

Original Article

Comparison of the therapeutic effect and impact of surgery following radiotherapy and chemotherapy following surgery for patients with cervical cancer

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Abstract: Objective: To compare the therapeutic effect and impact of surgery following radiotherapy and chemotherapy following surgery for patients with cervical cancer. Methods: A total of 329 cervical cancer patients admitted to Yantai Yuhuangding Hospital from May 2008 to December 2014 in the Gynecology and Oncology department were selected as the research objects. Retrospective analysis was carried out and according to different treatment methods, the patients were divided into a surgery-first group (surgery before radiotherapy) of 164 cases, and a chemotherapy-first group (chemotherapy before surgery) of 165 cases. The curative effect, postoperative adverse reactions, complications, and lymph node metastasis were compared between the two groups. All patients were followed up for 3 years, and the survival rate and quality of life in these 3 years were recorded. Results: The total effective rate of the chemotherapy-first group (97.0%) was significantly higher than that of the surgery-first group (89.0%, $P=0.019$). In regard to total postoperative adverse reactions, the chemotherapy-first group also surpassed the surgery-first group ($P<0.001$). In terms of survival rates, the 1-, 2- and 3-year survival rate of the chemotherapy-first group were 99.4%, 97.0%, 91.5% respectively, whereas those of the surgery-first group were 97.0%, 89.0%, 75.0% respectively. Compared with the 3 years total survival rate of the two groups, the chemotherapy-first group was significantly superior to the surgery-first group ($P=0.048$). The average score of quality of life in the chemotherapy-first group was (84.07 ± 7.69), which was significantly higher than that in the surgery-first group (70.12 ± 9.59), $P<0.001$. Conclusion: In treatment of cervical cancer, chemotherapy following surgery achieves better therapeutic effect than the surgery following radiotherapy, which greatly improves the survival rate and quality of life of patients. It is worth promoting in clinical practice.

Keywords: Cervical cancer, chemotherapy, radiotherapy, surgical treatment, survival rate

Introduction

Cervical cancer is a very common malignancy in gynecology [1]. According to the survey by Huh et al., more than 1.2 million new cases of cervical cancer are found in 2014 in the world [2]. With the deterioration of the social environment, cervical cancer has shown a younger trend [3]. More relevant reports show that the recurrence of cervical cancer is extremely serious, and the recurrence rate of disease within 2 years is up to 32.8% [4]. Research by Branca et al. have shown that the recurrence of cervical cancer is mainly due to residual lesions, since traditional tumor resection surgery is unable to excise all the potential lesions pre-

cisely [5]. With the rapid development of modern medical technology, treatment of cervical cancer has made a relatively outstanding breakthrough [6]. At present, the best treatment of cervical cancer can be achieved by a combination of surgery with radiotherapy or chemotherapy [7, 8]. However, there is no relevant research, either domestic or abroad, comparing treatment efficacy of surgery following radiotherapy and chemotherapy following surgery for patients with cervical cancer exactly. Whether the different treatment sequence will cause a different prognosis, and how to treat to achieve the best therapeutic effect are still in debate. Hence, through comparison of curative effect in cervical cancer patients with the two

Comparison of the effect and impact between two surgery treatments

treatment sequences (surgery following radiotherapy and chemotherapy following surgery), this study aimed at to provide reference and guidance for future clinical implementation of surgery combined with radiotherapy and chemotherapy for cervical cancer.

Materials and methods

Research object

A total of 329 patients with cervical cancer admitted to Yantai Yuhuangding Hospital from May 2008 to December 2014 in the Gynecology and Medical Oncology Department were selected as study subjected and their clinical data were analyzed retrospectively. The selected patients aged 30-60 years old with an average of 41.57 ± 12.44 years old. According to the different treatment methods, 164 cases were classified as surgery-first group (surgery before radiotherapy) and 165 cases as chemotherapy-first group (chemotherapy before surgery).

Inclusion criteria: The selected patients were diagnosed as cervical cancer by pathology biopsy in Yantai Yuhuangding Hospital. After diagnosis, they were admitted in for hospitalization to rehabilitation. The age was between 30-60 years old with complete case note and willing to cooperate with our medical staff scheduling.

Exclusion criteria: Patients with surgical contraindications and intolerant to surgery; patients with other cardiovascular and cerebrovascular diseases; patients with other upper respiratory diseases and lower digestive tract diseases; pregnancy patients; midway referral patients; severe physical disability patients; long-term bedridden patients; patients taking or receiving other medications or instrumentation during treatment in Yantai Yuhuangding Hospital. The study was approved by the Ethics Committee of Yantai Yuhuangding Hospital.

Methods

Pelvic lymphadenectomy or hysterectomy was performed for all the patients in the surgery-first group. After 7 days, the linear accelerator 6MV photon line was applied to the whole pelvic field for purely external irradiation therapy, and the 192 Iridium to the intracavitary for radiation therapy, respectively. The dose of the pel-

vic field was 400-600 Gy/time, the dose of A point was 300-500 Gy/time. Such treatment was carried on twice a week for 8 weeks.

A new adjuvant chemotherapy program namely TP program intravenous chemotherapy (paclitaxel 135~175 mg/m² dissolved in 500 mL saline was given via intravenous infusion or intraperitoneal administration, and cisplatin 75 mg/m² was given at intervals of 1 h) was performed in the chemotherapy-first group. The specific operation was strictly carried out by reference to the 2016 cancer chemotherapy manual [9]. The 5 th day after the completion of chemotherapy, pelvic lymphadenectomy or hysterectomy was performed. After the whole treatment was completed, the difference between the two groups was evaluated and a follow-up survey was conducted for a period of 3 years to record the survival of the patients.

Evaluation criteria

The main outcome measures were obtained according to the 2017 Gynecological Cancer Safety Guide as a reference guide to evaluate the efficacy of cervical cancer treatment: The complete regression of the tumor was evaluated as excellent; the reduction of the tumor volume by 50% and above was evaluated as good; the tumor volume decreased by less than 50% was evaluated as common; no significant improvement in tumor conditions or deterioration was evaluated as poor [10]. The total effective rate was the combination of cases with the evaluation of excellent and good.

Secondary outcome measures: the postoperative adverse reactions, complications and lymph node metastasis. The patient's 3-year survival rate and quality of life score were investigated, including physical function evaluation (whether there is disease recurrence, infection, etc.), social activity function evaluation (whether can perform life activities normally) and pain situation (whether there is ache, throes, press pain, etc.). The scores were based on percentiles, and comprehensive evaluation provided by the patients and their families after clearly understanding the exact meaning of each item.

The follow-up was in the form of telephone, letter, or hospital review with the deadline by 30 May 2017, patients' death or out of contact.

Comparison of the effect and impact between two surgery treatments

Table 1. Comparison of clinical data between the two groups (n, %)

	Surgery-first group (n=164)	Chemotherapy-first group (n=165)	χ^2	P
Age			1.154	0.283
<45 years	64 (39.0)	55 (33.3)		
≥45 years	100 (61.0)	110 (66.7)		
Residence			0.365	0.546
City	88 (53.7)	94 (57.0)		
Village	76 (46.3)	71 (43.0)		
Nationality			0.525	0.469
Han	159 (97.0)	162 (98.2)		
Minority	5 (3.0)	3 (1.8)		
Fertility conditions			0.112	0.738
Birth	139 (84.8)	142 (86.1)		
No birth	25 (15.2)	23 (13.9)		
Education level			0.365	0.546
<High school	84 (51.2)	90 (54.5)		
≥High school	80 (48.8)	75 (45.5)		
Smoking and drinking			2.437	0.118
Yes	47 (28.7)	35 (21.2)		
No	117 (71.3)	130 (78.8)		
Exercise habits			0.694	0.405
Yes	69 (42.1)	62 (37.6)		
No	95 (57.9)	103 (62.4)		
Weight			0.685	0.408
<60 kg	77 (47.0)	85 (51.5)		
≥60 kg	87 (53.0)	80 (48.5)		
Surgery mode			0.514	0.473
Pelvic lymphotomy	86 (52.4)	80 (48.5)		
Hysterectomy	78 (47.6)	85 (51.5)		
Pathology staging			1.374	0.241
Stage I-II	94 (57.3)	105 (63.6)		
Stage III-IV	70 (42.7)	60 (36.4)		

Statistical methods

SPSS 22.0 software was used for statistical analysis. The counting data such as the rate of efficacy assessment, adverse reaction, complications, and lymph node metastasis etc. were expressed as a rate and compared using Chi-square test between groups. The measurement data, such as the score of quality of life, are expressed as mean \pm standard deviation (\bar{x} false \pm sd) and were compared using t test between groups. The survival rate was calculated by the Kaplan-Meier method and compared with Log-rank test. $P < 0.05$ suggested

that the difference was statistically significant.

Results

Clinical data of the patients

Comparison of clinical data between the two groups showed that there was no significant difference between the two groups in terms of age, residence, nationality, marital status, fertility conditions, education level, smoking, drinking, exercise habits, weight, surgery mode, and pathology staging ($P > 0.05$), which suggested that the two groups of patients were comparable. See **Table 1**.

Assessment of efficacy

Comparing the efficacy assessment of the two groups shows that 50.6% (83 cases) were evaluated as excellent in the surgery-first group, which was significantly lower than that of 74.6% (123 cases) in the chemotherapy-first group. However, there were 7.9% (13 cases) and 3.0% (5 cases) were evaluated as good and common respectively in surgery-first group, which were significantly higher than those in the chemotherapy-first group 2.4% (4 cases) and 0.6% (1 case, $P < 0.05$). In terms of overall efficiency, 97.0% of the chemotherapy-first group was significantly

better than that of the surgery-first group 89.0% ($P = 0.001$). See **Table 2**.

Adverse reactions, complications, and lymph node metastasis

In the surgery-first group, adverse reactions occurred in 30.8% patients after surgery, of which 17.7% developed complications and 12.8% had lymphatic metastasis. The adverse reaction rate was 7.9% in chemotherapy-first group, of which 5.5% developed complications and 2.4% had lymphatic node metastasis. Compared with the adverse reactions between

Comparison of the effect and impact between two surgery treatments

Table 2. Assessment of efficacy in both groups of patients (n, %)

Effect	Surgery-first group (n=164)	Chemotherapy-first group (n=165)	X ²	P
Excellence	83 (50.6)	123 (74.6)		
Fine	63 (38.4)	37 (22.4)		
Common	13 (7.9)	4 (2.4)		
Poor	5 (3.0)	1 (0.6)		
Total effective rate (%)	89.0	97.0	21.000	0.001

Table 3. Adverse reactions in the both groups of patients (n, %)

	Surgery-first group (n=164)	Chemotherapy-first group (n=165)	X ²	P
Complication	29 (17.7)	9 (5.5)		
Lymph node transformation	21 (12.8)	4 (2.4)		
Total adverse reaction	30.8	7.9	27.16	<0.001

the two groups, the surgery-first group was significantly higher than the chemotherapy-first group ($P<0.001$). See **Table 3**.

Prognosis of survival

By the end of 30 May 2017, 329 cases of cervical cancer were followed-up and the success follow-up rate was 100.0%.

Among them, a total of 14 patients of chemotherapy-first group died within 3 years. The 1-, 2- and 3-year survival rates were 99.4%, 97.0% and 91.5%, respectively. The surgery-first group total 41 cases of death, the first, second and third year survival rates were 97.0%, 89.0%, 75.0%, respectively. Comparison of 3 years total survival rate between the two groups ($P=0.048$), and the difference were statistically significant. The graph is shown in **Figure 1**.

Quality of life assessment

The postoperative quality of life scores of the two groups were compared. The average score of the chemotherapy-first group was (84.07 ± 7.69), which was significantly higher than of the surgery-first group (70.12 ± 9.59 , $P=0.001$). Among which, the scores of physical function, social function, and pain situation were also better than surgery-first group (all $P<0.05$). See **Table 4**.

Discussion

Cervical cancer is a very common female gynecologic disease. Because of no obvious early

characteristics, the majority of patients have reached middle or late stages once diagnosed [11]. Currently in clinical practice, the effective method for the treatment of cervical cancer is still mainly based on surgery. Generally, hysterectomy or uterine cleaning has been adopted according to the patient's reproductive needs and the severity of the conditions [12]. Cervical cancer patients usually have large local lesions, para uterine infil-

tration, lymph node metastasis, and other conditions. Optimal results still cannot be achieved after surgery, and the probability of recurrence is extremely high [13]. Therefore, with the development of medical technology, radiotherapy, and chemotherapy have gradually been widely applied in the treatment of cervical cancer. The research results of Kitagawa et al. showed that chemotherapy could reduce the volume of cervical cancer to a certain extent and reduce the difficulty of the surgery as well [14]. The research of Mohamed et al. showed that postoperative radiotherapy could effectively inhibits lymph node metastasis and reduces the recurrence rate of cervical cancer patients [15].

The results from this research indicate that the treatment effect of chemotherapy following surgery is better than that of surgery following radiotherapy for cervical cancer treatment in regard to the following aspects, such as evaluation of curative effect, adverse reactions, complications, lymph node metastasis, prognosis of survival rate, and life quality score. The possible reasons may be that drugs used for chemotherapy are mainly taxane compounds paclitaxel, or platinum metal complex drugs such as cisplatin, of which paclitaxel has great ability to regulate on the polymerization of microtubules and stable microtubule structure [16]. Cisplatin is a board spectrum drug that has strong bactericidal ability [17]. Both drugs used in tumor patients can effectively inhibit microtubule division and destroy the dynamic balance during microtubule proliferation, so as to achieve the

Comparison of the effect and impact between two surgery treatments

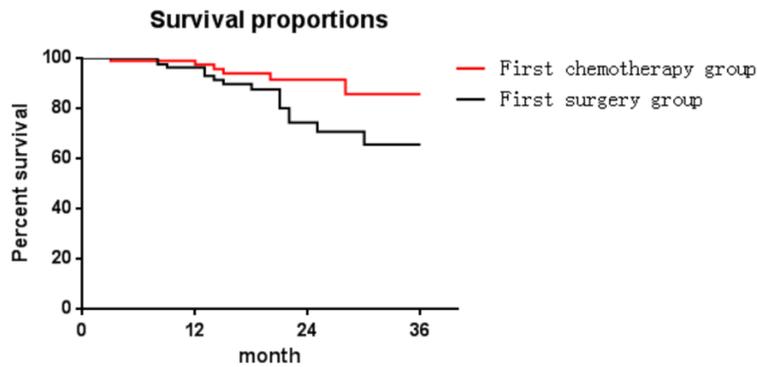


Figure 1. The 3-year prognosis survival graph of the two groups of patients. The 1-, 2- and 3-year survival rate of chemotherapy-first group was 99.4%, 97.0% and 91.5%, respectively. The 1-, 2- and 3-year survival rate of surgery-first group was 97.0%, 89.0%, and 75.0%, respectively. Comparison of 3-year total survival rate between the two groups ($P=0.048$).

Table 4. The quality of life assessment of two groups of patients (score)

	Surgery-first group (n=164)	Chemotherapy-first group (n=165)	χ^2	P
Somatic function	68.41±10.65	82.57±8.14	13.552	0.001
Social event feature	71.54±7.15	80.34±5.28	12.703	0.001
Pain intensity	70.41±10.97	89.31±9.66	16.594	0.001
Average	70.12±9.59	84.07±7.69	14.567	0.001

effect of killing tumor cells. This is also similar to the results of Vizza et al. research on the application of chemotherapy in ovarian cancer, which supported the conclusion of this experiment [18]. Furthermore, Isohashi's study also testified that chemotherapy could effectively kill the subclinical lesion near the tumor, reduce the amount of intraoperative bleeding, greatly reducing the risk of surgery [19]. Thereby enhancing the patient's prognosis conditions and rate of survival. Therefore, while patients are undergoing chemotherapy before surgery, it could effectively control cervical cancer by shrinking and peeling the lesion that in complex structure and closely linked to the tissue. The decisive factor in the prognosis of cervical cancer is the complete resection and cleaning of the cancer tissue lesion during the surgery. Patients after chemotherapy are more likely to achieve the perfect excision conditions in the surgery, resulting in a significant difference in prognosis between the two groups of patients. The main reason for the poor prognosis caused by postoperative radiotherapy might be the particularity of the female body structure: there are important organs such as the vagina, bladder, and rectum are present extremely close to

the uterus. Therefore the tolerance dose is significantly lower than that of the uterus, it is very easy to cause radioactivity related inflammation during radiotherapy, which seriously affects the clinical efficacy and prognosis of patients [20]. Owing to the inflammation of rectum, and which affects the normal operation of the digestive system, patients cannot absorb nutrients from food normally, so that the severity of inflammation is aggravated and forms a vicious circle, which directly affects prognosis.

There are still inadequacies in this experiment, such as small number of cases and short follow-up time. It does not rule out the possible differences in the experimental results may exist in cervical cancer patients of different races or different ages. It also does not exclude the possible survival

rate may be different from the results of this research after prognosis of 5 years or 10 years. However, the next experiment will improve upon these parameters.

In summary, chemotherapy following surgery can achieve the best therapeutic effect in the treatment of cervical cancer disease, which greatly improves the prognosis of survival and quality of life of patients. It is worth popularizing in clinical practice.

Disclosure of conflict of interest

None.

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Comparison of the effect and impact between two surgery treatments

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Comparison of the effect and impact between two surgery treatments

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