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# Clinical Efficacy and Adverse Reactions of VMAT Radiotherapy Combined with Raltitrexed Chemotherapy in the Treatment of Elderly Patients with Esophageal Cancer

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**Abstract:** *Objective*: To investigate the efficacy and adverse reactions of volumetric modulated arc therapy (VMAT) radiotherapy combined with raltitrexed chemotherapy in the treatment of elderly patients with esophageal cancer. *Methods*: A total of 86 elderly patients with esophageal cancer admitted to our hospital between February 2024 and February 2025 were enrolled in this study and equally divided into two groups: a control group receiving VMAT radiotherapy alone and a study group receiving VMAT radiotherapy combined with raltitrexed chemotherapy, with 43 patients in each group, to compare the therapeutic outcomes between the two treatment approaches. *Results*: The study group demonstrated significantly higher objective remission and disease control rates than the control group ($P < 0.05$). Post-treatment levels of HSP90α, Cyfra21-1, and CEA were markedly reduced in the study group relative to the control group ($P < 0.05$). Adverse reaction incidence showed no notable difference between the two groups ($P > 0.05$). Quality of life (QOL) scores were significantly elevated in the study group compared to the control group at both 3- and 6-month follow-ups ($P < 0.05$). *Conclusion*: VMAT radiotherapy combined with raltitrexed chemotherapy can improve the short-term efficacy, reduce tumor marker levels, and improve the quality of life of elderly patients with esophageal cancer. The treatment has fewer adverse reactions and better patient tolerance.

**Keywords:** Esophageal cancer; Elderly; Volumetric modulated arc therapy; Raltitrexed

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## 1. Introduction

Esophageal cancer is a common clinical gastrointestinal tumor, and its incidence increases with age. Its early symptoms are concealed, and the disease stage is often advanced at diagnosis. Many patients are already unable to undergo surgical treatment. Research shows that about 40–60% of patients are unable to undergo surgical

treatment due to the advanced stage of the disease at diagnosis [1]. For these patients, radical radiotherapy and chemotherapy have become the main treatment methods. As a new radiotherapy method, volumetric modulated arc therapy (VMAT) kills tumor cells by irradiating the tumor target area. Its measurement distribution effect is good and more precise and flexible, playing an important role in the treatment of solid tumors [2]. Studies have shown that radiotherapy combined with chemotherapy in the treatment of esophageal cancer can improve radiotherapy sensitivity and patient survival rates [3]. Based on this, this study explores the effect of VMAT radiotherapy combined with raltitrexed chemotherapy in the treatment of elderly patients with esophageal cancer, as detailed below.

## 2. Materials and methods

### 2.1. General information

A total of 86 elderly patients diagnosed with esophageal cancer and admitted to our hospital between February 2024 and February 2025 were enrolled in this study. Based on the treatment approaches, they were categorized into a control group and a study group, each comprising 43 patients. The baseline characteristics of both groups were comparable, with no statistically significant differences ($P > 0.05$), as detailed in **Table 1**.

**Table 1.** Comparison of general information between the two groups

| Group | Cases | Gender (%) | | Age (years) | Disease duration (months) | BMI (kg/m$^2$) | TNM stage | |
|---|---|---|---|---|---|---|---|---|
| | | Male | Female | | | | II | III |
| Control | 43 | 24 (55.81%) | 19 (44.19%) | 79.34 ± 4.32 | 11.35 ± 4.23 | 23.66 ± 3.51 | 25 (58.14%) | 18 (41.86%) |
| Study | 43 | 23 (53.48%) | 20 (46.51%) | 79.12 ± 4.61 | 11.23 ± 4.14 | 23.75 ± 3.62 | 24 (55.81%) | 19 (44.19%) |
| $\chi^2/t$ | | 0.047 | 0.228 | 0.133 | 0.117 | 0.047 | | |
| $P$ | | 0.829 | 0.820 | 0.894 | 0.907 | 0.828 | | |

### 2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Meet the diagnostic criteria [4] and confirmed by pathological examination; (2) Age is not less than 70 years old; (3) Unable to complete surgery and receiving radiotherapy and chemotherapy for the first time; (4) Estimated survival time is greater than 1 year; (5) Signed informed consent.

Exclusion criteria: (1) Those with esophageal bleeding, erosion, etc.; (2) Those with distant metastasis; (3) Those with severe mental illness and other serious organic diseases; (4) Those with incomplete information.

### 2.3. Methods

The control group received VMAT radiotherapy alone: Patients were placed in a supine position, with CT enhancement for positioning, a 5mm scanning layer thickness, and delineation based on examination results, including gross tumor volume, clinical target volume, planning target volume, and adjacent tissues and organs. A three-dimensional radiotherapy planning system was used to perform a counterclockwise 358° single-arc VMAT plan (179–181°) for VMAT-treated patients, with a maximum dose rate of 600 MU/min and a 4° sub-field interval. Treatment was administered 5 times per week, with a 21-day cycle, for 2 cycles.

The study group received raltitrexed on the basis of the control group's treatment: 3 mg/m$^2$ of the drug was

diluted in 100 mL of normal saline and administered intravenously to patients every 3 weeks, with 2 cycles of treatment during radiotherapy.

## 2.4. Observation indices

(1) The short-term outcomes of both groups were evaluated based on complete remission (CR), partial remission (PR), stable disease (SD), and progressive disease (PD) [5]. The objective response rate was determined by (CR + PR) divided by the total cases, while the disease control rate was calculated as (CR + PR + SD) divided by the total cases.

(2) Compare the tumor marker levels before and after treatment in the two groups. Fasting venous blood samples were collected to detect heat shock protein 90α (HSP90α), cytokeratin fragment 19 antigen 21-1 (Gyfra21-1), and carcinoembryonic antigen (CEA).

(3) Record adverse reactions during treatment in both groups.

(4) A 6-month follow-up study assessed the quality of life (QOL) in cancer patients across both groups, comparing baseline measurements taken before treatment with subsequent evaluations at 1, 3, and 6 months post-treatment to analyze changes over time.

## 2.5. Statistical methods

Data were analyzed using SPSS 24.0 software. Normally distributed measurement data with homogeneous variance were expressed as mean ± standard deviation (SD), and enumeration data were expressed as percentages (%). T-test and chi-square test ($\chi^2$) were performed accordingly. A $P$-value < 0.05 was considered statistically significant.

# 3. Results

## 3.1. Comparison of short-term efficacy between the two groups

The study group demonstrated a significantly greater objective remission rate and disease control rate than the control group ($P < 0.05$), as detailed in **Table 2**.

**Table 2.** Comparison of short-term efficacy between the two groups [*n*, (%)]

| Group | Cases | CR | PR | SD | PD | Objective response | Disease control |
|---|---|---|---|---|---|---|---|
| Control | 43 | 12 (27.91%) | 13 (30.23%) | 10 (23.26%) | 8 (18.60%) | 25 (58.14%) | 35 (81.40%) |
| Study | 43 | 20 (46.51%) | 20 (46.51%) | 2 (4.65%) | 1 (2.33%) | 40 (93.02%) | 42 (97.67%) |
| $\chi^2$ | | | | | | 14.176 | 6.081 |
| $P$ | | | | | | <0.001 | 0.014 |

## 3.2. Comparison of tumor marker levels before and after treatment in both groups

After treatment, the levels of HSP90α, Cyfra21-1, and CEA in the study group were significantly lower than those in the control group (P<0.05). See Table 3.

**Table 3.** Comparison of tumor marker levels before and after treatment in both groups (mean ± SD, ng/mL)

| Group | Cases | HSP90α (ng/mL) | | Cyfra21-1 (ng/mL) | | CEA (ng/mL) | |
|---|---|---|---|---|---|---|---|
| | | Before Treatment | After Treatment | Before Treatment | After Treatment | Before Treatment | After Treatment |
| Control | 43 | 110.87 ± 43.23 | 72.11 ± 26.43 | 6.67 ± 1.31 | 3.87 ± 1.03 | 6.49 ± 1.23 | 3.42 ± 1.01 |
| Study | 43 | 111.12 ± 45.24 | 54.61 ± 21.23 | 6.72 ± 1.18 | 2.37 ± 0.64 | 6.51 ± 1.16 | 2.48 ± 0.56 |
| *t* | | 0.026 | 3.385 | 0.186 | 8.111 | 0.078 | 5.337 |
| *P* | | 0.979 | 0.001 | 0.853 | <0.001 | 0.938 | <0.001 |

## 3.3. Comparison of adverse reactions between the two groups

No statistically significant variation was observed in the occurrence of adverse effects when comparing the two groups ($P > 0.05$), as detailed in **Table 4**.

**Table 4.** Comparison of adverse reactions between the two groups [*n*, (%)]

| Group | Cases | Radiation Esophagitis | Radiation Pneumonitis | Leukopenia | Thrombocytopenia | Gastrointestinal Reactions | Total Incidence |
|---|---|---|---|---|---|---|---|
| Control | 43 | 4 (9.30%) | 4 (9.30%) | 36 (83.72%) | 36 (83.72%) | 3 (6.98%) | 17 (39.53%) |
| Study | 43 | 4 (9.30%) | 36 (83.72%) | 4 (9.30%) | 4 (9.30%) | 4 (9.30%) | 19 (44.19%) |
| $\chi^2$ | | | | | | | 0.191 |
| *P* | | | | | | | 0.662 |

## 3.4. Comparison of QOL scores before and after treatment between the two groups

The quality of life (QOL) scores in the study group demonstrated a statistically significant improvement compared to the control group at both the 3-month and 6-month follow-up assessments ($P < 0.05$), as detailed in **Table 5**.

**Table 5.** Comparison of QOL scores before and after treatment between the two groups (mean ± SD, scores)

| Group | Cases | Baseline | 1 month post-treatment | 3 months post-treatment | 6 months post-treatment |
|---|---|---|---|---|---|
| Control | 43 | 75.64 ± 4.21 | 72.42 ± 3.43 | 77.35 ± 4.12 | 78.53 ± 3.32 |
| Study | 43 | 75.56 ± 4.31 | 71.43 ± 4.32 | 81.03 ± 3.24 | 86.33 ± 4.34 |
| *t*-value | | 0.087 | 1.177 | 4.604 | 9.360 |
| *p*-value | | 0.931 | 0.243 | < 0.001 | < 0.001 |

# 4. Discussion

Surgical treatment is a commonly used therapy for esophageal cancer. However, elderly patients may not tolerate surgery due to their physical condition and underlying diseases; thus, radiotherapy is often chosen as the treatment method [6]. As an advanced radiotherapy technique commonly used in clinical practice, Volumetric Modulated Arc Therapy (VMAT) can increase the local dose to the tumor without increasing the dose to critical organs. Its application can effectively shorten treatment time, and it has characteristics such as high

conformality and fewer jumps. It has demonstrated outstanding advantages in the treatment of tumors, including esophageal cancer [7]. Studies have shown that VMAT can shorten treatment time for esophageal cancer patients, protect critical organs, and reduce the occurrence of radiation pneumonitis [8]. Although VMAT can be effective in the treatment of esophageal cancer, monotherapy with radiotherapy often yields suboptimal results. Yan et al. [9] showed that concurrent radiotherapy and chemotherapy can lead to better long-term outcomes, improving local control rates and prolonging survival time for esophageal cancer patients.

As a specific inhibitor of thymidylate synthase (TS), raltitrexed has a higher binding affinity for TS and can competitively block TS activity, disrupting normal DNA replication in tumor cells and causing cell cycle arrest and apoptosis, thereby exerting an anti-tumor effect. Although its efficacy is similar to that of fluorouracil, its mechanism of action is different, and it has a lower incidence of adverse reactions [10]. Some scholars have pointed out that raltitrexed has lower cardiotoxicity compared to fluorouracil drugs, making it particularly advantageous for elderly cancer patients, especially those with cardiac insufficiency, as it can reduce the impact on cardiac function [11]. In this research, the study group demonstrated a greater objective response rate and disease control rate compared to the control group, along with significantly reduced tumor marker levels post-treatment. This indicates that concurrent VMAT radiotherapy and raltitrexed chemotherapy have good short-term efficacy in elderly esophageal cancer patients, improving disease control and reducing tumor marker levels. The two groups showed comparable rates of adverse effects, with no severe or life-threatening acute radiation toxicities observed, demonstrating that the combination of VMAT radiotherapy and raltitrexed chemotherapy has manageable toxicity and is well-tolerated by patients. The results also showed that the QOL scores of the study group were significantly higher than those of the control group at 3 and 6 months after treatment. Concurrent radiotherapy and chemotherapy can improve disease control, symptoms, prognosis, and quality of life for patients.

## 5. Conclusion

In summary, VMAT radiotherapy can shorten treatment time and improve tumor control effects, while raltitrexed chemotherapy has definite efficacy and lower adverse reactions. The synchronous treatment of both can improve the short-term efficacy of elderly patients with esophageal cancer, with good disease control effects, and can reduce patients' tumor marker levels, which is beneficial for improving patients' quality of life. Patients have good tolerance, indicating clinical value.

## Disclosure statement

The authors declare no conflict of interest.

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