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Salvage high-dose-rate brachytherapy for isolated vaginal recurrence of endometrial cancer

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ABSTRACT

PURPOSE: We have retrospectively analyzed the outcomes of high-dose-rate (HDR) brachytherapy as a salvage therapy for vaginal recurrence of endometrial cancer.

METHODS AND MATERIALS: From 1997 to 2012, salvage HDR brachytherapy was performed in 43 patients. The median age was 64 years (range, 41−88 years). HDR brachytherapy was performed by interstitial brachytherapy in 34 patients (79%) and by intracavity brachytherapy in nine patients (21%). Seventeen (40%) of the 43 patients were treated with external beam radiotherapy. The median followup period was 58 months (range, 6−179 months).

RESULTS: The 5-year overall survival (OS), progression-free survival (PFS), and local control rates (LC) were 84%, 52%, and 78%, respectively. Patients who received brachytherapy with external beam radiotherapy experienced no nodal recurrence (0 of 17 patients), whereas 23% of the patients (6 of 26 patients) who received brachytherapy alone experienced nodal recurrence ($p = 0.047$). The pathologic grade at the time of initial surgery (G1-2 vs. G3) was found to be a significant prognostic factor for both OS and PFS. The respective 5-year OS was 96% vs. 40% ($p < 0.01$), and the 5-year PFS was 58% vs. 0% ($p < 0.01$). Age (≥60 vs. <60) and modality (interstitial brachytherapy vs. intracavity brachytherapy) were significant prognostic factors for LC. The respective 5-year LC was 74% vs. 100% ($p = 0.020$) and 85% vs. 56% ($p = 0.035$).

CONCLUSIONS: HDR brachytherapy is effective and feasible in patients with isolated vaginal recurrence of endometrial cancer. Pathologic grade, age, and modality were significant prognostic factors.

Keywords: Endometrial cancer; Brachytherapy; Vaginal recurrence; High dose rate

Introduction

Endometrial cancer has a predominantly favorable outcome. Most patients will present at an early stage of the disease, and more than 80% of the patients are cured by surgery. However, 10−15% of patients with early-stage endometrial cancer experience pelvic recurrence after surgery (1). Most recurrences are in the vagina (2), and salvage radiotherapy has been performed with curative intent (3−10). However, most studies have had a limited number of patients and have used a variety of modalities (external beam radiotherapy [EBRT] or brachytherapy), schedules, and total doses. Therefore, there remains some uncertainty regarding the most appropriate treatment approach. Recurrent tumor size is considered a prognostic factor related to success of the salvage therapy (3, 4). Therefore, since 1997, when we have performed salvage

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high-dose-rate (HDR) brachytherapy for isolated vaginal recurrence of endometrial cancer. We have used either HDR intracavity brachytherapy (ICBT) or interstitial brachytherapy (ISBT). The decision on whether to use HDR ICBT vs. HDR ISBT was dependent on the diameter (thickness) of the tumor at the time of brachytherapy. Here, we present a retrospective analysis of salvage HDR brachytherapy for isolated vaginal recurrence of endometrial cancer at our hospital (Osaka University Hospital) and at a nearby hospital (National Hospital Organization Osaka National Hospital). The goal of this study was to determine the effectiveness and feasibility of HDR brachytherapy, especially ISBT, for treating endometrial cancer recurrence.

Methods and materials

Patients

Permission to proceed with the data acquisition and analysis was obtained from the Osaka University Hospital Institutional Review Board and from the National Hospital Organization Osaka National Hospital Review Board. A list of patients who had been treated with HDR brachytherapy for isolated vaginal recurrence of endometrial cancer after the initial surgical treatment from 1997 to 2012 was collected by retrospective chart review. Patients had the initial surgery based on our institutional protocol. Basically, patients with a grade 1 endometroid adenocarcinoma without myometrial invasion had a total abdominal hysterectomy (TAH) plus bilateral salpingo-oophorectomy (BSO). Patients with either a grade 1−2 endometroid adenocarcinoma who had invaded <50% of the myometrium or patients with a grade 2 endometroid adenocarcinoma without myometrial invasion were treated with TAH, BSO, and pelvic lymphadenectomy. Patients with either grade 3 endometroid adenocarcinoma, nonendometroid histology, or extrauterine disease were treated with TAH, BSO, and pelvic and para-aortic lymphadenectomy. Some exceptions occurred for the patients with complications. Patients who had either regional lymph node recurrence or distant metastases were excluded from this analysis. Finally, the data from a total 43 patients were analyzed.

Radiotherapy

All of the patients received HDR brachytherapy using an iridium-192 source. Patients who had previous radiotherapy in the pelvic region were treated with brachytherapy alone. If the tumor was ≥5 mm in diameter, we proceeded with ISBT (42 Gy/seven fractions; four patients), whereas we used ICBT when the tumor was <5 mm in diameter. On the other hand, patients without previous radiotherapy received ICBT alone when tumor was <5 mm in diameter (seven patients). If the tumor was ≥5 mm in diameter, we proceeded with either ISBT alone (48−60 Gy/8−10 fractions; 14 patients) or with combined EBRT and brachytherapy. Seventeen (40%) of the 43 patients were treated with EBRT. EBRT was delivered to the whole pelvis at 30−50 Gy/15−25 fractions. Two patients received ICBT because an adequate regression of the tumor had been achieved, whereas 17 patients received ISBT because the tumor diameter was ≥5 mm at the time of brachytherapy. The total brachytherapy dose combined with EBRT was 30−60 Gy/5−10 fractions. In all patients, the median EQD2 of recurrent tumor was 69 Gy (range, 40−86 Gy). In HDR ICBT, the dose was administered to the vaginal wall at a 5-mm depth from the surface of the vagina. In the first four sessions, we used a cylinder for the applicator. At the last session, we used an ovoid pair for the applicator to make up for the dosage deficiency at the vaginal stump. For the HDR ISBT, the implant technique and treatment planning have been described elsewhere (11, 12). HDR ISBT was performed using 3D planning in all 11 patients at National Hospital Organization Osaka National Hospital and in 14 patients out 32 patients (44%) at Osaka University Hospital.

Outcome assessment

The overall survival (OS), progression-free survival (PFS), and local control rates (LC) were estimated from the first day of salvage radiotherapy to the day of the event or, if no event occurred, to the day of last followup. Local failure was defined as disease progression of the initial recurrent tumor by either clinical or radiographic examination. Nodal failure was defined as disease progression within the pelvis by either clinical or radiographic examination. Distant failure was defined as distant metastasis without either local or nodal failure. The rates were estimated using the Kaplan−Meier method, and the differences between the factors were examined by the log-rank test. A Cox proportional hazard model was used for multivariate analysis. p values of <0.05 was considered statistically significant. Toxicities were graded according to the Common Terminology Criteria for Adverse Events, version 4. Toxicity data, including the grade of the complications, were collected retrospectively through hospitalization and followup records.

Results

Patient characteristics

The characteristics of the patients are summarized in Table 1. The median age was 64 years (range, 41−88 years). The initial the International Federation of Gynecology and Obstetrics stage was I−II in 26 patients (60%) and III in 17 patients (40%). Based on the histology, 38 patients (88%) had endometroid adenocarcinoma. The pathologic grade was 1−2 in 34 patients (79%) and grade 3 in 5 patients (12%). The median tumor size was 20 mm (range, 3−50 mm).