CLINICAL ARTICLE

The effects of combined microwave ablation and open surgery for the treatment of lung cancer-derived thoracolumbar metastases

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Objective: To investigate the clinical effects of microwave ablation (MWA) in addition to open surgery for the treatment of lung cancer-derived thoracolumbar metastases.

Methods: This was a single-institution, retrospective, cohort study. From January 2019 to December 2020, a total of 47 patients with lung cancer-derived thoracolumbar metastases underwent posterior spinal canal decompression and fixation surgery in our hospital. Two independent surgical teams treated these patients. One group underwent open surgery combined with MWA therapy, while the other had open surgery only (control). The pre- and post-operative visual analog scale (VAS) scores and the overall survival (OS) were compared between the MWA and control groups. The Frankel Grade classification was applied for the evaluation of the post-surgical spinal cord function. Improvement was defined as an increase of at least one rank from the pre-operative scores. Each patient was evaluated pre- and post-operatively at 48 h, 1 month, and 3-month intervals. Data on surgical-related complications were recorded.

Results: Thirty men and 17 women were included, with an average age of 57.9 ± 11.4 years (range, 26–81 years). Twenty-eight patients underwent MWA and were in the MWA group, and 19 patients were included in the control group. Post-operatively all patients were followed up regularly; the median follow-up time was 12 months (range, 3–24 months), and their median OS was 14 months. Patients in the MWA group had a lower VAS score than those in the control group at the 48-h (1.75 ± 1.01 *vs* 2.47 ± 0.96, $P = 0.01$) and 1-month (1.79 ± 0.92 *vs* 2.53 ± 1.35, $P = 0.048$) check-ups. At the 3-month evaluation, the VAS score differences between the two groups were not significant ($P = 0.133$). After surgery, spinal cord function improvement was not significantly different between the MWA and control groups ($P = 0.515$). MWA therapy combined with open surgery was not associated with increased OS compared with the control group ($P = 0.492$).

Conclusion: MWA can be an effective and safe pain-relief method but may not extend the OS of patients with lung cancer.

Key words: Lung cancer; Microwave ablation; Open decompression; Pain relief; Spine metastases

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Introduction

The occurrence rate of bone metastases in lung cancer is 10%–30%.[1,2] Spinal metastases are the most common site of bone metastases, leading to severe skeletal-related events, such as refractory pain, pathological fractures, and spinal cord compression.[3] The life expectancy and quality of life of these patients are severely affected by the skeletal-related events in the terminal stages of lung cancer.[4] Approximately 40% of the patients with cancer experience pain due to spinal metastases.[5] Therefore, timely and effective treatment is imperative for patients with severe skeletal-related events. Conventional management strategies include radiation therapy, chemotherapy, and surgical intervention. Radiation therapy can partially relieve the symptoms of spinal metastases, but there is a 5.7% incidence of local failure after radiotherapy.[6] Moreover, some patients with metastatic spinal cord compression may be unable to tolerate high doses of radiation. Therefore, surgical intervention is often required to restore the spine's stability, save the spinal cord function, and control severe pain. The traditional open decompression surgical options include total unblock spondylectomy, vertebrectomy, sagittal resection, piecemeal excision, and eggshell curettage. However, they are associated with a high incidence (approximately 25%) of complications.[7] Complications mainly include extensive blood loss and post-operative infection, resulting in a high mortality rate and prolonged hospital stay.[8,9] Moreover, many patients cannot tolerate a large open decompression (surgical intervention) due to neoplasm-associated comorbidities, such as malnourishment and impaired immune system.

Thermal ablation therapies have become increasingly popular for treating bone tumors. Microwave ablation (MWA) is a novel technique that has several advantages over the existing ablation systems. Compared to the radiofrequency ablation, the MWA can offer larger ablation zones, shorter procedural times, and more effective heating through high impedance tissues, such as the bone, thus, achieving favorable results as quick recovery, effective pain relief, and local tumorcontrol.[5] Both benign and malignant bone tumors treated with MWA showed satisfactory clinical results. A prospective pilot study of computerized tomography (CT)-guided MWA in treating13 patients with osteoid osteomas showed a 92.3% success rate in the complete patient's pain relief 1 month after surgery.[10] Aubry *et al.*[11] reported16 bone and soft-tissue malignant tumors treated by CT-guided MWA. They achieved a high percentage of tumor necrosis, and 36.3% of the lesions had no recurrence at the 12-month follow-up.

Microwave ablation has recently become available for spinal metastases treatment.[12] As it pertains to patients with cancer in advanced stages, the MWA technology is always attractive as an alternative or adjunct option for spinal metastases treatment. A systematic review[13] demonstrated that the percutaneous MWA could achieve an estimated pain reduction on the numerical rating scale of 5.3/10 at one month. There are limited studies on open decompression surgery combined with MWA. Liu *et al.*[14] found a low recurrence rate (16.6%) in 12 cases of breast cancer-derived thoracic metastases treated with a combination of MWA and invasive spine surgery during a 10-month follow-up period. MWA with open decompression therapy in 23 patients with breast cancer-derived thoracic metastases showed that 78.3% of them improved their score.[15] However, these two findings were from retrospective studies without a control group and a limited sample size. Zhang *et al.*[16] showed that applying MWA in 69 patients with pathological spinal fractures had more advantages in alleviating pain and improving the quality of life when combined with decompression and pedicle screw fixation than not performing MWA. MWA combined with decompression surgery for patients with cancer-derived spinal metastatic tumors is an effective treatment improving clinical outcomes, especially pain relief. However, it is unclear whether using MWA treatment for spinal metastases can improve the survival time and quality of life in the terminal stages of the illness. In addition, there is no reported research on patients with lung cancer-derived spinal metastases with poor survival because of the rapidly growing primary cancer.[17]

This study aimed to investigate: (i) whether MWA in addition to open depression and fixation surgery is a safe treatment method for patients with lung cancer-derived thoracolumbar metastases; (ii) whether MWA in addition to surgery can improve pain-relief scores and neurology in those patients; and (iii) whether patients with lung cancer-derived thoracolumbar metastases, who undergo MWA in addition to surgery, have improved overall survival (OS) after surgery.

Patients and Methods

Patient Selection

The inclusion criteria were as follows: patients with: (i) diagnosis of lung cancer pathologically confirmed (both the primary lesion and the thoracolumbar metastatic lesion); (ii) spinal cord compression and neurological function deficits, spinal instability according to the Spinal Instability Neoplastic Score,[18] or refractory pain; (iii) symptoms that were not effectively alleviated by radiation therapy or chemotherapy; and (iv) physical condition good enough to tolerate surgery. The exclusion criteria were as follows: (i) patients with radiation myelopathy; and (ii) who underwent percutaneous vertebroplasty or percutaneous biopsy.

We included in the study all patients with lung cancer-derived thoracolumbar metastases attended by the orthopedic doctors in Guangdong Provincial People's Hospital between January 2019 and December 2020. They were referred either by a medical oncologist or from an outpatient clinic. Two independent orthopedic teams received the patients. One team (chief surgeon Z.Y.) performed open surgery combined with MWA(MWA group), while the other team (chief surgeon C.Y.B.) performed open surgery conventionally without MWA (control group). In addition, computed tomography and magnetic resonance imaging of the spine were performed to confirm the diagnosis of spinal metastases in patients with a history of lung cancer. The site of the lesion and the degree of neurologic compression were also determined during this exploration.

This was a single-institution, retrospective, cohort study. The institutional review board of the Guangdong Provincial People's Hospital approved our research (No. GDREC2019560H(R1)), and it was considered to meet the ethical requirements. Written informed consent was obtained from all the patients.

Surgical Procedure and Microwave Ablation Technique

The posterior approach was considered for this surgery. Under general anesthesia, poster anterior fluoroscopic control was used to identify the pedicles of the target vertebrae, and the skin was marked. The first step involved instrument fixation. The Wilts approach was used to expose the entry site of the pedicle screws. Next, the insertion angle of the pedicles was adjusted using C-arm fluoroscopy. The adjacent one-level or two-level vertebrae above and below the tumor were fixed with cannulated pedicle screws. The second step of the surgical procedure was neurological decompression and partial tumor resection in the cases of spinal cord compression. Generally, a short midline incision was made to expose the spinal process and lamina of the target vertebra. The spinal process, lamina, facets, and pedicle were resected completely or partially according to the need for surgical exposure of the lesion. The compressed spinal cord and tumor were carefully separated to achieve complete decompression. The neural structures were decompressed by creating a safety zone of a few millimeters around the spinal cord and nerve roots.

After partial tumor resection, one team (chief surgeon Z.Y.) used a MWA antenna (2450 Hz, Changchun, and MTI-5DT, Nanjing, China) to perform ablation of the vertebral bone. The antenna was precisely placed into the metastatic lesion inside the vertebral body and through the pedicle under the guidance of C-arm fluoroscopy. Depending on the case, 30–60W power was used for 1.5–5 min a thermometer was used to monitor the temperature during the MWA. Thermometers were placed at the vertebra's anterior, center, and posterior margins to protect the spinal cord and peripheral blood vessels. The center of the lesion was maintained at 70–85 °C for 2–10 min to ensure effective destruction of the tumor; the temperature of the surrounding tissues was maintained at <43 °C by a repeated frozen saline flush. The intraoperative ablation and monitoring are illustrated in Figure 1. In the control group where no MWA was used (chief surgeon C.Y.B.) if the lesion was determined to be osteolytic, polymethyl methacrylate (PMMA) bone cement was injected into the vertebral metastasis to reinforce the stability of the vertebra. The bone cement injection was performed under X-ray fluoroscopy to prevent PMMA leakage. In addition, patients were required to wear a body brace for 1 month post-operatively during out-of-bed activities. Images of the surgical procedures and important imaging findings are shown in Figures 2–4.

Evaluation

During a routine follow-up, the patient's clinical information, visual analog scale (VAS) score for pain assessment, Frankel Grade classification for spinal cord function assessment, and the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale score were recorded. Demographic information was obtained from the electronic medical

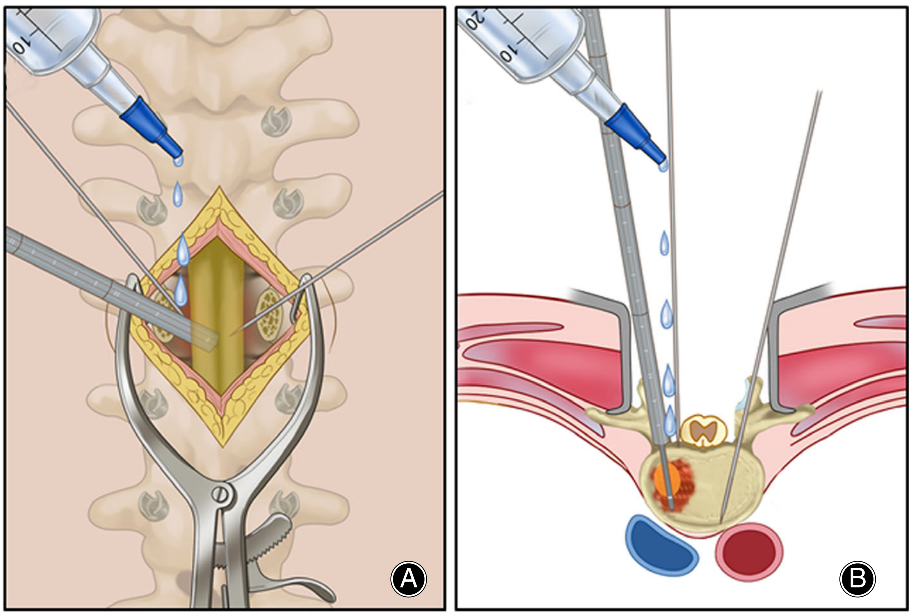

Fig. 1 Schematic diagrams of the intraoperative ablation and monitoring in the rear view (a) and top view (b).The microwave needle was placed into the metastatic lesion in the vertebral body. Two thermometers were used to monitor the temperature. Thermometers were placed at the vertebral anterior, and vertebral posterior margins. A repeated frozen saline flush was used to maintain the temperature of the surrounding tissues at 43 degrees or below. The thick white line of the ablation probe tip represents the source of microwave needle emission. The orange region represents the heating range of the microwave

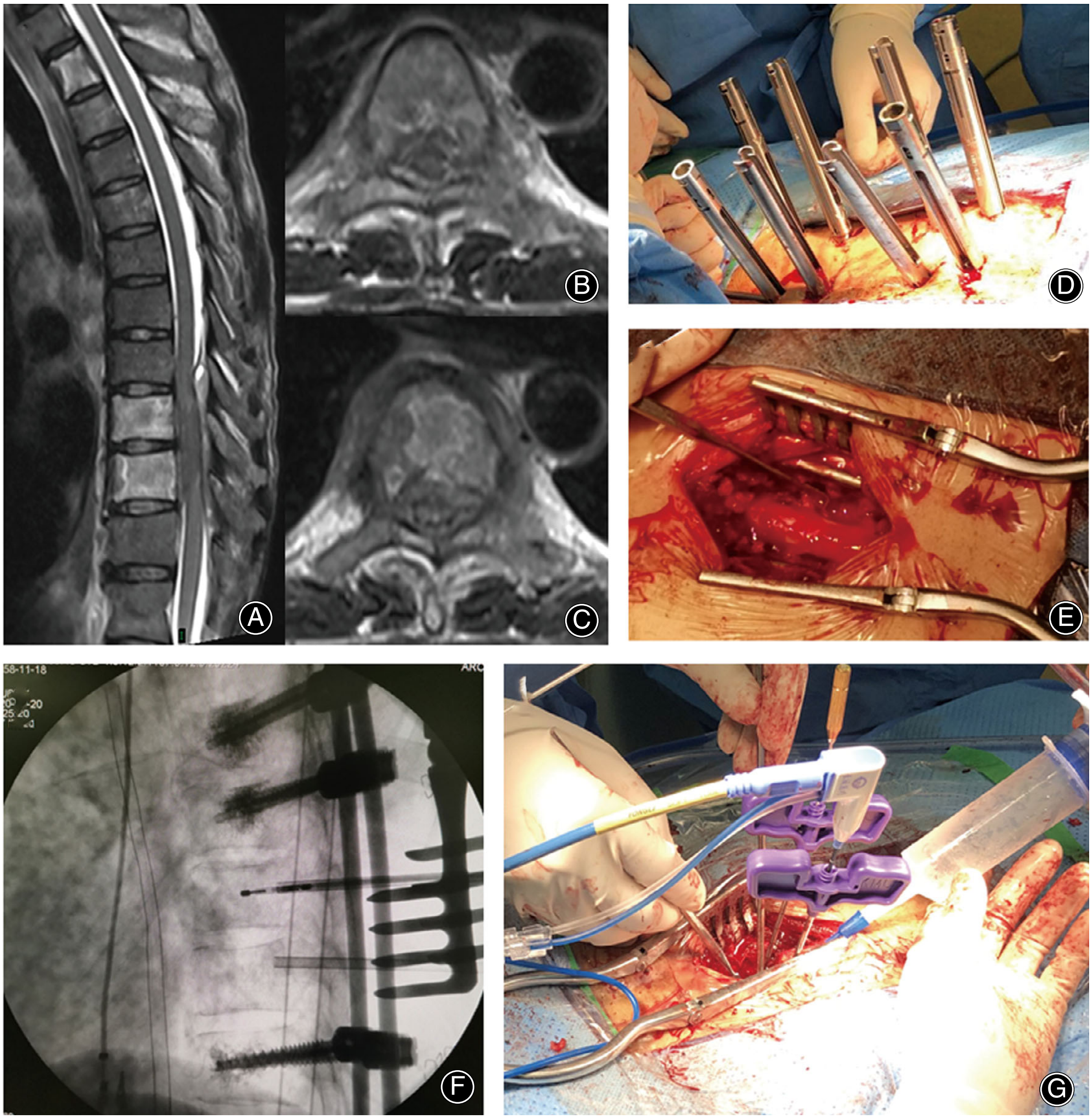

Fig. 2 Preoperative sagittal (a) and axial (b, c) magnetic resonance (MR) images show metastasis of T_9, T_{10} from lung cancer with neurologic compression in a 59-year-old man. Placement of pedicle screws into the vertebrae using a minimally invasive technique (d). After pedicle screw fixation, the spinal process and lamina were removed to expose the Dural sac involved using the midline approach for neurologic decompression (e). The precise position of microwave needles was monitored by intraoperative fluoroscopy (f). Microwave ablation needle and thermometer were inserted into the vertebral metastases through the pedicle (g)

records. The OS was defined as the interval between the date of the initial surgery in the orthopedic department and the date of death or the last date of follow-up. Each patient was evaluated in the outpatient clinic 1 month after the operation and then at 3-month intervals until death.

Visual Analog Scale

The pain was evaluated using the VAS, ranging from 0 (no pain) to 10 (worst possible pain). The VAS score was recorded in continuous data pre- and post-operatively at 48 h, 1 month, and 3 months. A higher score indicated a greater pain intensity.

Functional Outcome

After the operation, spinal cord function improvement evaluation was defined as a Frankel Grade classification increase of at least one rank from the pre-operative levels. Otherwise, it was considered as worse or unchanged. Frankel Grade classification scores were recorded pre- and post-operatively at 48 h, 1 month, and 3 months.

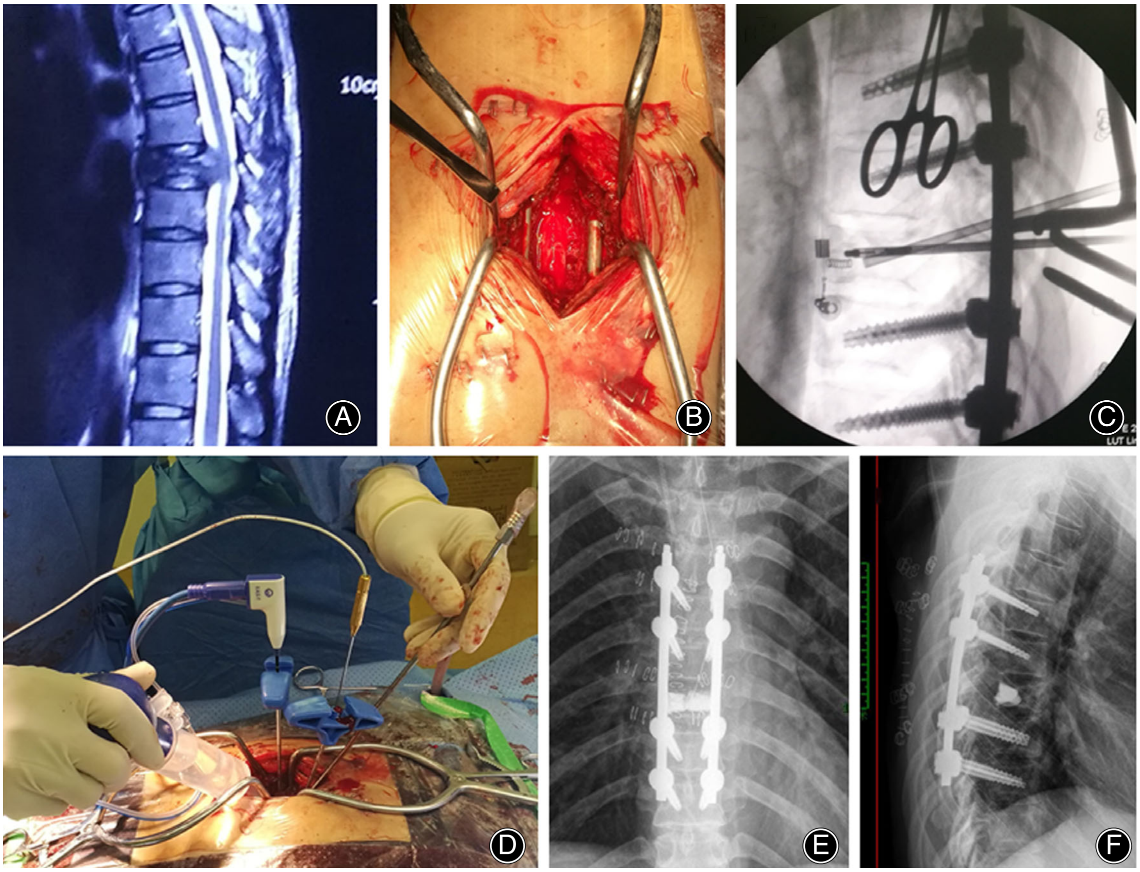

Fig. 3 Preoperative sagittal magnetic resonance images (a) show metastasis of T8 from lung cancer with neurologic compression in a 46-year-old man. After pedicle screw fixation, the spinal process and lamina were removed to expose the Dural sac involved (b). The precise position of microwave needle was monitored by intraoperative fluoroscopy (c). Microwave ablation needle and thermometer were inserted into the vertebral metastases through the pedicle (d). Postoperative frontal (e) and lateral (f) X-rays were taken

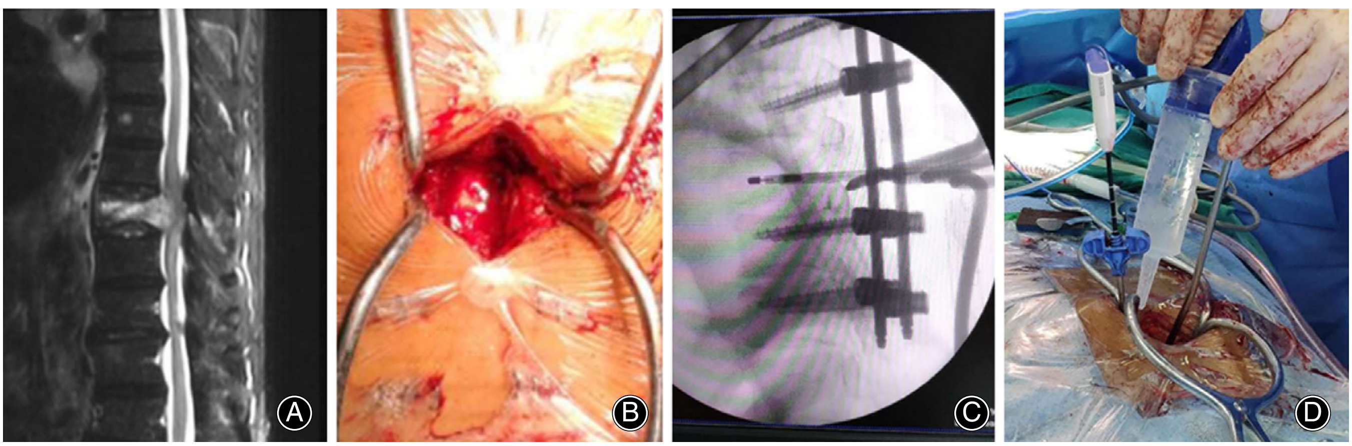

Fig. 4 Preoperative sagittal magnetic resonance images (a) show metastasis of T9 from lung cancer with neurologic compression in a 68-year-old man. The spinal process and lamina were removed to expose the dural sac after fixation (b). The position of microwave needle was monitored by fluoroscopy (c). Microwave ablation needle and thermometer were inserted into the vertebral metastases through the pedicle (d)

Statistical Analysis

SPSS Statistics for Windows, version 22.0 (IBM Corp, Armonk, NY, USA),was used for the statistical analyses. Continuous variables are shown as mean ± standard deviation. The Mann–Whitney U test compared variables when a normal distribution could not be guaranteed. Categorical variables were compared using the chi-squared test. The post-operative OS rate was estimated using the Kaplan–Meier method, and differences were analyzed using the log-rank test. The statistical significance value was set at P <0.05.

Results

Patient Demographics

There were 47 patients with lung cancer-derived thoracolumbar metastases who met the inclusion criteria (30 men and 17 women). Twenty-eight patients underwent MWA therapy. Their average age was 57.9 ± 11.4 years. The patients' characteristics are shown in Table 1. There were no significant differences in sex, age, ECOG score, and Frankel Grade classification between the two groups before the operation. All patients were treated following the oncological department protocols of standardized medical treatment. Thirty-six patients underwent targeted therapy.

Operative Data and Functional Outcomes

Surgical operations were successfully performed in all patients without any serious complications like iatrogenic spinal nerve injuries or vascular injury during operation. The range of patients' blood loss during the operation was 100–1700 ml, with an average of 814.2 ± 852.3 ml. The mean total operating time was 5.52 ± 1.73 h. No difference was found in the operation duration and the blood loss during the operation between the two groups (Table 1). Nine (19.1%) patients did not achieve spinal cord function improvement according to the Frankel Grade classification at the 1-month follow-up visit. Spinal cord function improvement after surgery was not significantly different between the MWA and control groups ($P = 0.515$).

Complications

One patient of the MWA group had cerebrospinal fluid leaks after the operation. He received conservative treatment after drainage tube removal and recovered promptly. No nerve function complications caused by MWA were identified. There was no wound infection or fixation failure observed in any patient. Therefore, no further surgical intervention was necessary.

Pain Management

The mean pre-operative VAS score was 6.77 ± 1.65, and the difference between the MWA and control groups was not significant (6.79 ± 1.8 *vs* 6.74 ± 1.4, $z = -0.35$, $P = 0.72$) (Figure 5). Post-operatively, the mean VAS score of the two groups decreased significantly at the 48-h, 1-month, and 3-month reviews compared to the pre-operative values. Patients in the MWA group had a lower VAS score than those in the control group at the 48-h (1.75 ± 1.01 *vs* 2.47 ± 0.96, $z = -2.59$, $P = 0.01$) and 1-month (1.79 ± 0.92 *vs* 2.53 ± 1.35, $z = -1.98$, $P = 0.048$) evaluations. At the 3-month check-up, the two groups' differences were no longer significant ($P = 0.133$).

Survival Analysis

All patients received regular follow-up visits, and the median follow-up time was 12 months (range, 3–24 months) post-operatively. The Kaplan–Meier curves for post-operative survival of the patients with lung cancer between the MWA and the control group are shown in Figure 6.The median OS was 14 months (range, 1–24 months) post-operatively. Hence,

TABLE 1 Characteristics of 47 patients with thoracolumbar metastases of lung cancer between the MWA group and no MWA group

Characteristics	Microwave ablation group	No ablation group	Statistic	*P* value
Sex (cases)			$\chi^2 = 1.341$	0.247
Male	16	14		
Female	12	5		
Age (years, mean ± SD)	59.1 ± 11.3	56.3 ± 11.9	$t = 0.814$	0.42
ECOG score			$\chi^2 = 0.037$	0.847
0,1	11	8		
2,3,4	17	11		
Operation duration (h, mean ± SD)	5.8 ± 1.4	5.1 ± 1.9	$t = 1.528$	0.134
Blood loss(ml, mean ± SD)	806.8 ± 778.5	829.5 ± 863.3	$t = -0.094$	0.926
Frankel Grade classification(cases)			$\chi^2 = 0.01$	>0.99
A, B	6	4		
C, D	22	15		
Evaluation of spinal cord injury improvement(cases)			$\chi^2 = 0.424$	0.515
yes	24	14		
no	4	5		

Abbreviations: ECOG score, Eastern Cooperative Oncology Group (ECOG) Performance Status score, SD, standard deviation.

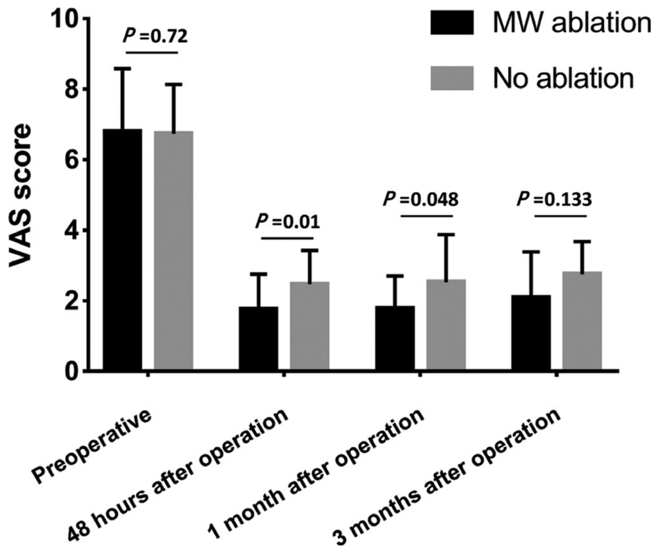

Fig. 5 The mean visual analog scale (VAS) score preoperatively and postoperatively at 48 h, one month, and three months

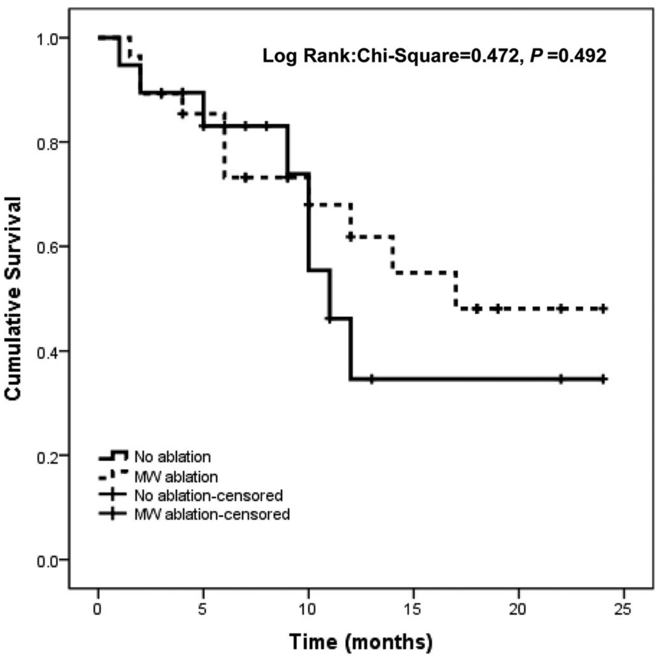

Fig. 6 Kaplan–Meier curves for postoperative survival of the lung cancer patients between the MWA group and no MWA group

the MWA therapy was not associated with extended OS ($P = 0.492$).

Discussion

This study aimed to investigate and compare the clinical effects of open surgery combined with MWA and just open surgery (without MWA) in treating lung cancer-derived spinal metastases. We determined that the MWA combined with the open surgery method was more effective in achieving short-term pain relief than the only surgery group. However, the MWA therapy did not improve the OS.

With the rapid growth of the targeted therapy for lung cancer, spinal metastases (the most common bone metastases) have received increasing attention. The main goal of the surgical treatment is to relieve refractory pain, alleviate symptoms of nerve compression, and rebuild the stability of the vertebral body. Several advanced surgical techniques have reported satisfactory clinical results.[19] Open decompression surgery is an effective method of relieving neurological symptoms and restoring spinal instability. All open decompression surgeries for cancer with spinal metastases are palliative, except for the total en bloc spondylectomy.[20] Many ablation adjuvant therapies, such as radiofrequency ablation, MWA ablation, and cryoablation, have been used in open decompression surgery to relieve pain or improve tumor control.[5,21,22]

Pain Relief after Ablation

Microwaves are more effective than radiofrequency ablation because of the poor heat conduction of bone in the latter.[23] In addition, MWA has the advantages of larger ablation zones and shorter operational times.[24,25] So, the precision of ablation temperature and region is of great importance.[26] Thermometers, which can be placed at the vertebra's anterior and posterior margins, are used to monitor the temperature during the MWA.[27] The temperature of the lesion center can reach 70–85°C to destroy the tumor, while the temperature of the surrounding tissues can be maintained at <43°C by a repeated frozen saline flush.

An increasing number of studies have focused on the application of MWA to treat spinal metastases.[5] Percutaneous MWA for metastases has been reported to be effective in achieving analgesia in the short term.[12,27,28] Khan *et al.*[27] reported a dramatic reduction of the pain score after percutaneous MWA and cementoplasty in 84 thoracolumbar sites of painful spinal metastases and myeloma. Liu *et al.*[14,15] demonstrated that MWA combined with open decompression surgery for patients with breast cancer-derived thoracic metastatic tumors is an effective treatment that maintains or improves functional outcomes better than open surgery. However, Kastler *et al.*[28] did not use cement augmentation combined with MWA and reported moderate pain improvement. Therefore, Sagoo *et al.*[5] suggested that the significant improvement of pain in patients with spinal metastases may be due to a synergistic mechanism of the combined therapy. Few previous studies have included a control group. Furthermore, the primary tumor types of spinal metastases vary, and they may have a heterogeneous response to the treatment. Our findings determined that compared to the control group, MWA combined with open surgery in patients with lung cancer achieved excellent pain relief at the 1-month follow-up visit. The mean VAS score improved from 6.79 before the operation to 1.79 at the 1-month follow-up visit in the MWA group. For the control group, the pre-operative and 1-month post-operative VAS scores were 6.74 and 2.47, respectively. However, at the 3-month follow-up visit, the pain levels of the two groups showed no difference. Therefore, the analgesic effect of MWA therapy may last shortly after open surgery for spinal metastases, which supports a previous study's findings.[13] Both nociceptive and neuropathic components cause refractory pain in patients with bone metastasis. The nociceptive component is the release of algogenic substances. The neuropathic component is driven by tumor cell growth, which destroys the nerve fibers and induces pathological sensory and sympathetic nerve fibers.[22] Microwave ablation may destruct the nerve fibers of a local lesion and reduce the number of inflammatory factors by destroying the tumor cells.[15]

Overall Survival after Operation

Patients with lung cancer-derived spinal metastases have a poor OS because of the rapid growth of primary lung cancer.[17] This study demonstrated that the median post-operative OS was 14 months, similar to Xu's report on a massive spondylectomy for metastatic spinal cord compression from non-small cell lung cancer.[29] Zhang *et al.*[30] found that the median OS was 11 months after radiofrequency ablation combined with posterior decompression surgery. In this study, our findings showed that the MWA therapy was not associated with an increased OS post-operatively. Therefore, we believe that combining MWA with open surgery may not prolong OS in patients with lung cancer.

Local Tumor Control

Previous studies showed that combined MWA therapy could achieve reasonable local tumor control.[26,27,31] In a study of massive spondylectomy for metastatic spinal cord compression from non-small cell lung cancer,[29] there was no reported post-operative local recurrence during the follow-up period. Our analysis also confirmed there was no readmission to the orthopedic department because of local tumor recurrence. Surgery for spinal metastases is a palliative therapy. Therefore, combining this with MWA may improve local tumor control.

Limitations

This study had some limitations. First, the chief surgeons of the MWA and control groups were not the same, which may have contributed to some bias, although the baseline characteristics were not significantly different. Second, local tumor control was not supported by radiological examination but was reflected by readmission to the orthopedic department because patients with lung cancer-derived spinal metastases have a poor OS. Finally, this was a retrospective analysis from one institution with a median 12-month follow-up. A randomized controlled trial with a more extended follow-up period is warranted. Future studies should involve multicenter collaborations to define further the indications, outcomes, and cancer-free survival and recurrence rates associated with this procedure.

Conclusions

The MWA therapy combined with open surgery for lung cancer-derived thoracolumbar metastases can provide excellent short-term pain relief. However, at the 3-month follow-up visits, there was no significant difference in the reported pain scores between patients treated with and without MWA. Thus, MWA can be an alternative and effective adjuvant therapy for pain relief, but it may not prolong the OS of patients with lung cancer.

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