)
T2	26 (83.9%)
Lymph node metastasis	
Yes	0 (0%)
No	31 (100%)
Surgical margin	
Positive	1 (3.2%)
Negative	30 (96.8%)
LVSI	
Yes	20 (64.5%)
No	11 (35.5%)
Tumor grade	
Grade 1	7 (22.6%)
Grade 2	16 (51.6%)
Grade 3	8 (25.8%)

LVSI:Lymphovascular space invasion

Table 2: Treatment Details

	Patients (n:31,%)
Lymphadenectomy	
Only pelvic	13(42 %)
Pelvic + paraaortic/ Paraaortic sampling	8 (25.8 %)
None	10 (32.2 %)
Number of LNs removed	
Number of pelvic LNs removed	Median; 16 (range 5-64)
Number of paraaortic LNs removed	Median; 7 (range 2-30)
Chemotherapy	
No	27 (87.1 %)
Yes	4 (2.9 %)
Local recurrence	
Yes	1 (3.2%)
No	30 (96.8%)
Distant metastasis	
Yes	1 (3.2%)
No	30 (96.8%)

**Figure 1.** Kaplan-Meier plots of disease free survival.**Figure 2.** Kaplan-Meier plots of overall survival.

DISCUSSION

Fragility in the geriatric population reflects damage to the functionality of biological systems and it is important in the geriatric population to cope with the side effects of treatments such as surgery, CT and RT.^[10,11] Each geriatric patient may have different characteristics from each other

in terms of comorbidity, need for care, physical and mental health status, etc. Therefore, it would be beneficial to develop specific assessment tools for different cancer types, as opposed to a single assessment method.^[12]

Sourdret et al.^[13] established a geriatric oncology treatment evaluation team at Toulouse University Hospital consisting of medical oncology, radiation oncology, surgeon and nurse who are experts in the field of geriatrics. Patients aged 65 years or older diagnosed with cancer were evaluated by this team during the treatment planning phase. In 16.7% of 384 patients, the treatment plan was changed as a result of the geriatric team evaluation. It was observed that the most effective factors in the change of treatment plan were cognitive impairment ($p=0.020$), malnutrition ($p=0.023$), and low physical performance ($p=0.010$).

Racin et al.^[14] evaluated geriatric patients with high intermediate risk and higher risk endometrial cancer according to whether lymphadenectomy was performed. Adjuvant therapy was observed to be similar between the two groups. In this study, where the median age of the patients was 76.9, it was observed that the rates of DFS, cancer specific survival (CSS), and OS were statistically significantly lower in the group that did not undergo lymphadenectomy ($p=0.076$, $p<0.001$, and $p<0.001$, respectively). As a result of the study, it was emphasized that lymphadenectomy should be performed in geriatric patients with indications. However, in this study, the rate of adjuvant RT was only 45% in the group of patients who did not undergo lymphadenectomy, and perhaps higher local control and survival rates could have been achieved if a higher rate of adjuvant RT had been applied to these patients.

Xie et al.^[15] examined 36,816 uterine cervical cancer patients in their review on the Surveillance, Epidemiology, and End Results Program (SEER) database covering the years 2004-2015. When the two groups under 65 years of age and over were compared, it was observed that the 1- and 5-year CSS in the geriatric group was statistically significantly worse than the younger group. It was observed that patients who received surgery, radiotherapy or chemotherapy in the geriatric group had better survival outcomes than patients who did not receive any treatment. In the subgroup analyzes, it was observed that even in early stage geriatric patients, the group that received inadequate treatment or did not receive treatment had a statistically significant worsening course.

Cushman et al.^[16] compared postoperative chemoradiotherapy (CRT) with RT alone in 166 geriatric uterine cervical cancer patients over 70 years of age with high risk factors such as parametrial invasion, positive surgical margins, or lymph node metastasis. No difference in OS was observed between the two groups, despite the number of accompanying risk factors or the evaluation of each factor separately. As a result of the study, it was emphasized that treatment selection can be made for geriatric patients on a patient basis, considering patient performance, toxicity and tolerability.

In our study, 39% of the patients were 71 years or older. 67.5% of the patients had lymphadenectomy and external pelvic RT was applied to all of the patients and intracavitary vaginal brachytherapy (VBT) was applied to 90.3% of them. Only 3.2% of the patients had local recurrence and 3.2% had distant metastases. However, as seen in the above-mentioned studies, many factors seem to be effective on survival success while forming multidisciplinary treatments in the geriatric patient group. It seems useful to decide on a patient basis how surgical treatment, RT and CT should be performed and to evaluate the geriatric patient in detail.

CONCLUSION

Uterine cancers are among the most common cancers in women. Surgery followed by adjuvant RT also has tolerable and excellent oncological results in early stage geriatric uterine cancer patients. In order to increase the success of oncological treatment in the geriatric patient group, multimodality randomized studies shaped according to the patient group-specific prognostic factors, comorbidity and age group are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Istanbul Prof. Dr. Cemil Tascioglu City Hospital Ethics Committee (Date: 20.10.2022, No: E-48670771-514.99)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

- Bourgin C, Saidani M, Poupon C, et al. Endometrial cancer in elderly women: Which disease, which surgical management? A systematic review of the literature. *Eur J Surg Oncol.* 2016 Feb;42(2):166-75.
- Swaminathan D, Swaminathan V. Geriatric oncology: problems with under-treatment within this population. *Cancer Biol Med.* 2015 Dec;12(4):275-83.
- Barton MB, Jacob S, Shafiq J, et al. Estimating the demand for radiotherapy from the evidence: a review of changes from 2003 to 2012. *Radiother Oncol.* 2014;112(1):140-4.
- Asli LM, Kvaløy SO, Jetne V, et al. Utilization of radiation therapy in Norway after the implementation of the national cancer plan—a national, population-based study. *Int J Radiat Oncol Biol Phys.* 2014;90(3):707-14.
- Diver EJ, Hinchcliff EM, Gockley AA, et al. Assessment of treatment factors and clinical outcomes in cervical cancer in older women compared to women under 65 years old. *J Geriatr Oncol.* 2018;9(5):516-9.
- Wright JD, Lewin SN, Barrena Medel NI, et al. Endometrial cancer in the oldest old: Tumor characteristics, patterns of care, and outcome. *Gynecol Oncol.* 2011;122:69-74.
- Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. *J Clin Oncol.* 2011;29(25):3457-65.
- Wildiers H, Heeren P, Puts M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol.* 2014;32(24):2595-603.
- Røyset I, Saltvedt I, Rostoft S, et al. Geriatric assessment with management for older patients with cancer receiving radiotherapy. Protocol of a Norwegian cluster-randomised controlled pilot study. *J Geriatr Oncol.* 2022;13(3):363-73.
- Huisingh-Scheetz M, Walston J. How should older adults with cancer be evaluated for frailty? *J Geriatr Oncol.* 2017;8(1):8-15.
- Handforth C, Clegg A, Young C, et al. The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Ann Oncol Off J Eur Soc Med Oncol.* 2015;26(6):1091-101.
- Dumas L, Ring A, Butler J, Kalsi T, Harari D, Banerjee S. Improving outcomes for older women with gynaecological malignancies. *Cancer Treat Rev.* 2016;50:99-108.
- Sourdet S, Brechemier D, Steinmeyer Z, Gerard S, Balardy L. Impact of the comprehensive geriatric assessment on treatment decision in geriatric oncology. *BMC Cancer.* 2020;20(1):384.
- Racin A, Raimond E, Bendifallah S, et al. Lymphadenectomy in elderly patients with high-intermediate-risk, high-risk or advanced endometrial cancer: Time to move from personalized cancer medicine to personalized patient medicine! *Eur J Surg Oncol.* 2019;45(8):1388-95.
- Xie S, Pan S, Zou S, Zhu H, Zhu X. Characteristics and Treatments of Patients Aged 65 Years or Over with Cervical Cancer. *Clin Interv Aging.* 2020 Jun 3;15:841-51.
- Cushman TR, Haque W, Menon H, et al. Postoperative chemoradiotherapy versus radiotherapy alone for elderly cervical cancer patients with positive margins, lymph nodes, or parametrial invasion. *J Gynecol Oncol.* 2018;29(6):e97.