Journal of the Formosan Medical Association (2017) xx, 1–8

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com

Original Article

Role of adjuvant radiotherapy in FIGO stage IIIC endometrial carcinoma: Treatment outcomes and prognostic factors in 52 irradiated patients

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Received 23 May 2017; received in revised form 16 July 2017; accepted 2 August 2017

KEYWORDS
Adjuvant radiotherapy;
Endometrial cancer;
Stage IIIC

Background: To retrospectively review the postoperative radiotherapy treatment outcomes and the prognostic factors for the International Federation of Gynecology and Obstetrics (FIGO) stage IIIC endometrial carcinoma.
Methods: Fifty-two patients who were newly diagnosed and previously untreated FIGO stage IIIC endometrial carcinoma over a 33-year period (September 1983 to April 2015) were retrospectively reviewed. They had received radical surgery followed by adjuvant radiotherapy with or without adjuvant chemotherapy. Those excluded patients had initial distant metastasis disease, palliative intent or incomplete adjuvant radiotherapy. Different subgroups of the stage III patients were compared statistically in terms of their rates of overall survival (OS), loco-regional recurrence-free survival (LRRFS) and distant metastasis-free survival (DMFS).
Results: The median follow up duration was 51.5 months (range, 5–298). The loco-regional recurrence was found in 4 patients and distant metastasis in 15 patients. Comparing stage IIIC1 vs. IIIC2 patients, their 5-year OS were 69.9% vs. 55% ($p = 0.0954$), LRRFS 90.3% vs. 94.4% ($p = 0.6151$), and DMFS 82.5% vs. 53.3% ($p = 0.0080$). The FIGO stage was a significant factor for DMFS (hazard ratio [HR], 5.440, 95% confidence interval [95% CI] 1.379–21.451, $p = 0.0155$), but only marginal for OS (HR, 2.137, 95% CI 0.930–4.913, $p = 0.0738$). The ECOG performance status was marginal significant for DMFS (HR, 4.777, 95% CI 0.976–23.378, $p = 0.0536$).
Conclusion: Adjuvant radiotherapy decreased loco-regional recurrence and had good local control in FIGO stage IIIC endometrial carcinoma. The stage IIIC2 patients showed a greater tendency

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http://dx.doi.org/10.1016/j.jfma.2017.08.002

of distant metastases and poorer overall survival rate when compared to patients of stage IIIC1.

Introduction

Endometrial cancer is the top seven commonest malignancy in the women of Taiwan.[1] Although mostly diagnosed at the early-stages, about 15–20% of them are at locally-advanced stages.[2]

As the endometrial cancer can express heterogenous tumor characteristics, it has variable prognoses.[2,3] For the International Federation of Gynecology and Obstetrics (FIGO) stage IIIC patients who had regional lymph nodes involvement, the treatment modalities included radical surgery with postoperative adjuvant treatment.[4] Also the current guidelines of the National Comprehensive Cancer Network (NCCN) (Version 1, 2017), adjuvant chemotherapy with or without tumor-directed radiotherapy is the choice of treatment for locally-advanced endometrial cancer.[5] However, the FIGO stage IIIC disease is a distinct subgroup with different failure pattern and a consensus of the optimal treatment modalities remains to be reached.[2,4]

According to Gynecologic Oncology Group 122, in terms of the progression-free and overall survival, treating patients with locally-advanced endometrial cancer, the combination of adjuvant chemotherapy, cisplatin and doxorubicin is better than whole abdominal radiotherapy.[6] However, the eligible stage IIIC patients in GOG study constituted only half (51.5%) of the cases. On the other hand, a number of other studies reported the improved loco-regional control with the combined treatment of post-operative radiotherapy for stage IIIC patients.[2,3,7–11] Two recent studies analyzing the SEER and NCDB database reported the advantages in overall survival when the stage IIIC patients had been treated with a combined chemotherapy and radiotherapy.[12,13]

Here we retrospectively reviewed 52 FIGO stage IIIC patients in our institute. They were treated with radical surgery and then followed by adjuvant radiotherapy in combination with or without chemotherapy. Their respective treatment outcomes and prognostic factors were analyzed.

Materials and methods

Patients

The study was approved by the Institutional Review Board in our institution (IRB TCVGH No: CE17056A) and database was taken from our institute (Veteran General Hospital, Taichung, Taiwan, Republic of China) during a 33-year period (September 1983 to April 2015). One-hundred and thirty-seven patients with FIGO stage III endometrial carcinoma were documented. The inclusion criteria were (1) newly diagnosed and previously untreated endometrial carcinoma, (2) no evidence of distant metastasis at initial diagnosis, (3) receipt of staging operation as initial treatment, (4) pathologically-proved pelvic or para-aortic lymph node metastasis (FIGO stage IIIC1 or IIIC2), and (5) patients received postoperative adjuvant radiotherapy with or without chemotherapy at our institute. The exclusion criteria included (1) initial distant metastasis disease, (2) treatment with palliative intent, and (3) incomplete adjuvant radiotherapy course. Of the 137 patients with stage III endometrial carcinoma, 59 patients belonged to stage IIIA, 17 belonged to IIIB and 61 belonged to IIIC. Two patients received staging operation followed by chemotherapy, but disease progression with distant metastasis and then underwent palliative radiotherapy, 1 patient underwent incomplete staging operation, 1 patient received radiotherapy alone without staging operation, 2 patients received radiotherapy at other hospital, and 3 patients had incomplete radiotherapy course. Therefore, a total of 52 patients were enrolled in this study.

Before surgery, all patients received physical examinations, routine blood cell counts and chemistry, chest X-ray and abdominal/pelvic computed tomography. The positron emission tomography/computed tomography was performed whenever indicated clinically.

Most patients (n = 42, 80.8%) had endometrioid histology. The remaining patients showed non-endometrioid histology, which were undifferentiated carcinoma (n = 2), malignant mixed mullerian tumor (n = 2), squamous cell carcinoma (n = 2), adenosquamous carcinoma (n = 2), leiomyosarcoma (n = 1), or serous papillary carcinoma (n = 1).

Surgery

All patients received radical surgery, including total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph node dissection with or without para-aortic lymph node sampling/dissection, and followed by post-operative adjuvant radiotherapy with or without chemotherapy.

Radiotherapy

The postoperative radiotherapy included external beam radiotherapy with or without vaginal brachytherapy. The external beam radiotherapy was delivered by a 10-MV photon beam directed to post-operative tumor bed and regional lymph node area using different therapeutic techniques which included intensity-modulated radiotherapy (n = 27), 3D conformal radiotherapy (n = 4) or 2D radiotherapy (n = 21). For the stage IIIC1 patients, the median radiation doses were 50.4 Gy (range, 46.8 Gy–66.2 Gy) for postoperative tumor bed and 50.4 Gy

Please cite this article in press as: Hsieh H-Y, et al., Role of adjuvant radiotherapy in FIGO stage IIIC endometrial carcinoma: Treatment outcomes and prognostic factors in 52 irradiated patients, Journal of the Formosan Medical Association (2017), http://dx.doi.org/10.1016/j.jfma.2017.08.002