

Observation of the short- and long-term effects of parametrial implant radiotherapy technique in treating patients with mid- and late-stage cervical cancer.

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Abstract

Purpose: To explore and discuss the short- and long-term effects of parametrial implant radiotherapy technique on cervical cancer treatment.

Methods: The study recruited 124 subjects from the Department of Radiotherapy of the hospital where the author is employed. The subjects were patients with mid- and late-stage localized cervical cancer who received treatment from October 2011 to May 2016. Patients were classified into the treatment and control groups. Each group comprised 62 subjects. The same synchronous sensitization chemotherapy regimen was observed for all subjects. Patients in the control group received pelvic cavity external irradiation and single after-loading intracavitary brachytherapy, whereas patients in the treatment group received parametrial implants combined with after-loading intracavitary brachytherapy. Tumor shrinkage, negative side effects of treatment, and one-, three-, and five-year survival rates were observed.

Results: The recent effective rate of therapy for the treatment group was 100.0% and higher than that of the control group (96.8%). The difference in effective rates between the two groups was statistically significant ($P < 0.05$). The treatment group had higher one-, three-, and five-year survival rates than the control group. The difference in survival rates between the two groups was statistically significant ($P < 0.05$). The patients in the treatment group who survived for one, three, and five years were 22.6%, 41.9%, and 35.5%, respectively. The patients in the control group who survived for one, three, and five years were 16.1%, 38.7%, and 45.2%, respectively. The rectitis incidence rates of patients in the treatment group who survived for one, three, and five years were 32.2%, 46.8%, and 21.0%, respectively. The rectitis incidence rates of patients in the control group who survived for one, three, and five years were 25.8%, 40.3%, and 33.9%, respectively. The incidence of untoward effects was not statistically significant ($P > 0.05$).

Conclusion: Parametrial implant radiotherapy technique effectively treats mid- and late-stage cervical cancer without causing new untoward effects. Therefore, the further promotion and application of parametrial implant radiotherapy technique are encouraged.

Keywords: Mid- and late-stage cervical cancer, Parametrial implant, After-loading therapy.

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Introduction

Cervical cancer is common among Chinese women and has the highest incidence rate next to breast cancer. According to the National Health and Family Planning Commission of the People's Republic of China, the mortality rate of recently diagnosed cervical cancer patients is 30,000 out of 130,000 [1].

Three treatment techniques for cervical cancer are surgery, radiotherapy, and chemotherapy. Most patients are diagnosed during the late stage of cervical cancer, therefore missing the best time for surgery. Radiotherapy is the major treatment technique for mid- and late-stage cervical cancer.

However, conventional techniques rarely achieve the ideal treatment effect [2]. Local tumors are only effectively shrunk by increased local radiotherapy doses, thus increasing the patients' survival period and treatment ratios.

The combination of parametrial implants and after-loading intracavitary brachytherapy significantly increases irradiation doses for tumors and significantly decreases radioactive damage to organs. It is a new treatment strategy for mid- and late-stage cervical cancer and has drawn the attention of an increasing number of clinical workers [3].

Materials and Methods

General materials

The 124 research subjects were recruited from the Department of Radiotherapy of the hospital where the author is employed. The subjects were patients with mid- and late-stage local cervical cancer who received treatment from October 2011 to May 2016.

The cases were selected according to the Cervical Cancer Diagnosis and Treatment Guidance issued by the National Health and Family Planning Commission of the People's Republic of China and Performance Score (KPS) standards. Subjects were limited to those with:

1. Detailed clinical pathological examination data with clear terms of their cervical cancer period
2. No cancer metastasis to other organs
3. No other diseases that caused cervical cancer
4. Tumors with sizes of 2-7 cm
5. No radiotherapy contraindication
6. No problems with communication and in full agreement to participate in the research program
7. No prior treatment received
8. KPS>70.

Patients who exhibited the following conditions were excluded:

1. Serious co-infection
2. Other serious diseases
3. Other cancer types
4. Cervical stump cancer
5. Failed to finish all treatments

The subjects were randomly divided into the treatment and control groups. Each group comprised 62 patients. The average age of the control group was (44.7 ± 8.5) years old. According to FIGO's period division standards, there was one case in the IB2 period, 33 cases in the IIB period, 9 cases in the IIIA period, 15 cases in the IIIB period, and 4 cases in the IVB period. Based on pathological type division, there were 44 cases of squamous cancer, seven cases of adenocancer, six cases of small cell cancer, and five cases of clear cell cancer. Patients in the two groups were not significantly different in terms of baseline age and pathological division; thus, the two groups were comparable.

Treatment strategies

All patients underwent the synchronous chemosensitization regimen. Nedaplatin (NDP) chemosensitization monotherapy was performed. On the first day of radiotherapy, patients received intravenous drips of 20 mg/m² NDP mixed with normal saline (NS). Treatment occurred once a week at a total of four to five treatments. After the conclusion of radiotherapy, sequential treatment with TP chemotherapy was conducted once every four weeks. The chemotherapy period lasted for six

weeks. The control group received pelvic cavity external irradiation combined with single after-loading intracavitary brachytherapy; the treatment group received parametrial implants combined with after-loading intracavitary brachytherapy [4]. Pelvic cavity external irradiation was performed with 6MV linear accelerator (VARIAN, Elekta AB). The referential dosage was set at 95% PTV 50.4 Gy and 1.8 Gy. Pelvic cavity external irradiation was performed one to five times a week over a treatment period of six to seven weeks. The radiation dosage was increased to 8–10 Gy when positive lymph glands near the aorta abdominalis and within the pelvic cavity were present. The dosage for single after-loading intracavitary brachytherapy was 42 Gy/7 times. The treatment group received parametrial implants two to five times based on tumor size. The parametrial implant procedure was as follows: the metal tube source applicator was placed in the uterine cavity and one needle was implanted in Cervix Uteri Point 3 and/or Cervix Uteri Point 9. The dosage was 20 mm, 6 Gy outside the tube and 13 mm, 8 GY outside the needle.

Observation of indexes

Recent effective rate: The evaluation standards of the recent effective rate were based on the WTO's treatment judgment standards and were as follows: 1) complete remission (CR)-complete remission of tumor tissues without new growths; 2) partial remission (PR)- gross tumor volume (GTV) shrunk by $\geq 50\%$ without new growths; 3) stable disease (SD)- GTV shrunk considerably by $<50\%$; 4) progressive disease (PD)- GTV did not shrink or new growths are present. This study considered effective CR and PR.

Patients' survival rate: The long-term follow-up of patients was conducted. The patients' one-, three-, and five-year survival rates were recorded.

Untoward effects: The rectitis and urocystitis incidence rates among patients who survived for one, three, or five years were recorded.

Statistical treatment

Statistical analysis and processing of all data were conducted with SPSS 18.0. Patients' current effective rate, survival rates over one-, three-, and five-years, and complication incidence rate were expressed as mean \pm standard deviation ($\bar{x} \pm S$). Mean comparison was performed by one-way analysis of variance. T-test was also conducted. $P < 0.05$ indicated that the difference was statistically significant.

Results

Current effective rate

The treatment group had a 100.0% current effective rate and was higher than that of the control group (96.8%). The

effective rates of the two groups were statistically different ($P < 0.05$) (Table 1).

Table 1. Comparison of recent effective rates between the control and treatment groups [n (%)].

Group	Effective	CR	PR	SD	PD
Treatment group (n=62)	62 (100.0)	60 (96.8)	2 (3.2)	0	0
Control group (n=62)	60 (96.8)	56 (90.3)	4 (6.4)	2 (3.2)	0
χ^2	5.106	3.975	3.976	3.852	
P	$P < 0.05$	$P < 0.05$	$P < 0.05$	$P < 0.05$	

Patients' survival rate

The one-, three-, and five-year survival rates of the treatment group were higher than that of the control group. The difference in survival rates between the two groups was statistically significant ($P < 0.05$) (Table 2).

Table 2. Comparison of the survival rates between the two groups [n (%)].

Group	One-year survival rate	Three-year survival rate	Five-year survival rate
Treatment group (n=62)	62 (100.0)	60 (96.8)	2 (3.2)
Control group (n=62)	60 (96.8)	56 (90.3)	4 (6.4)

Table 3. Untoward effect incidence rates of patients in the two groups [n (%)].

Group	Untoward effects of patients surviving for one year		Untoward effects of patients surviving for three years		Untoward effects of patients surviving for five years	
	Urocytitis	Rectitis	Urocytitis	Rectitis	Urocytitis	Rectitis
Treatment group (n=62)	14 (22.6)	20 (32.2)	26 (41.9)	29 (46.8)	22 (35.5)	13 (21.0)
Control group (n=62)	10 (16.1)	16 (25.8)	24 (38.7)	25 (40.3)	28 (45.2)	21 (33.9)
χ^2	0.587	0.326	0.211	1.258	0.956	1.023
P	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$

Discussion

After-loading radiotherapy with high dose implants in tissues has developed rapidly in recent years; this treatment approach not only efficiently increases radiotherapy dose to the tumor area, but also prevents bleeding from local tumor combinations [5,6]. ZENG Siyuan et al. studied 20 cases of exogenous late-stage cervical cancer patients who received tissue implant radiotherapy; they found that the effective rate was as high as 92%. This finding suggests that tissue implant radiotherapy favorably affects the treatment of exogenous cervical cancer. However, their research findings require more in-depth study.

Tumors will quickly shrink or even undergo complete remission two to three weeks after three rounds of implant radiotherapy. In this research, the effective rate of the treatment group was 100.0% and was higher than that of the control group (96.8%). The difference between the two groups was statistically significant ($P < 0.05$). This result also suggests that the combination of parametrial implants and after-loading

Treatment group (n=62)	60 (96.8)	51 (82.2)	37 (59.7)
Control group (n=62)	55 (88.7)	42 (67.7)	31 (50.0)
χ^2	4.498	2.536	5.194
P	$P < 0.05$	$P < 0.05$	$P < 0.05$

Untoward effects

Untoward effects in the two groups are shown in Table 3. Patients in the treatment group who survived for one, three, and five years had urocytitis incidence rates of 22.6%, 41.9%, and 35.5%, respectively. The urocytitis incidence rates of patients in the control group who survived for one, three, and five years were 16.1%, 38.7%, and 45.2%, respectively. The patients in the treatment group who survived for one, three, and five years had rectitis incidence rates of 32.2%, 46.8%, and 21.0%, respectively. Patients in the control group who survived for one, three, and five years had rectitis incidence rates of 25.8%, 40.3%, and 33.9%. Differences in incidence rates between groups were not statistically significant ($P > 0.05$).

intracavitary brachytherapy efficiently shrinks tumors. The research subjects in this study were late-stage cervical cancer patients with high GTV, poor blood circulation within the tumor, and serious cell hypoxia. The tumors' central parts exhibited necrosis and liquidation. The tumors were also less sensitive to radiotherapy. Inserting a metal tube source applicator in the uterine cavity can help solve these problems to some extent, because tube is functionally situated nearer to the tumor and the unit radiotherapy dose to the tumor can be greatly increased. Radiotherapy can inhibit the damage repair of tumor cells, reduce GTV through toxic effects, and reinforce parametrial implants. The combined therapies maximally reduced GTV by functioning on cancer cells for different periods. New research findings have suggested that radioactive rays can change cell membrane permeability and increase the amount of chemicals, such as platinum, entering the cells. Therefore, radiotherapy can enhance the effect of chemicals and increase the effective rate of treatment.

Previous studies reported that parametrial implant radiotherapy faces long-term recurrence rates in the treatment of mid- and late-stage cervical cancer, and that recurrence rates and dosage are negatively correlated. The follow-up period in this research was relatively long, and the author found that the one-, three-, and five-year survival rates of patients in the treatment group were higher [7]. This suggests that parametrial implant radiotherapy has favorable long-term effects on the treatment of mid- and late-stage cervical cancer. The combination of parametrial implant radiotherapy and after-loading intracavitary brachytherapy most likely contributed to more accurate targeting, proper adjustment of dosage, short irradiation duration, and lower individual exposure dose compared with traditional radiotherapy [8].

According to relevant literature, the urocystitis and rectitis incidence rates are 14.3% and 32.3%, respectively, among patients with mid- and late-stage cervical cancer and receiving external irradiation or single intracavitary brachytherapy. Urocystitis and rectitis incidence rates were 6.5% and 19.3%, respectively, among patients who received parametrial implant and intracavitary brachytherapy.

In this research, the urocystitis incidence rates among patients in the treatment group who survived for one, three, and five years were 22.6%, 41.9%, and 35.5%, respectively. The urocystitis incidence rates among patients in the control group who survived for one, three, and five years were 16.1%, 38.7%, and 45.2%, respectively. The rectitis incidence rates among patients in the treatment group who survived for one, three, and five years were 32.2%, 46.8%, and 21.0%, respectively. The rectitis incidence rates among patients in the control group who survived for one, three, and five years were 25.8%, 40.3%, and 33.9%. The untoward effect incidence rate was higher than that reported by previous studies. The high dosage and older age of patients adopted in this research may account for the higher incidence rates of untoward effects. Meanwhile, GTV shrunk and the tumor location changed after radiotherapy. The implanted metal tube source applicator was vulnerable to the influence of the full state of the uterus. These factors might decrease the radiotherapy dose received by the tumor. Three-dimensional intensity-modulated radiotherapy (IMRT) offers a solution to this problem [9,10].

In future research, the TPS treatment plan and system should be adopted to achieve optimal dosage and more accurate radiotherapy to reduce the incidence rates of untoward effects. The untoward effect incidence rate of patients in the treatment group was higher than that of the control group, but was not statistically significant. This result suggests that parametrial implant radiotherapy is a relatively safe treatment for mid- and late-stage cervical cancer.

Conclusion

The parametrial implant technique has definite short- and long-term effects in treating mid- and late-stage cervical cancer

patients. More importantly, this treatment approach has no new untoward effects. Thus, parametrial implant technique is worth further promoting and applying in the treatment of cervical cancer.

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