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Original Article

Pulmonary recurrence in patients with endometrial cancer

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Abstract

Background: In this article, we aimed to define the clinical, pathological, and surgical factors predicting pulmonary recurrence (PR) and determining survival after PR in patients with endometrial cancer.

Methods: Thirty-six (2.7%) patients were analyzed who suffered pulmonary failure in the first recurrence out of 1345 patients who had at least extrafascial hysterectomy plus bilateral salpingo-oophorectomy for endometrial cancer between January 1993 and May 2013. The recurrence was designated as an isolated PR in cases of the presence of recurrence only in the lung, while it was called a synchronized PR if the patient had extrapulmonary recurrence in addition to PR.

Results: In the multivariate analysis in the entire cohort, only International Federation of Gynecology and Obstetrics stage was an independent prognostic factor for PR. Two-year overall survival (OS) was 52% in patients with PR. In the univariate analysis, early International Federation of Gynecology and Obstetrics stage, absence of lymphatic metastasis, negative lymphovascular space invasion, absence of cervical invasion, negative adnexal spread, negative peritoneal cytology, negative omental metastasis, adjuvant radiotherapy after initial surgery, isolated PR, and chemotherapy upon recurrence were associated with improved OS after PR. The OS was 54 months for patients with isolated PR, while it was 10 months for patients who had synchronized PR. Furthermore, OS was 43 months and 13 months for the patients who took chemotherapy and radiotherapy, respectively.

Conclusion: Advanced stage is associated with PR. If recurrence is only in the lung, survival is better. Systemic treatment after PR is associated with improved survival. However, multi-center studies are required to standardize the treatment for PR.

Keywords: endometrial cancer; pulmonary recurrence; survival

1. Introduction

Endometrial cancer is the sixth most frequent cancer in women worldwide and 320,000 women are annually diagnosed with this challenging disease according to 2012 GLOBOCAN data.[1] Endometrial cancer is usually diagnosed in the early stages; however, 20% of patients have extrauterine disease.[2] The 5-year overall survival (OS) rate is above 80% for patients in the early stages.[3] Recurrence develops in 11–13% of all patients with endometrial cancer in the first 2 years following initial treatment, depending on the clinical factors, stage, previous surgery, and pathological factors.[4–6] In the presence of poor prognostic factors, recurrence is observed in up to 60% of the patients.[7–9] Additionally, extrapelvic failure is detected in >75% of the patients with recurrence.[6,10,11]

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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The lung is a common site for endometrial cancer metastasis, and pulmonary metastasis is primarily the result of hematogeneous spread. Pulmonary failure was reported to be observed in 1.9–9% of patients with first recurrence.[11–17] There is limited data about the factors predicting pulmonary recurrence (PR). However, PR was reported to be associated with Stage IV disease and deep myometrial invasion.[15] Earlier reports stated that PR was associated with poor prognosis. In these reports, 75% of patients with PR were shown to expire from cancer in the 1st year.[14] However, in a recent paper, patients with isolated lung metastasis that was ≤2 cm and low grade were detected to have 98-months OS following recurrence.[16] Additionally, the 5-year OS of patients with endometrial cancer who had pulmonary metastasectomy after the initial recurrence was reported to be up to 76%.[18–21]

The factors predisposing patients to PR, how PR progresses, and what its treatment should be have not been clarified. The data regarding PR in endometrial cancer is limited and it is not without limitations. Usually, PR was included in distant recurrences in previous reports and not analyzed separately. Patients with sarcomas in addition to epithelial tumors were generally included or patients with endometrial cancer were evaluated with patients who had cancer of other primary sites in those reports.

In the present study, we aimed to define the clinical, pathological, and surgical factors predicting PR and determining survival after PR.

2. Methods

A total of 1640 patients with diagnosed epithelial endometrial cancer were treated in our clinic between January 1993 and May 2013. The data of 1413 patients who had at least extrafascial hysterectomy plus bilateral salpingo-oophorectomy were obtained from the Gynecological Oncology Clinic (Ankara, Turkey) electronic database and patient files. Among these 1413 patients, 68 patients either were deemed lost to follow-up or died of surgery-related complications in the early postoperative period. Clinical, surgical, and pathological data of the remaining 1345 patients was collected. The patients who had a sarcomatous component in their final pathology report and who were treated for pulmonary failure in the second or subsequent recurrences were not included. The first recurrence was in the lung in 36 of the 1345 patients who were retrospectively evaluated. The entire cohort was analyzed in order to define the factors determining PR. In this group, patients with recurrence except PR and patients who had no recurrence were defined as PR negative group.

The clinical, surgical, and pathological factors determining OS in patients with PR ($n = 36$) were defined. The recurrence was labeled as an isolated PR in cases of the presence of recurrence only in the lung, while it was called synchronized PR if the patient had extrapulmonary recurrence in addition to PR. The extent of disease in the lung was stratified as single pulmonary nodule (1 nodule) and multiple pulmonary nodules (>1 nodule) according to the number of tumoral nodules in the lung. Recurrence tumor size was accepted as the largest diameter of the tumor in the lung or other sites, while the largest diameter of tumor in the lung was defined as pulmonary tumor size. Disease-free interval (DFI) was the period between initial surgery and PR, and OS was defined as the period between PR and death or the last contact with the patients. Institutional Review Board (Ankara, Turkey) approval was obtained.

The patients were staged according to the 2009 International Federation of Gynecology and Obstetrics (FIGO) criteria. Serous, clear cell, and undifferentiated tumors were accepted as Grade 3 tumors in the pathological evaluation following initial surgery.

PR and extrapulmonary recurrence was diagnosed by the clinical and radiological signs obtained from the pelvic and systemic examination, chest X-ray, abdominopelvic and thoracic computerized tomography, or magnetic resonance imaging. Additionally, tissue diagnosis was available in five patients. The decision of the treatment that would be performed was taken by the gynecologic oncology council. The status of disease after treatment was evaluated according to the World Health Organization.[22] According to the assessment made in the 1st month after treatment, we defined clinical response as the following: (1) complete clinical response: disappearance of the macroscopic tumor; (2) partial clinical response: shrinkage over 50% in the macroscopic tumor; (3) stable disease: macroscopic tumor shrinkage less than 50% or not less than 25% growth; and (4) progressive disease: > 25% growth in the macroscopic tumor or macroscopic appearance of new tumor foci.

Patients who had complete clinical response after the therapy for recurrence were followed-up every 3 months for 2 years, every 6 months until the 5th year following treatment, and yearly thereafter. In the follow-up, pelvic examination, abdominopelvic ultrasonography, complete blood count, and blood chemistry were performed. At every patient visit, chest X-ray was performed. Thoracic and/or abdominal computerized tomography was used when there was an abnormality in the pelvic examination or ultrasonography or chest X-ray or when there was clinical suspicion. Ca-125 level was utilized in the follow-up, even though it was not routinely used. The same follow-up protocol except for the chest X-ray had been performed after the initial treatment that the patients had received, subsequent to the initial diagnosis of endometrial cancer. In the follow-up after treatment following the initial diagnosis of endometrial cancer, chest X-ray was utilized yearly or more commonly in cases of clinical suspicion such as the presence of cough and/or dyspnea.

In the entire cohort, the factors determining PR were compared using Chi-square test. Factors having a p value < 0.25 in univariate analyses were included as candidate variables in multivariate analyses with logistic regression analysis. The isolated PR group was compared with the synchronized PR group with Chi-square test for the categorical parameters and by analysis of variance table test for continuous parameters. In the PR group, OS estimates were determinated by using the Kaplan–Meier method, and survival