Oncology Treatment Discovery, 2024, Volume 2, Issue 1
http://ojs.bbwpublisher.com/index.php/OTD

Comparative Efficacy of Whole-Brain Radiotherapy Combined with Supplemental Precision Radiotherapy and Whole-Brain Radiotherapy Alone for Brain Metastases

Weiwei Dong*, Yun Zhou, Xiangyang Jiang, Yan Zhou

Zhangjiagang AoYang Hospital, Suzhou 215600, Jiangsu Province, China

***Corresponding author:** Weiwei Dong, Dongweiwei2007@126.com

Abstract: *Objective:* To investigate the efficacy of whole-brain radiotherapy combined with supplemental precision radiotherapy compared to whole-brain radiotherapy alone for brain metastasis. *Methods:* Twenty-six cases of patients with brain metastasis were observed from January 2020 to June 2023. Thirteen cases each were randomly assigned to the observation group and the control group. The patients in the observation group received whole-brain radiotherapy combined with supplemental precision radiotherapy, while those in the control group received only whole-brain radiotherapy. *Results:* Comparing the quality of life scores between the two groups, the data from the observation group was significantly superior ($P < 0.05$). The survival rate of the observation group was higher than that of the control group, and their survival time was longer ($P < 0.05$). Additionally, compared with the control group, the observation group exhibited lower levels of various serum tumor factors after treatment ($P < 0.05$). *Conclusion:* Whole-brain radiotherapy combined with supplemental precision radiotherapy demonstrates improved clinical efficacy, prolonged survival time, and enhanced quality of life for patients with brain metastasis. These findings warrant further study and promotion.

Keywords: Brain metastasis; Whole-brain radiotherapy; Supplemental precision radiotherapy; Therapeutic efficacy

Online publication: March 29, 2024

1. Introduction

Brain metastasis occurs in approximately 30% of all cancers, with lung cancer being particularly prevalent, accounting for up to 80%. When brain metastasis develops in lung cancer patients, it not only diminishes their quality of life (QoL) but also shortens their survival time, thereby adversely affecting their prognosis. Currently, whole-brain radiotherapy (WBRT) is the primary treatment modality for brain metastasis in lung cancer patients. It aims to eradicate metastatic cancer cells using radiation, alleviate clinical symptoms, and enhance survival rates, thus becoming the preferred treatment option [1].

However, studies have indicated that WBRT often leads to adverse side effects and fails to achieve

satisfactory therapeutic outcomes. Supplemental precision radiotherapy, on the other hand, targets lesions with precision, thereby enhancing treatment accuracy and improving patients' quality of survival. By combining these modalities, a synergistic effect can be achieved, leading to improved patient outcomes [2,3]. This paper aims to investigate the efficacy of WBRT combined with supplemental precision radiotherapy.

2. Materials and methods

2.1. General information

The primary cases in this study were patients diagnosed with brain metastasis between January 2020 and June 2023), divided into 2 groups, each comprising 13 cases.

Inclusion criteria: (1) Diagnosis of brain metastasis confirmed by imaging with a measurable or evaluable intracranial lesion [4]; (2) Informed consent obtained from patients and their families; (3) No history of previous radiotherapy treatments.

Exclusion criteria: (1) Presence of cerebral infarction or other severe brain diseases; (2) Existence of drug contraindications; (3) Presence of comorbid mental health disorders.

In the observation group of 13 cases, there were 8 males and 5 females, with an average age of 68.25 ± 2.41 years, ranging from 52 to 84 years. The duration of illness ranged from 1 to 4 years, with an average of 2.51 ± 0.32 years. Pathological types included squamous carcinoma (5 cases), adenocarcinoma (5 cases), and adenosquamous carcinoma (3 cases). ECOG scores ranged from 0 to 2 points, with an average of 1.13 ± 0.03. In the control group of 13 cases, there were 9 males and 4 females, with an average age of 68.25 ± 2.41 years, ranging from 53 to 84 years. The duration of illness ranged from 2 to 4 years, with an average of 2.99 ± 0.41 years. Pathologic types included squamous carcinoma (4 cases), adenocarcinoma (8 cases), and adenosquamous carcinoma (1 case). ECOG scores ranged from 1 to 2 points, with an average of 1.58 ± 0.05 points. Comparison of the aforementioned indicators (age, gender, disease duration, pathologic type, and ECOG score) showed no significant differences ($P > 0.05$), allowing for valid comparisons.

2.2. Methods

Prior to radiotherapy implementation, both groups underwent magnetic resonance imaging (MRI) and computed tomography (CT) examinations to determine the initial lesion state. The control group received standard WBRT (irradiation of the patient's entire brain), delivering a dose of 30 Gy per day, five times a week. The observation group received supplemental precision radiotherapy in addition to standard WBRT. This involved targeting the lesion directly and interpolating distant tumors, utilizing gyro-rotating cobalt-60 stereotactic radiation technology. Approximately 80%–90% of the isodose curve covered the tumor edge, with a total dose ranging from 16 to 30 Gy, a single dose of 10 to 12 Gy, and an average target area dose of 17.1 Gy (ranging from 10 to 30 Gy).

2.3. Observation indexes

Various parameters were assessed for comparison between the two groups after treatment, including QoL scores, adverse reactions, survival time and rate, and serum tumor factors.

The SF-36 scale was employed to evaluate patient QoL, comprising four items, with scores indicating a positive correlation with patient QoL [5].

The ELISA method was utilized to analyze serum tumor factors in both groups, with pre-treatment and post-treatment serving as the observation points. Three milliliters of venous blood were collected from fasting patients in the early morning, placed in Eppendorf tubes, centrifuged at 2000 revolutions per minute for 5

minutes, and then stored at -80°C until examination.

2.4. Statistical analysis

Data analysis was conducted using SPSS 20.0, employing statistical methods appropriate for the dataset. All measurement data followed a normal distribution and were expressed as mean ± standard deviation (SD), with *t*-tests performed accordingly. Count data were expressed as *n* (%), with χ^2 tests applied. A significance level of $P < 0.05$ indicated statistical significance.

3. Results

3.1. Comparison of quality of life scores between the two groups

Table 1 shows that the observation group had higher QoL scores as compared to the control group ($P < 0.05$).

Table 1. Comparison of quality of life scores (mean ± SD, points)

Group	*n*	Environment	Physical health	Social relationships	Psychological health
Observation group	13	49.63 ± 2.11	58.96 ± 2.41	77.85 ± 3.45	13.85 ± 1.17
Control group	13	34.52 ± 2.01	44.25 ± 1.09	63.21 ± 2.08	5.22 ± 1.06
t	-	18.695	20.052	13.103	19.709
P	-	0.000	0.000	0.000	0.000

3.2. Comparison of adverse reactions between the two groups

There were no significant differences in adverse reactions for both groups ($P > 0.05$), as shown in **Table 2**.

Table 2. Comparison of the incidence of adverse reactions in the two groups

Group	*n*	Gastrointestinal reactions (*n*)	Bone marrow suppression (*n*)	Liver impairment (*n*)	Total [*n* (%)]
Observation group	13	1	0	0	1 (7.79)
Control group	13	1	0	1	2 (15.38)
χ^2	-				0.377
P	-				0.539

3.3. Comparison of survival time and rate

Table 3 shows that the survival rate of the observation group was significantly higher than that of the control group, and the survival time was significantly longer as compared to the control group ($P < 0.05$).

Table 3. Comparing the survival time and rate of the two groups

Group	*n*	Overall survival rate [*n* (%)]	PFS time (mean ± SD, months)
Observation group	13	12 (92.31)	26.58 ± 2.11
Control group	13	3 (23.08)	5.63 ± 1.02
t / χ^2	-	12.764	32.231
P	-	0.000	0.000

3.4. Comparison of serum tumor factor levels between the two groups

After treatment, the observation group had significantly lower levels of various serum tumor factors as compared to the control group ($P < 0.05$), as shown in **Table 4**.

Table 4. Comparison of serum tumor factor levels before and after treatment (mean ± SD)

Group	TNF-α (pg/mL)		NSE (ng/mL)		SCC Ag (ng/mL)		CEA (ng/mL)	
	Before	After	Before	After	Before	After	Before	After
Observation group (n = 13)	26.58 ± 2.01	17.25 ± 1.02*	25.85 ± 1.46	7.22 ± 1.01*	24.77 ± 1.63	11.02 ± 1.45*	97.85 ± 2.41	43.55 ± 2.32*
Control group (n = 13)	26.55 ± 2.02	21.66 ± 1.36*	25.86 ± 1.47	12.85 ± 1.79*	24.78 ± 1.65	18.52 ± 1.09*	97.86 ± 2.40	84.85 ± 5.49*
t	0.038	9.353	0.017	9.877	0.016	14.907	0.011	24.984
P	0.970	0.000	0.986	0.000	0.988	0.000	0.992	0.000

* $P < 0.05$ compared to pre-treatment.

4. Discussion

With the continuous advancement of medical research and the enhancement of medical capabilities, the cure rates for malignant tumors have significantly improved. Among these, brain metastasis from lung cancer, characterized by its challenging treatment and poor prognosis, saw a turning point in the mid-1970s with the gradual inclusion of radiotherapy in its treatment regimen, leading to a significant increase in patient survival rates [6]. The scope of intracranial tumor radiotherapy applications primarily includes incompletely resected tumors, tumors spreading within the central nervous system, and preventing tumor recurrence post-resection. However, these treatments are contraindicated for children under three years of age. In cases where children cannot tolerate radiotherapy, chemotherapy may be administered to manage the condition [7].

In this study, the observation group exhibited superior survival times and rates compared to the control group, along with higher QoL scores. This suggests that combined treatment prolongs patient survival, positively impacting therapeutic outcomes and enhancing patient QoL. Research indicates that WBRT can eliminate microscopic foci and residual cancer cells, thereby extending patient survival. However, traditional radiotherapy often necessitates high drug doses, leading to various irreversible neurotoxicities such as dementia and cerebral necrosis [8]. Modern selective WBRT, facilitated by MRI, offers an alternative. Supplemental precision radiotherapy, employing advanced techniques like three-dimensional treatment planning, multi-leaf grating, and CT simulation positioning, enhances treatment efficacy while safeguarding normal brain tissue. The synergistic effect of combining these modalities surpasses that of WBRT alone, improving patient prognosis [9].

Comparing tumor factor levels between the two groups post-treatment, the observation group exhibited lower serum tumor factor levels, suggesting that combined treatment enhances patient immune function, thereby preventing disease deterioration. Tumor necrosis factor-alpha (TNF-α), a pro-inflammatory factor, is implicated in immune and inflammatory responses, particularly in malignant tumors, where elevated levels promote cancer cell growth and metastasis. Neuron-specific enolase (NSE), abundant in human nerve cells, aids in disease recurrence prediction, while squamous cell carcinoma antigen (SCC Ag) and carcinoembryonic antigen (CEA) serve as specific markers for squamous cell carcinoma (SCC) and various tumors, respectively. Monitoring these indices enables timely assessment of patient condition changes and treatment efficacy. Brain metastasis typically spreads via the bloodstream, detectable through imaging examinations. However, due to subclinical lesions, WBRT remains the primary treatment modality [10]. Despite extending survival, high-dose

radiotherapy may induce radiation encephalopathy, with doses generally limited to 30–40 Gy. Consequently, clinical efficacy may be compromised, with some patients experiencing recurrence or inadequate tumor control. Precision radiotherapy, a newer modality, ensures accurate patient positioning and preserves QoL [11].

Although controversial, some scholars advocate for combining WBRT with supplemental precision radiotherapy to enhance patient prognosis and reduce toxicity. This study aligns with this perspective. However, uncertainties remain regarding the selection criteria for different chemotherapeutic regimens. Moreover, this study's small sample size and short duration introduce bias in treatment selection and outcomes assessment, limiting its generalizability. Therefore, future studies should expand sample sizes and extend study durations to validate the efficacy of WBRT combined with supplemental precision radiotherapy.

In conclusion, compared to WBRT alone, the combination of WBRT and supplemental precision radiotherapy yields significantly improved efficacy, increasing patient survival rates and enhancing QoL. This warrants further investigation and promotion.

Disclosure statement

The authors declare no conflict of interest.

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