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A comparison between cyberknife and neurosurgery in solitary brain metastases from non-small cell lung cancer

Li-Jun Tian, Hong-Qing Zhuang, Zhi-Yong Yuan*

Department of Radiation Oncology, Tianjin Medical University Cancer Hospital & Institute, Tianjin 300060 PR China

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ABSTRACT

Purpose: To evaluate the efficacy of cyberknife (CK) and neurosurgery (NS) in patients newly diagnosed as solitary brain metastasis (SBM) from non-small cell lung cancer (NSCLC).
Methods and materials: We retrospectively analyzed 76 patients between 1990 and 2012 from our institution, including 38 patients performing CK and the other half performing NS. The observation end point was overall survival time (OS), local control of treated metastasis (LC) and intracranial control (IC). Kaplan–Meier OS curves were compared with the log-rank test. Cox regression analysis was used to determine prognosticators for OS, LC and IC.
Results: The baseline characteristic between the two groups was not significantly different. The 1-year OS rates were 53.5% and 30.5% in the CK group and NS group, respectively, ($p = 0.121$). The 1-year LC rates were 50.8% and 31.3%, respectively, ($p = 0.078$). The 1-year IC rates were 50.8% and 27.7%, respectively, ($p = 0.066$). In multivariate analysis, improved OS was significantly associated with younger age ($p = 0.016$), better ECOG performance status ($p = 0.000$) and graded prognostic assessment (GPA, 3.5–4.0, $p = 0.006$). The LC was also associated with better ECOG performance status ($p = 0.000$). The IC was associated with both better ECOG performance status ($p = 0.000$) and GPA (3.5–4.0, $p = 0.005$).
Conclusions: There was no statistical difference between CK and NS for SBM from NSCLC in OS, LC and IC. However, CK is less invasive and may be more acceptable for patients. The result needs randomized trials to confirm and further study.

1. Introduction

Brain metastases usually occur in 20–40% of all cancer patients in the clinical oncology [1] and lead to approximately 25% of patients dying from neurologic causes [2]. In patients of diagnosing as non-small cell lung cancer (NSCLC), about a quarter of them would develop brain metastases in their life time [3] and roughly half of these are solitary brain metastasis (SBM) [4]. As the more successful treatment with NSCLC and earlier detection by more sensitive imaging, the incidence of SBM would be higher than before [5].

It is suggested that the prognosis of SBM would be better than multiple brain metastases and benefit from more aggressive therapies [6,7]. There are various treatment to be chosen, including cyberknife (CK) or neurosurgery (NS) with or without whole-brain radiotherapy (WBRT). However, the optional treatment for SBM of NSCLC still remains controversial.

Compared to the WBRT, both CK and NS appeared to be more effective in improving survival time, local control of treated metastasis (LC). However there was no class 1 evidence to support one method over the other. The purpose of this study is to determine whether CK or NS could provide longer OS, better LC and IC.

2. Methods and materials

2.1. Patient eligibility

We retrospectively collected all medical records of 76 patients who were newly diagnosed as SBM of NSCLC from 1990 to 2012 at our institution. The further inclusion criteria were the following: (1) all the brain lesions were evaluated with magnetic resonance imaging (MRI) at the initial examination; (2) patients performed CK or NS aimed at brain lesion without performing WBRT; (3) the surgical resection was complete which was confirmed by the surgeon's impression and postoperative MRI ($\leq$24 h); (4) patients did not perform CK or NS aimed for the brain metastasis before; (5) patients did not adopt chemical or targeted drugs that could pass the blood–brain barrier.

2.2. Treatment schedule

All patients in the CK group adopted linac-based cyberknife. Patients were requested to use a noninvasive mask and subsequently perform contrast dye-enhanced computed tomography

* Corresponding author. Tel.: +86 22 23341405; fax: +86 22 23344105.
E-mail address: yuanzhiyongradiotherapy@hotmail.com (Z.-Y. Yuan).

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Table 1
Patient baseline characteristics of the treatment groups.

	Number of patients			
	Entire cohort	SRS ($n=38$)	OP ($n=38$)	p value
Gender				
Male	47	24	23	0.813
Female	29	14	15	
Age (years)				
≤60	44	21	23	0.642
>60	32	17	15	
ECOG performance status				
0–1	41	20	21	0.818
2	35	18	17	
Side of brain				
Left	30	16	14	0.670
Right	40	20	20	
Midline	6	2	4	
Pathology of NSCLC				
Squamous	25	10	15	0.375
Adenocarcinoma	44	25	19	
Other	7	3	4	
Status of systemic disease				
Stable	24	16	8	0.064
Progression	12	7	5	
Synchronous	40	15	25	
Extracranial metastases				
Yes	31	16	15	0.815
No	45	22	23	
GPA				
3.5–4	18	7	11	0.550
3	20	11	9	
1.5–2.5	38	20	18	

Abbreviations: SRS, stereotactic radiosurgery; OP, surgical resection; ECOG, Eastern Cooperative Oncology Group; GPA, graded prognostic assessment; NSCLC, non-small cell lung cancer.

(CT) of 1.5 mm thickness. MRI was also requested to perform for all patients after or before 2–3 days. Then we define gross target volume (GTV) in the fusion image using image fusion software. PTV expanded 1–2 mm on the basis of GTV. We outlined vital structures, such as brain stem, optic chiasm and lens. The dose of CK was 15–20 Gy and prescribed to the 80% isodose.

The metastasis site was requested to be complete resection in the NS group. The evaluating criteria was by the impression of surgeon's impression in the operation and MRI (≤24 h). It was also no limited for the brain metastasis size.

2.3. Prognostic factor

The baseline characteristics of patients were compared in the two groups, including gender, age, ECOG performance status, brain metastasis site, pathology of NSCLC, status of systemic disease, extracranial metastases and GPA score. Systemic disease status was classified into 3 groups: stable (duration ≥ 3 months) [8], progression and synchronous (duration ≤ 15 days between brain metastasis and primary lung cancer of diagnosis).

The survival of brain metastases from NSCLC was confirmed to be associated with the graded prognostic assessment (GPA) [9,10]. The GPA uses four criteria (age, Karnofsky performance status [KPS], number of BMs, and whether extracranial metastases are present or absent) and scores each with a 0, 0.5, or 1.0 value. The patient with the best prognosis would have a GPA of 4.0.

2.4. Follow up and observation end point

Data were collected about baseline characteristics, treatment regimen, and treatment outcome. In the first time follow up, CT or MRI scans were scheduled at 4 weeks after the treatment, then every 3 months for one year, and at least every 6 months after that. The follow-up time was measured from the date of ending the brain treatment. The observation end point is OS, LC and IC. LC was defined as stable or decreased area of treated metastasis on follow up scans. If there was no recurrence in the local and remote brain, it was thought to be IC.

Table 2
Results of the univariate analysis regarding survival.

Variable	At 6 mo (%)	At 12 mo (%)	At 18 mo (%)	At 24 mo (%)	P
Gender					
Male	65.7	40.3	24.3	20.8	0.115
Female	82.8	45.4	35.7	30.6	
Age (year)					
≤60	86.4	51.9	40.4	37	0.001
>60	55.7	25.2	11.2	11.2	
ECOG performance status					
0–1	100	71.4	48.3	44.8	0.000
2	45.0	5.1	0	0	
Side of brain					
Left	70.0	52.1	29.8	22.3	0.328
Right	74.8	29.5	22.1	22.1	
Pathology of NSCLC					
Squamous	68.0	25.8	17.2	17.2	0.017
Adenocarcinoma	81.6	53.9	37.6	33.4	
Status of systemic disease					
Stable	75.0	56.7	45.8	45.8	0.016
Synchronous	77.3	34.0	20.0	17.0	
Extracranial metastases					
Yes	61.3	37.4	22.9	19.9	0.306
No	82.1	45.4	31.5	27.5	
Treatment regimen					
SRS	76.1	53.5	32.8	28.7	0.121
OP	73.7	30.5	24.0	20.0	
GPA					
3.5–4	91.0	59.3	46.1	46.1	0.005
3	90.2	57.7	32.5	24.3	
1.5–2.5	54.8	25.9	18.5	13.9	

Abbreviations as in Table 1.