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Original Article

Efficacy and prognosis of concurrent chemoradiotherapy in the management of recurrent cervical cancer: a retrospective study

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Abstract: Objective: This retrospective study aimed to evaluate the efficacy of concurrent chemoradiotherapy (CCRT) in the treatment of recurrent cervical cancer (RCC) and its effect on patient prognosis. Methods: A total of 106 RCC patients, treated at Nanfang Hospital and Southern Medical University from January 2015 to January 2019, were retrospectively analyzed. Of these, 56 patients who received CCRT served as the research group, while 50 patients treated with radiotherapy alone formed the control group. Outcomes compared between groups included treatment efficacy, tumor-free survival (TFS), 5-year overall survival (OS) rate, incidence of adverse reactions, serum tumor marker levels (carbohydrate antigen 15-3 [CA15-3], squamous cell carcinoma antigen [SCCA], and carcinoembryonic antigen [CEA]) and quality of life at 6 months post-treatment. Prognostic factors for poor outcomes were also analyzed. Results: Compared to the control group, the CCRT group exhibited significantly higher total response rate, prolonged TFS, improved 5-year OS rate, and better quality of life at 6 months post-treatment (all $P<0.05$). Serum levels of CA15-3, SCCA, and CEA decreased significantly post-treatment in the CCRT group and were lower than those in the control group (all $P<0.05$). Although the incidence of adverse reactions in the research group was slightly higher, the difference was not significant ($P>0.05$), and all side effects were alleviated after treatment. Multivariate analysis identified age, pathologic stage, treatment response, and treatment modality as independent prognostic risk factors (all $P<0.05$). Conclusions: CCRT demonstrated superior efficacy, favorable prognosis, and low complication rate in the treatment of RCC. It effectively suppressed serum tumor markers and improves patient quality of life, supporting its broader clinical application.

Keywords: Recurrent cervical cancer, concurrent chemoradiotherapy, treatment efficacy, prognosis

Introduction

Cervical cancer is a common malignancy with a high incidence among women aged 30 to 55 years, with a growing tendency to affect younger individuals. Timely intervention has been shown to effectively reduce both morbidity and mortality rates [1]. However, due to the lack of typical symptoms in the early stage, approximately 50% of patients have been diagnosed at an intermediate or advanced stage, often presenting with local tumor enlargement, tissue invasion, or distant metastasis. Moreover, up to about 21% of patients develop recurrent cervical cancer (RCC), posing great challenges to clinical treatment [2, 3]. At present, radiotherapy remains the primary treatment modality for RCC both in China and abroad, largely due to the limited efficacy of surgical intervention for managing recurrent disease [4]. However, radiotherapy alone has limited therapeutic effect, often resulting in only modest clinical improvement and a low 5-year survival rate [5]. Therefore, combining radiotherapy with other therapeutic modalities to improve clinical efficacy and prolong survival in patients with RCC has become a focal point of current clinical research.

In recent years, advances in medical science and ongoing research in cervical cancer have demonstrated that neoadjuvant chemotherapy, as a systemic treatment modality, exerts a potent cytotoxic effect on tumor micrometastases and enhances the sensitivity and efficacy of radiotherapy [6]. Some studies have found that

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concurrent chemoradiotherapy (CCRT) can target tumor cells at different phases of the cell cycle, modulate the hypoxic microenvironment, enhance radiosensitivity, eliminate residual microscopic lesions not addressed by radiotherapy alone, and improve cell membrane permeability to optimize the efficacy of chemotherapy [7, 8]. In recent years, CCRT has been increasingly applied in the treatment of RCC; however, relevant research remains limited and lacks depth [9].

This study enrolled 106 patients with RCC to evaluate the efficacy and prognostic value of CCRT for early-stage RCC, aiming to provide clinical evidence to support more effective treatment strategies.

Materials and methods

Clinical information

A total of 106 patients with RCC, who received treatment at the Nanfang Hospital and Southern Medical University from January 2015 to January 2019, were retrospectively enrolled. Based on treatment modality, 56 patients who received CCRT comprised the research group, while the remaining 50 patients who underwent radiotherapy alone constituted the control group. All participants were rigorously screened according to predefined inclusion and exclusion criteria. The sample size met the minimum statistical requirement (approximately 40 participants per group), as determined by the following sample size estimation formula:

$$n = \frac{((Z_{1-\alpha/2} + Z_{1-\beta})^2 \times (p_1(1 - p_1) + p_2(1 - p_2)))}{(p_1 - p_2)^2}$$

Inclusion criteria: (1) II-IV RCC confirmed by pathology or cytology; (2) diagnosis of postoperative recurrence [10]; (3) met the indications for radiotherapy and chemotherapy; (4) Karnofsky Performance Status score ≥60; and (5) complete clinical and follow-up data.

Exclusion criteria: (1) hematologic disorders; (2) autoimmune diseases; (3) acute or chronic infections; (4) psychiatric disorders; (5) severe dysfunction of major organs (e.g., heart, liver, brain, and kidneys); (6) were pregnant or breastfeeding; or (7) had other primary malignancies besides cervical cancer.

The study protocol was approved by the Ethics Committee of Nanfang Hospital, Southern Medical University, and conducted in accordance with the Declaration of Helsinki.

Treatment plan

Patients in the control group received radiotherapy alone, with the irradiation field determined using a simulation positioning machine. Patients received whole pelvic radiotherapy using irregular anterior-posterior fields and central irradiation delivered by a Siemens Primus linear accelerator with 6MV X-ray beams. Concurrent rectal lead shielding and supplementary intracavitary radiotherapy brachytherapy were applied. The prescribed dose was 55 Gy to the anterior and posterior pelvic fields and 25 Gy to the central pelvic region. If parametrial infiltration was present, an additional dose of 10-15 Gy was administered; for vaginal infiltration, the dose was escalated to 32-48 Gy. Radiotherapy was administered once every 6 weeks, for a total of five sessions. On the basis of radiotherapy, patients in the research group received concurrent chemotherapy. The regimen included: Cisplatin (20 mg; Yunnan Botanical Pharmaceutical Co., Ltd., China; approval number: H53021679), administered via intravenous infusion three times per week, on alternate days; Cyclophosphamide (400 mg; Jiangsu Hengrui Medical Co., Ltd., China; approval number: H3202085), administered via intravenous infusion once daily for five consecutive days; Pingyangmycin (8 mg; Hisun Pfizer Pharmaceutical Co., Ltd., China; approval number: H20059038), administered via intravenous infusion once daily for five consecutive days.

Observation indicators

(1) Therapeutic efficacy was evaluated and compared between the two groups according to the Response Evaluation Criteria in Solid Tumors [11]. Treatment responses were categorized as follows: complete response (CR; complete disappearance of the target lesion after treatment), partial response (PR; a reduction of more than 50% in the volume of the target lesion), stable disease (less than 50% reduction, no significant change in lesion size, and no new lesions), and progressive disease (enlargement of the lesion or the appearance of new lesions). The overall response rate was calculated as: (CR + PR) cases/total cases × 100%.

Table 1. General information

Factor	Research Group n=56	Control Group n=50	χ^2	P
Age (years)			0.001	0.976
≤57	20 (35.71)	18 (36.00)		
>57	36 (64.29)	32 (64.00)		
BMI (kg/m^2)			0.089	0.766
≤23	24 (42.86)	20 (40.00)		
>23	32 (57.14)	30 (60.00)		
History of Pelvic Surgery			0.284	0.594
YES	16 (28.57)	12 (24.00)		
NO	40 (71.43)	38 (76.00)		
Pregnancy times			0.065	0.799
≥2	10 (17.86)	8 (16.00)		
<2	46 (82.14)	42 (84.00)		
Pathologic Type			0.015	0.993
Adenocarcinoma	20 (35.71)	18 (36.00)		
Squamous Cell Carcinoma	22 (39.29)	20 (40.00)		
Adenosquamous Carcinoma	14 (25.00)	12 (24.00)		
Pathologic Stage			0.026	0.873
Stage II-III	35 (62.50)	32 (64.00)		
Stage IV	21 (37.50)	18 (36.00)		

Note: BMI, body mass index.

(2) Serum tumor markers including squamous cell carcinoma antigen (SCCA), carbohydrate antigen 15-3 (CA15-3), and carcinoembryonic antigen (CEA) were measured in both groups before and after treatment. Enzyme-linked immunosorbent assay kits were used for detection (Whenzhou KeMiao Biological Technology Co., Ltd., China; catalog numbers: KM091271, KM090926, KM090091).

(3) The tumor-free survival and 5-year overall survival rates were recorded and compared between the two groups. All patients underwent a 5-year follow-up, with assessments conducted quarterly by telephone interviews, home visits, medical record reviews, and clinical re-examinations. Overall survival (OS) was defined as the time from treatment initiation to death from any cause.

(4) Adverse reactions were assessed according to the radiation toxicity grading criteria and hematological toxicity evaluation standards of the American Radiation Oncology Cooperative Group [12]. Observed adverse events included leukopenia, gastrointestinal reactions, myelosuppression, and hepatic and renal insufficiency. Toxicities were graded on a scale of 0-4, and the incidence rates were recorded and compared between the two groups.

(5) Quality of life was assessed 6 months after treatment using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 [13]. The scale evaluates five functional domains: physical, role, emotional, cognitive, and social functioning. Higher scores indicate better quality of life.

Statistical methods

All data were analyzed using SPSS version 18.0 (IBM Corp., Armonk, NY, USA), and figures were generated using GraphPad Prism version 8 (GraphPad Software, San Diego, CA, USA). Categorical variables were compared using the chi-square test, while continuous variables were analyzed using Student's t test. Survival analysis was conducted using the Kaplan-Meier method, and differences between survival curves were assessed using the log-rank test. A *P*-value <0.05 was considered significant.

Results

Clinical information

No statistically significant differences were observed between the research and control groups regarding gender, age, and obstetric history, indicating comparability of the subjects (all P>0.05, **Table 1**).

Table 2. Comparison of therapeutic efficacy

Therapeutic Efficacy	Research Group n=56	Control Group n=50	χ^2	P
Complete response	10 (17.86)	4 (8.00)	-	-
Partial response	35 (62.50)	26 (52.00)	-	-
Stable Disease	10 (17.86)	15 (30.00)	-	-
Progressive disease	1 (1.79)	5 (10.00)	-	-
Total Response Rate	45 (80.36)	30 (60.00)	5.290	0.021

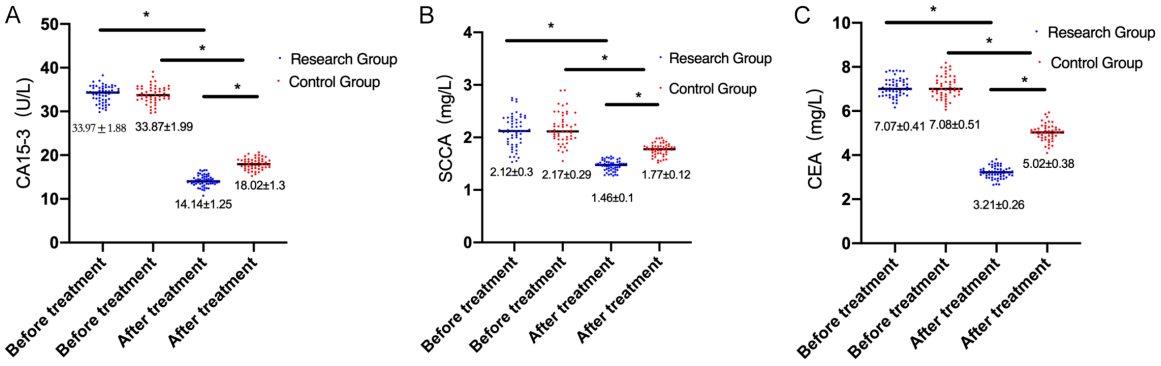

Figure 1. Comparison of tumor markers before and after treatment. A: Comparison of serum CA15-3 between two groups before and after treatment; B: Comparison of serum SCCA between two groups before and after treatment; C: Comparison of serum CEA between two groups before and after treatment. Note: * indicates P<0.05. CA15-3, carbohydrate antigen 15-3; SCCA, squamous cell carcinoma antigen; CEA, carcinoembryonic antigen.

Table 3. Comparison of tumor-free survival and 5-year survival rates

Item	Research Group n=56	Control Group n=50	t/χ^2	P
Tumor-free survival rate	13.28±0.41	11±0.31	31.99	<0.001
5-year overall survival rate	20 (35.71)	9 (18.00)	4.171	0.041

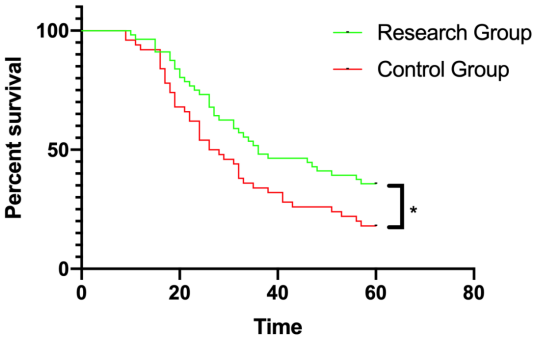

Figure 2. Comparison of the 5-year survival rate. Note: * indicates P<0.05.

Comparison of therapeutic efficacy

In the research group, the number of patients achieving CR, PR, stable disease and progressive disease was 10, 35, 10, and 1, respectively. In the control group, the corresponding numbers were 4, 26, 15, and 5, respectively. The total response rate in the research group was statistically higher than that in the control group (80.36% *vs.* 60.00%, P<0.05, **Table 2**).

Comparison of tumor markers before and after treatment

No significant differences were observed in serum levels of CA15-3, SCCA, and CEA between the two groups before treatment (all P>0.05). After treatment, all tumor markers declined markedly in both groups, with the decrease in the research group being more pronounced compared to the control group (all P<0.05, **Figure 1**).

Comparison of tumor-free survival and 5-year survival rates

The mean tumor-free survival in the research group was 13.28±0.41 months, with a 5-year OS rate of 35.71% (20/56). In the control group, the corresponding values were 11±0.31 months and 18.00% (9/50), respectively. Kaplan-Meier survival analysis showed that the

Table 4. Comparison of incidence of adverse reaction during treatment

Adverse Reaction	Research Group n=56	Control Group n=50	χ^2	P
Leukopenia	5 (8.93)	2 (4.00)	-	-
Gastrointestinal Reactions	6 (10.71)	2 (4.00)	-	-
Bone Marrow Suppression	1 (1.79)	1 (1.00)	-	-
Liver and Kidney Insufficiency	1 (1.79)	0	-	-
Incidence of Adverse Reaction	13 (23.21)	5 (10.00)	3.272	0.071

Table 5. Univariate analysis

Factor	Good Prognosis Group (n=29)	Poor Prognosis Group (n=77)	χ^2	P
Age			44.022	<0.001
≤57 years old (n=38)	25 (86.21)	13 (16.88)		
>57 years old (n=68)	4 (13.79)	64 (83.12)		
Pathological Type			1.404	0.496
Adenocarcinoma (n=38)	13 (44.83)	25 (32.47)		
Squamous carcinoma (n=42)	10 (34.48)	32 (41.56)		
Adenosquamous carcinoma (n=26)	6 (20.69)	20 (25.97)		
Pathological Stage			12.008	<0.001
II-III (n=67)	26 (89.66)	41 (53.25)		
IV (n=39)	3 (10.34)	36 (46.75)		
Treatment Response			12.840	<0.001
Complete/Partial Response (n=75)	28 (96.55)	47 (61.04)		
Stable/Progressive Disease (n=31)	1 (3.45)	30 (38.96)		
Treatment Regimen			25.984	<0.001
Concurrent Chemoradiation (n=56)	27 (93.10)	29 (37.66)		
Radiation Alone (n=50)	2 (6.90)	48 (62.34)		

research group had markedly higher tumor-free survival and 5-year OS rates compared to the control group (both P<0.05, **Table 3**; **Figure 2**).

Comparison of incidence of adverse reactions during treatment

After treatment, the number of patients in the research group experiencing leukopenia, gastrointestinal reactions, bone marrow suppression, and liver and kidney insufficiency was 5, 6, 1, and 1, respectively. In the control group, the corresponding numbers were 2, 2, 1, and 0, respectively. The incidence of complications was slightly higher in the research group than in the control group, but the difference was not statistically significant (P>0.05, 23.21% vs. 10.00%, **Table 4**).

Multivariate analysis of prognostic factors

Based on outcomes, patients were categorized into a poor prognosis group (n=77) and a good prognosis group (n=29). Univariate analysis identified age, pathologic stage, treatment response, and treatment regimen as potential factors associated with poor prognosis in RCC patients (**Table 5**). Variables with significant differences were subsequently included in multivariate logistic regression analysis. The results demonstrated that age, pathological stage, treatment response, and treatment regimen were all independent risk factors for patient prognosis (**Table 6**).

Comparison of quality of life after treatment

The quality of life of all patients was evaluated 6 months after treatment. The research group showed evidently higher scores across various dimensions compared to the control group (P<0.05, **Figure 3**).

Discussion

In the clinical treatment of cervical cancer, chemotherapy and radiotherapy are commonly

Table 6. Multivariate analysis

Factors	B	S.E.	Wald	P	OR	95% C.I.	
						Lower	Upper
Age	4.518	1.180	14.664	<0.001	91.680	9.077	925.983
Pathological Stage	3.317	1.331	6.214	0.013	27.575	2.032	374.244
Treatment Response	2.886	1.291	4.996	0.025	17.914	1.427	224.953
Treatment Regimen	3.828	1.303	8.633	0.003	45.979	3.577	590.972

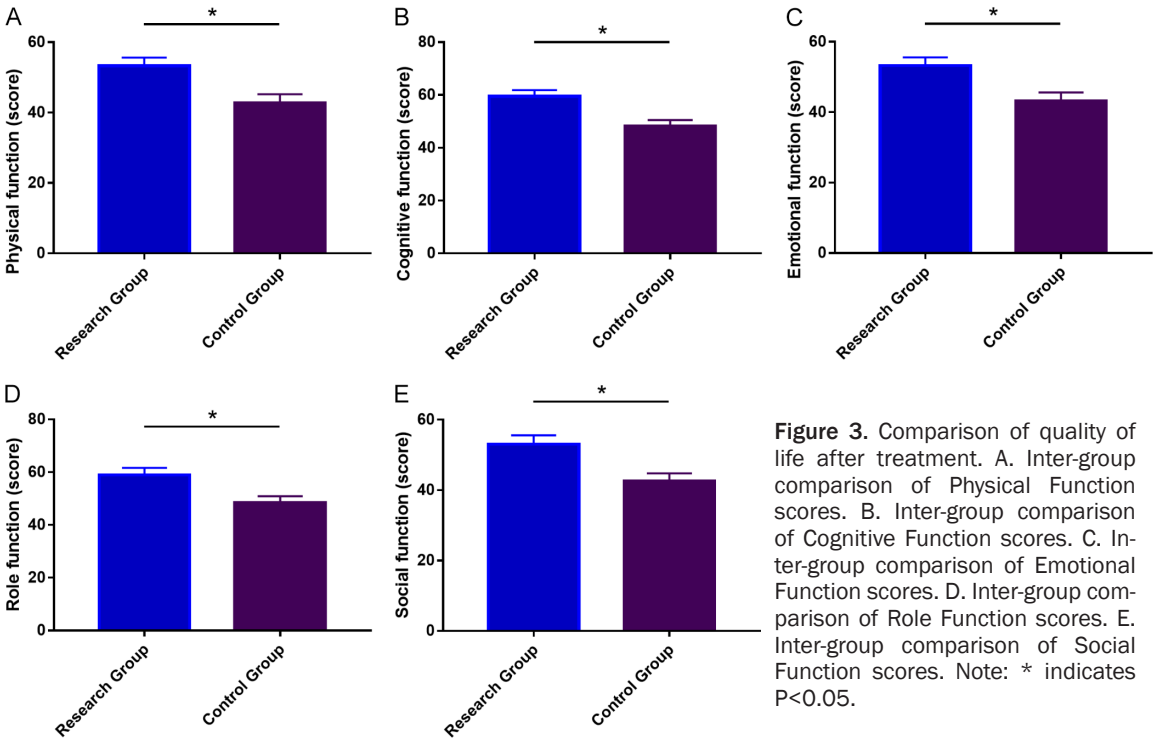

Figure 3. Comparison of quality of life after treatment. A. Inter-group comparison of Physical Function scores. B. Inter-group comparison of Cognitive Function scores. C. Inter-group comparison of Emotional Function scores. D. Inter-group comparison of Role Function scores. E. Inter-group comparison of Social Function scores. Note: * indicates P<0.05.

employed to reduce tumor size and improve the likelihood of a radical cure [14]. However, RCC often develops within 2 years of initial treatment. Although radiotherapy remains a cornerstone of RCC treatment, it is insufficient on its own to fully suppress tumor growth and recurrence. Increasing the radiotherapy dose can markedly increase toxicities and side effects, making it difficult for patients to tolerate [15]. Therefore, identifying effective treatment strategies is crucial for improving the therapeutic outcome of RCC.

In recent years, advances in clinical research on new chemotherapeutic agents and the improvement in administration methods have led to the widespread use of chemotherapy regimens in patients with advanced cervical cancer [16]. The main advantage of CCRT is that chemotherapeutic agents can increase the effects of ionizing radiation in aerobic cells by generating peroxide free radicals, while also acting as oxygen in hypoxic cells, thereby amplifying and strengthening the radiation damage mechanism [17]. In addition, chemotherapeutic agents can inhibit DNA repair enzymes and impair the repair mechanisms of tumor cells, effectively reducing lesion size and regulating tumor blood supply, thus strengthening the overall therapeutic effect [18]. In recent years, CCRT has been increasingly applied in the treatment of RCC, but the related research remains incomplete. In this study, we observed that the total response rate in the research group was statistically higher than that of the control group, suggesting that CCRT has a more effective short-term curative effect than radiotherapy alone, and further improves the therapeutic outcomes for RCC patients. The study by You et al. [19] reported an overall response rate of 75% for CCRT in locally recurrent rectal cancer, which is comparable to the

80.36% response rate observed in the present study for RCC treated with the same modality.

With advancements in molecular biology and immunology, tumor markers have become essential tools for the auxiliary diagnosis and disease monitoring of cervical cancer. CEA is a broad-spectrum tumor marker that is elevated in various malignancies, such as colon cancer, breast cancer, and cervical cancer [20]. SCCA is the primary tumor marker for cervical squamous cell carcinoma, with research indicating elevated serum SCCA levels in cervical cancer patients compared to healthy individuals [21]. CA15-3, a glycoprotein antigen initially used for the differential diagnosis of breast cancer, has also been reported to be overexpressed in cervical cancer patients [22]. This study showed that the serum levels of CEA, SCCA and CA15-3 were highly expressed in the two groups before treatment, which was consistent with previous studies. After treatment, levels of the three markers decreased in both groups, with a more significant reduction in the research group. This may be attributed to the enhanced anti-tumor effect of the combination of radiotherapy and chemotherapy. Studies [23, 24] have shown that CCRT exerts a strong synergistic effect, with chemotherapeutic agents inhibiting the repair of radiation-induced damage and tumor cell proliferation. This, in turn, enhances tumor cell permeability, improving the absorption of platinum and other drugs, and enhancing the sensitivity to radiotherapy. Chemotherapy, moreover, effectively kills tumor cells in both distant metastases and local tissues, inhibiting tumor cell invasion into normal tissues. This reduces the levels of serum tumor markers and contributes to favorable disease outcomes, which supports our findings. The findings of Chen et al. [25] demonstrated that CCRT in patients with locally advanced cervical cancer significantly downregulated serum tumor markers, including CEA and SCCA levels, which is consistent with the results of our study.

We then compared tumor-free survival and 5-year OS rates between the research group and control groups. The results showed significantly higher rates in the research group, although this was accompanied by more pronounced toxicities and side effects. Fortunately, further analysis revealed that the most common adverse reactions in the research group were gastrointestinal reactions and leukopenia, both of which were relieved with symptomatic treatment and did not affect normal daily activities. Fewer patients experienced myelosuppression, and complications such as liver and kidney injury were also reversible with appropriate treatment. Therefore, the application of CCRT for RCC is crucial for improving both therapeutic outcome and patient prognosis. Additionally, CCRT offers significant advantages in terms of patient health and safety. As reported by Tang et al. [26], patients with early-stage cervical cancer who received postoperative CCRT had significantly higher progression-free survival and 5-year OS rates compared to those treated with radiotherapy alone, consistent with our findings. Finally, we compared the quality of life between the two groups after treatment and found that the research group had significantly higher scores 6 months post-treatment compared to the control group. This suggests that CCRT not only improves therapeutic outcomes and survival but also has a positive effect on patients' quality of life. This is the first comprehensive evaluation of CCRT's effects on RCC in terms of efficacy, safety, and quality of life. The findings of Stuopelytė et al. [27] align with those of the present study, indicating that cervical cancer survivors receiving CCRT experience a relatively favorable quality of life with regard to symptom burden.

This study has several limitations. First, the relatively small sample size from a single center may limit the generalizability of the findings. Additionally, factors influencing treatment efficacy were not explored in depth. Lastly, certain indicators, such as fatigue, negative emotions, and treatment adherence, were not investigated. To address these limitations, future studies should consider expanding the sample size and incorporating data from multiple centers to reduce potential bias. Moreover, including additional analyses on the unexamined factors could help optimize treatment strategies and provide a more comprehensive assessment of treatment outcomes.

Conclusion

CCRT demonstrated definite curative effects, a favorable prognosis, and a low complication rate for RCC treatment. It significantly inhibited serum tumor markers and improved patients' quality of life.

Disclosure of conflict of interest

None.

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