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Original research

Effect of preoperative radiotherapy on stage IB2 and IIA2 cervical cancer: A retrospective cohort study

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HIGHLIGHTS

- Efficiency of the preoperative radiotherapy on early stage CC was evaluated.
- There was no difference for complication, blood loss and surgery time between two groups.
- Preoperative radiotherapy did not improve the postoperative pathology.
- 1-, 3- and 5-year survival rates were similar between two groups.
- 3- and 5-year locoregional control rates were much higher in radiotherapy group.

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ABSTRACT

Introduction: The aim of the retrospective study was to investigate the therapeutic efficiency of the preoperative intracavitary radiotherapy combined with radical surgery on postoperative complications and long-term survival in patients with stage IB2 and IIA2 cervical cancer (CC).

Methods: From January 1995 to December 2012, a total of 171 patients with stage IB2 or IIA2 CC were recruited into the study. They were divided into two groups according to the treatment modality provided: preoperative radiotherapy followed by radical surgery (n = 80), and radical surgery alone (n = 91). The clinical curative effect, postoperative complications and the postoperative prognosis of patients were evaluated and compared in two groups. The tumor response and survival of patients in two groups were observed in follow-up study.

Results: There were no significant differences in the incidence of postoperative complications, intraoperative blood loss and surgery duration ($P > 0.05$) between the two groups. Preoperative radiotherapy did not improve the postoperative prognosis yet. Though patients undergoing preoperative radiotherapy showed the similar 1- (92.50% vs. 84.62%), 3- (85.00% vs. 81.32%) and 5-year (80.00% vs. 74.72%) survival rates, the 3- and 5-year locoregional control rates of them were much higher than those undergoing surgery alone ($P < 0.05$).

Conclusion: Preoperative radiotherapy combined with radical surgery could improve locoregional control rate and would not increase the risk of postoperative complications. It may be a feasible treatment mode for early stage CC carcinoma.

1. Introduction

Cervical cancer (CC) is the third most commonly diagnosed primary carcinoma and the leading cause of cancer death among women in the world [1]. The prognosis of patients with early stage CC (stage IB2 and IIA2) is usually poor due to high risk of recurrence and metastasis of CC [2].

Traditionally, patients with early stage cancer are treated with radiation therapy and surgery. Radical hysterectomy followed by primary chemoradiation therapy and tailored adjuvant therapy has been suggested in the treatment of early stage IB2 and IIA2 CC [3]. However, there were some inconsistencies on curative effects of

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surgery and radiotherapy in patients with stage IB2 or stage IIA2 CC. Previous studies have proved that radical surgery and radiotherapy are equally effective in the treatment of stage IB2 and IIA CC, but the type and rate of complications and morbidity between them were different [4,5]. Rungruang and his partners found that early stage CC patients treated with surgery first had improved outcomes than those treated with radiation first [6]. Park et al. [7] suggested that radical hysterectomy had better survival outcomes and lower treatment-related morbidities as compared to primary chemo-radiation therapy in patients with IB2 and IIA2 CC. Therefore, the roles of radical hysterectomy and primary chemoradiation therapy in early stage CC patients should be re-evaluated.

To investigate the curative effect of preoperative radiotherapy plus immediate radical surgery, a retrospective cohort study was performed to compare it with radical hysterectomy alone in stage IB2 and IIA2 CC patients.

2. Materials and methods

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (http://www.strobe-statement.org/) [8] for cohort studies was developed to enhance the quality of the present study.

2.1. Inclusion and exclusion criteria and group assignment

From January 1995 to December 2012, the consecutive medical records of patients with early stage CC admitted to Beijing Gynecology and Obstetrics Hospital were retrospectively reviewed. Patients were eligible for the study if they (1) were diagnosed with stage IB2 or IIA2 CC according to the International Federation of Obstetrics and Gynecology (FIGO) staging system [9]; (2) had a tumor more than 4 cm in diameter; (3) had normal liver and kidney function; (4) had karnofsky score [10] of over 90 points. Patients who were diagnosed with non-squamous cell cancer or during pregnancy were excluded.

Patients were divided into two groups according to the treatment techniques: preoperative radiotherapy group and immediate radical surgery group. The study protocol was approved by the ethics committee of this hospital, and informed consents were obtained from all of these patients.

2.2. Treatment procedures

Patients in preoperative radiotherapy group received preoperative intracavitary brachytherapy at a dose of 2000–3000 cGy (centigray) (radioactive source at 1 cm distance) using sources ^{192}Ir once a week (2–3 times in total). After 2–3 weeks of rest, radical hysterectomy and lymphadenectomy was performed. Patients in the surgery alone group received radical surgery directly.

After radical surgery, patients with vascular space invasion and cervical stromal invasion≥1/2 received subsequent therapy: external radiotherapy ± concurrent cisplatin-containing chemotherapy, patients with lymph node metastasis and a positive margin received external radiotherapy plus concurrent cisplatin-containing chemotherapy, while those with para-aortic lymph node metastasis received nodal radiotherapy plus pelvic radiation.

2.3. Curative effect evaluation

The efficacy of radiotherapy for early stage CC was assessed by tumor response, including complete response (CR, clinical disappearance of all target lesions and no new lesions), partial response (PR, >50% tumor shrinking and no new lesions), stable disease (SD, <50% tumor shrinking and no new lesions) and progressive disease (PD, no change in tumor size or the appearance of new lesions). CR and PR were considered effective, while SD and PD were considered ineffective.

Intraoperative blood loss, surgery duration, postoperative complications, and postoperative prognosis (such as the lymph node metastasis, the deep cervical stromal invasion, the vascular space invasion and the number of unfavorable prognostic factors) were recorded.

2.4. Statistical analysis

The data collected were analyzed using SPSS for Windows (version 17.0, SPSS Inc., Chicago, IL, USA). The χ^2 test and student *t*-test were used in univariate analysis of quantitative data and qualitative data respectively. The locoregional control rate and the survival rate at 1 year, 3 years and 5 years were observed and evaluated. $P < 0.05$ was regarded as significant difference.

3. Results

3.1. Characteristics of patients

Finally, a total of 171 patients with median age of 43 years (range, 21–75 years) were included in our study. Total 80 patients received preoperative intracavitary radiotherapy followed by radical surgery, and 91 underwent radical surgery alone. Basic characteristics of the patients were shown in Table 1. There were no significant differences in age, FIGO stage, tumor size and tumor grade between the two groups ($P > 0.05$).

3.2. Duration of surgery and surgical bleeding

Both surgery duration and bleeding volume of the two groups were found to confirm to normal distributions. Compared with the surgery alone group, the operation duration ($P = 0.061$) and intraoperative blood loss ($P = 0.405$) in preoperative radiotherapy group were all decreased, but the differences did not reach statistical significance ($P > 0.05$). Detailed results were shown in Table 2.

3.3. Postoperative complication

All patients completed treatment and no treatment-related deaths occurred. The common postoperative complications of two group patients were lymphocystis virus infection, the impaired wound healing, postoperative urinary retention and urinary tract infection. There were no significant differences between the preoperative radiotherapy group and the surgery alone group in the incidence of postoperative complications ($P > 0.05$, Table 3). These results indicated that preoperative radiotherapy did not increase the risk of postoperative complications.

3.4. Postoperative prognosis

Postoperative pathologic examination showed that 67 (83.75%) patients in preoperative radiotherapy group had poor prognosis: 22 cases had lymph node metastasis; 55 cases had deep cervical stromal invasion; 40 cases had vascular space invasion. In surgery alone group, 82 of them (90.11%) had poor prognosis, including 29 cases had lymph node metastasis, 72 cases had deep cervical stromal invasion and 50 cases had vascular space invasion. However, there were no significant differences between the two groups in lymph node metastasis, deep cervical stromal invasion, vascular space invasion, and other invasion or metastasis ($P > 0.05$, Table 4). These results indicated that preoperative radiotherapy did not improve the postoperative prognosis.