



Comparison of the therapeutic effects of surgery combined with postoperative radiotherapy and standalone radiotherapy in treating spinal metastases of lung cancer

Chao Zhang, Guowen Wang*, Xiuxin Han, Zhiwu Ren, Jian Duo

Department of Bone and Soft Tissue Tumor, Tianjin Medical University Cancer Institute and Hospital, Key Laboratory of Cancer Prevention and Therapy, China

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ABSTRACT

Object: There are few studies comparing the therapeutic efficacy between surgery combined with postoperative radiotherapy and standalone radiotherapy in treating spinal metastases of lung cancer. The aim of this clinical study was to compare the clinical and functional efficacy, quality of life, and survival outcomes between surgery combined with postoperative radiotherapy and standalone radiotherapy in treating spinal metastases of lung cancer.

Methods: A retrospective analysis of clinical data from June 2008 to December 2013 was performed with 46 patients suffering spinal metastases of lung cancer. Among the studied patients, 25 patients received standalone radiotherapy (radiotherapy group), and the other 21 patients received surgery combined with postoperative radiotherapy (surgery group). Follow-up and survival time were analyzed. Pain levels of the patients were assessed by visual analogue scale (VAS) from pre-treatment to one month and three months after starting treatment. 3 months after surgery, Neurologic deficit of the patients was evaluated using Frankel Grade, and functional impairment were classified by Karnofsky Score. The quality of life (QOL) was assessed by EORTC QLQ-C30 questionnaire.

Results: The follow-up period of the patients ranged from 2 to 25 months with the average of 8.8 months. In radiotherapy group, the mean survival was 8.5 months with median survival time of 7.8 months. In surgery group, the mean survival was 10.6 months with median survival of 8.4 months. The difference in survival times between the two groups was not statistically significant ($P=0.24>0.05$). From pre-treatment to one month and three months after treatment initiation, the VAS in both groups showed statistical significant improvement (One month: $P<0.01$ Three months: $P=0.001$, $p<0.01$). In the surgery group, 85.7% of all patients had functionally useful Frankel Grade D or E after surgery, compared with 71.4% pre-operatively. The percentage was 72.0% in the radiotherapy group post-treatment, compared with 68.0% pre-treatment. The relief of Frankel Grade in surgical group was superior to that of the radiotherapy group ($p=0.025$, $p<0.01$). KPS score (80–100) percentages in surgery group and in radiotherapy group were increased by 19% and 13.3%, respectively. The improvement of KPS was more in the surgery group ($p=0.013$, $P<0.01$). In radiotherapy group, the EORTC QLQ-C30 score was 86.13 ± 12.11 before treatment and 68.39 ± 14.96 after treatment. In surgery group, the EORTC QLQ-C30 score was 84.09 ± 9.48 before treatment and 54.64 ± 15.17 after treatment. The improvement of patient QOL was more in the surgery group ($p=0.004$, $p<0.01$).

Conclusion: Compared with standalone radiotherapy, surgery combined with postoperative radiotherapy did not significantly prolong the survival time. However, surgery can improve pain, function and QOL of patients with spinal metastases of lung cancer.

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* Corresponding author at: Department of Bone and Soft Tissue Tumor, Tianjin Medical University Cancer Institute and Hospital, Key Laboratory of Cancer Prevention and Therapy, Huan–Hu–Xi Road, Ti–Yuan–Bei, He Xi District, Tianjin, 300060, China. Fax: +86 13820036047.

E-mail addresses: zhangchao198409@163.com (C. Zhang), wanguowendr@163.com (G. Wang).

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1. Introduction

Lung cancer (LC) is responsible for 1.3 million deaths annually worldwide [20]. Lung cancer commonly metastasizes to liver, lymph nodes, adrenals, bones, and brain. Approximately 65% of patients with lung cancer develop bone metastases. The spine is the

most common site of bone metastasis of LC. Spinal metastases could lead to one or combination of the following symptoms: severe pain, paralysis and urinary or fecal incontinence, which in turn, adversely affects ambulatory ability, function and quality of life (QOL) of the patients. The median survival time for patients with LC and bone metastases is typically less than 6 months [2].

In the 1980s, the treatment of spinal cord compression secondary to spinal metastasis was posterior laminectomy, regardless of the location of the metastatic tumor. Emerging Evidence demonstrated that not only that conventional radiotherapy alone had equal benefit compared with laminectomy followed by radiotherapy [21], but also that laminectomy was associated with high rates of perioperative mortality and postoperative complications [3]. Therefore radiotherapy became the best choice for treatment of spinal cord compression secondary to spinal metastasis.

However, over the last couple of decades, significant advances in technique and spinal instrumentation have led to improved patient outcomes. The surgical treatment paradigm has changed significantly, with development from laminectomy alone to anterior decompression with instrumented stabilization. In a meta-analysis by Klimo et al., after treatment, surgery patients were demonstrated with a 1.3-fold greater chance of being ambulatory than radiotherapy patients [8]. Recovery of ambulatory function and pain reduction were also better in surgery patients. In a multicenter randomized study, Patchell et al. [10] found that patients who underwent surgical therapy with postoperative radiotherapy for metastatic epidural spine compression had a significantly better outcome with regard to survival, mobility, incontinence, and reduced opioid analgesia than patients who were treated conservatively with radiotherapy alone.

Although, the survival time of patient with spinal metastasis has increased over the last 10 years, the overall outcome is still poor. Conceding that surgery in spinal metastases cannot be curative, the goal of surgery is to provide symptomatic pain relief, restore structural stability to the spine and to prevent or reverse neurological compromise without causing excessive morbidity. However, whether to undergo operative treatment still remains controversial [1,15,16,17,18], especially in spinal metastases of lung cancer. Surgery should be considered only if the anticipated improvement in pain, function and QOL outweighs the risks of surgery. In this study, we compare the clinical, functional, QOL and survival outcomes between surgery combined with postoperative radiotherapy and standalone radiotherapy for patients with spinal metastases of LC.

2. Material and methods

2.1. Patients

A retrospective analysis of clinical data from June 2008 to December 2013 was performed with 46 patients suffering spinal metastases of lung cancer. There are 26 males and 20 female patients with average age of 54.17 years old (ranging from 40–65 years old). 25 patients received standalone radiotherapy (radiotherapy group), 21 patients received surgery with postoperative radiotherapy (surgery group). In radiotherapy group, there were 22 patients with Tomita Score of 6–7, and three patients with Tomita Score of 8. In the surgery group, all the patients demonstrated Tomita Score 6–7. In radiotherapy group Tomita classification [10]:

Tomita Type 2 (4), Tomita Type 3 (3), Tomita Type 4 (2), Tomita Type 5 (3), Tomita Type 6 (6), Tomita Type 7 (7). In surgery group: Tomita Score 6–7. Tomita classification: Tomita Type 1 (3), Tomita Type 2 (3), Tomita Type 3 (3), Tomita Type 4 (4), Tomita Type 5 (1), Tomita Type 6 (2), Tomita Type 7 (5) (Table 1).

Before treatment, the data including pain, neurologic deficit, functional impairment and QOL of patients were assessed. Pain levels were assessed by visual analogue scale (VAS). Neurologic deficit was evaluated by Frankel Grade (A, complete paralysis; B, sensory function only; C, incomplete motor function; D, fair/good motor function; E, normal function). The functional impairment was classified by Karnofsky Score. The QOL of patients was assessed by EORTC QLQ-C30 questionnaire. Furthermore, metastasized vertebrae segment of patients was also analyzed. (Fig. 1).

2.2. Procedures

The study was a non-randomized, uni-institutional clinical trial with two treatment groups. Patients must have met the following inclusion criteria: 1. Life expectancy > 3 months; 2. Histological type must be adenocarcinoma. 3. Axial and radicular pain. All patients had MRI of the entire spinal cord and X-rays of the spine before treatment. Gene expression profiling (using DNA microarrays) identified subtypes of lung adenocarcinomas. Mutation analysis was used to determine the EGFR status in tumor cells.

25 patients received standalone radiotherapy. The total dose was 30–45 Gy given in 10–15 fractions. Treatments were delivered to a port that encompassed one vertebral body above and below the visible lesion. 7 patients received additional chemotherapy (paclitaxel and carboplatin) and 4 patients who had EGFR mutation received targeted therapy (Erlotinib) as well.

21 patients underwent surgery combined with postoperative radiotherapy. The tumors of 7 patients was removed with wide excisional margins through a variety of approaches: anterior, posterior, or combinational, and then had instrumental spinal fixation of the vertebral column. 14 patients underwent palliative surgery with minimal level of resection, among which 11 patients received 2-step surgery consisted of posterior laminectomy and radiofrequency ablation (RFA) combined vertebroplasty (VP), followed by instrumented fixation, with the jump lesions of 5 patients treated by RFA combined PVP for Tomita Type 7, and 3 patients received simple posterior decompression and instrumented fixation. Among the 21 patients in the surgical group, 9 received chemotherapy (paclitaxel and carboplatin) and 6 patients received targeted therapy (Erlotinib).

Follow-up and survival time of the patients was analyzed. Pain levels were assessed using visual analogue scale (VAS) from pre-treatment to one month and three months after treatment. Neurologic deficit was evaluated by Frankel Grade and functional impairment was classified by Karnofsky Score. The QOL was assessed by EORTC QLQ-C30 questionnaire.

2.3. Statistical analysis

Statistical analysis was conducted using a commercially available statistical software package (SPSS version 16.0). $P < 0.05$ was considered statistically significant. Survival rate was analyzed with Kaplan–Meier method. In-group comparison of the VAS was carried out using analysis of variance. Between-group comparison

Table 1
Tomita type of patients.

Tomita Type (NO.)	Type 1	Type 2	Type 3	Type 4	Type 5	Type 6	Type 7
Radiotherapy group (25)	0	4	3	2	3	6	7
Surgery group (21)	3	3	3	4	1	2	5

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