Skeletal Radiol
DOI 10.1007/s00256-015-2195-4

SCIENTIFIC ARTICLE

Computed tomography-guided percutaneous microwave ablation combined with osteoplasty for palliative treatment of painful extraspinal bone metastases from lung cancer

Zhigang Wei[1] · Kaixian Zhang[2] · Xin Ye[1] · Xia Yang[1] · Aimin Zheng[1] · Guanghui Huang[1] · Jiao Wang[1]

Received: 13 March 2015 / Revised: 31 May 2015 / Accepted: 9 June 2015

Abstract
Objective To retrospectively evaluate the efficacy and safety of microwave ablation (MWA) combined with osteoplasty in lung cancer patients with painful extraspinal bone metastases.
Materials and methods From January 2011 to July 2014, 26 lung cancer patients with 33 painful extraspinal bone metastases underwent percutaneous MWA combined with osteoplasty. Effectiveness was evaluated by visual analog scale (VAS) and daily morphine dose with a follow-up of 6-months. Complications were also recorded.
Results Mean VAS score and morphine dose pre-procedure were 7.4±1.6 (range, 5–10) and 47.7±30.1 mg (range, 20–120 mg), respectively. Technical success and pain relief were achieved in all patients. Mean VAS scores and daily morphine doses post-procedure were as follows: 48 h, 1.7±1.2 (p<0.001) and 29.6±16.1 mg (p=0.003); 7 days, 1.9±1.7 (p<0.001) and 16.1±12.0 mg (p<0.001); 1 month, 1.5±0.9 (p<0.001) and 10.8±10.9 (p<0.001); 3 months, 0.9±0.7 (p<0.001) and 8.4±9.2 mg (p<0.001); and 6 months, 1.2±0.8 (p<0.001) and 9.2±12.3 mg (p<0.001). Complications were observed in eight patients (28 %); among these, major complications were reported in two (7.7 %) patients, one with local infection and the other with a bone fracture. The minor complication rate was 23.1 % (6/26).
Conclusion MWA combination with osteoplasty appeared to be an effective and safe treatment for lung cancer patients with painful extraspinal bone metastases.

Keywords Microwave ablation · Osteoplasty · Lung cancer · Extraspinal bone metastases

Zhigang Wei and Kaixian Zhang contributed equally to this work.

✉ Xin Ye
yexintaian2014@163.com

Zhigang Wei
weizhigang321321@163.com

Kaixian Zhang
kaixianzhang@aliyun.com

Xia Yang
yangxjinan@163.com

Aimin Zheng
am-zheng@163.com

Guanghui Huang
hgh3612@163.com

Jiao Wang
wangjiao22@126.com

[1] Department of Oncology, Shandong Provincial Hospital Affiliated to Shandong University, 324 Jingwuweiqi Road, Jinan, Shandong Province 250021, China

[2] Department of Oncology, Teng Zhou Central People's Hospital Affiliated to Jining Medical College, 181 Xingtan Road, Tengzhou, Shandong Province 277500, China

Introduction

Bone metastases occur in 20–80 % of cases during the evolution of malignant tumors [1, 2]. The most common primary sources are the lung, breast and prostate [3]. Among patients with bone metastases, the main symptom is intractable pain, which results in a significantly decreased quality of life [4, 5]. As a result of the short life expectancy and high systemic tumor burdens, treatments for these patients are palliative [6]. The traditional treatments for painful bone metastases include analgesic drugs, chemotherapy, radiotherapy, and surgery [5, 7–9]. Recently, minimally invasive treatments such as radiofrequency ablation, microwave ablation, cryoablation, high-intensity focused ultrasound, 125I seed implantation and osteoplasty [10–19] have been developed to treat patients

Published online: 26 June 2015

with bone metastases who have obtained limited benefit from conventional treatment management. However, few studies have focused on the combination of minimally invasive treatments [20–23]. Consequently, we conducted this retrospective study aimed at assessing the efficacy and safety of MWA combined with osteoplasty in lung cancer patients with painful extraspinal bone metastases.

Materials and methods

Lung cancer patients who met the following criteria were enrolled: (1) intractable pain that was resistant to conventional treatments; (2) focal pain localized to one or two regions with imaging confirmation of the presence of bone tumor involvement; (3) a life expectancy of ≥3 months and a tumor size no larger than 6 cm. Exclusion criteria included: (1) uncontrolled infection around the lesions or systemic infections; (2) coagulation disorder, especially in patients with a platelet count of $<50\times109$/L who had received continuous anti-coagulation therapy; (3) severely deficient hepatical, renal and cardiopulmonary function unfit for MWA; (4) Eastern Cooperative Oncology Group performance status was >3.

From January 2011 to July 2014, 26 lung cancer patients with extraspinal bone metastases, including 15 men and 11 women with a mean age of 69.4 (range, 56–82) years, underwent computed tomography (CT)-guided percutaneous MWA combined with osteoplasty. Among these 26 patients, 21 (80.8 %) had one lesion, 3 (11.5 %) had two lesions and 2 (7.7 %) had three lesions. The total 33 bone metastases included 11 iliums, 9 acetabulums, 8 ischiums, 2 femurs, 1 clavicle, 1 sacrum and 1 tibia. All patients had a histological diagnosis and underwent imaging scans before the procedure. Baseline characteristics are listed in details in Table 1. All patients were evaluated by an interdisciplinary group consisting of a radiologist, pain physician, surgeon, and medical oncologist. Ethics approval was obtained from the Institutional Review Board of Shandong Provincial Hospital Affiliated to Shandong University and Teng Zhou Central People's Hospital Affiliated to Jining Medical College. All patients provided written informed consent pre-procedure.

Table 1 Baseline characteristics of 26 lung cancer patients with 33 bone metastatic lesions

	Number	Percent
Age	69.4 (56–82)	
Sex		
Male	15	57.7
Female	11	42.3
Pathology		
Adenocarcinoma	14	53.8
Squamous cell carcinoma	8	30.8
Others[a]	4	15.4
Location		
Ilium	11	33.3
Acetabulum	9	27.3
Ischium	8	24.2
Others[b]	5	19.2
Size	3.4 (2.4–5.4)	
>3.5 cm	11	33.3
≤3.5 cm	22	66.7
MWA		
60 W	17	65.4
70 W	9	34.6
MWA		
Median (min)	5 (3–12)	
Amount of bone cement injection (ml)		
Mean±SD	8.0±2.9 (4–16)	
Follow-up time (months)		
Median	8.5 (5–16)	

[a] Others include two small-cell lung cancers, one large-cell lung cancer, and one carcinoid

[b] Others include two femurs, one clavicle, one tibia, and one sacrum

MWA microwave ablation; *SD* standard deviation

CT-guided MWA combined with osteoplasty

The MTC-3C microwave ablation system (Qi Ya Research Institute of Microwave Electronic, Nanjing, China. Registration standard: YZB/country 1408–2003. No: SFDA (III) 20073251059), or the ECO-2450B microwave ablation system (ECO Microwave Electronic Institute, Nanjing, China. Registration standard: YZB/country 1475–2013. No: SFDA (III) 20112251456) were used for MWA. A 13-gauge bone needle (Cook Inc., Bloomington, IN, USA) and polymethyl methacrylate (Simplex P; Howmedica Osteonics, Kalamazoo, Michigan, USA) were applied for the ablation and bone cement injection. Local anesthesia (lidocaine and bupivacaine) and preemptive analgesia (morphine) were used. Generally, the selected power of ablation was 60–70 W and the ablative duration ranged from 3 to 12 min. The ablation procedure has been reported in previous studies [24, 25]. When lesions were >3.5 cm (11 instances), two or more overlapping energy applications were done by repositioning the microwave antenna. Immediately after the MWA procedure, mixed bone cement was injected into the ablative lesion by means of a "working channel" (the channel of bone-cement syringe). The amount of the bone cement injection delivered under the guidance of CT was determined by the tumor size and the location of the injection. The mean volume of bone cement injected per lesion was 8.0±2.9 (range, 4–16) ml. Once the cement had solidified, the bone needle was immediately extracted. A CT scan was conducted post-procedure to observe the size and shape of the bone cement injection, the correlation with

nearby organs, and to determine if there were any signs of bleeding or leakage of bone cement (Figs. 1, 2, and 3).

Outcome assessment

A 10-point score was used for VAS evaluation [21]. VAS scores were assessed by physicians before (baseline) and at 48 h, 1 week, 1, 3, and 6 months after the procedure. The dose of daily morphine was also recorded.

Assessment of complications

Complications were assessed according to the standards drafted by the International Working Group on Imagine-Guided Tumor Ablation in 2005 [26]. Major complications were defined as clinical symptoms during or after ablation that may be life threatening, resulting in substantial damage and dysfunction and requiring hospitalization or prolonged hospitalization. Minor complications were defined as follows: self-limiting complications without sequelae and requiring only a short hospital stay for observation or treatment. Side effects referred to pain, post-ablation syndrome, and asymptomatic minor bleeding or fluid accumulation on CT. Post-ablation syndrome is induced by the absorption of the necrotic material and the release of inflammatory factors. The main symptoms are fever, fatigue, malaise, nausea, vomiting, which usually lasts 3–5 days.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous variables were expressed as mean±standard deviation. The paired Student's *t* test was applied to evaluate the visual analog scale (VAS) score and the dose of morphine before and after the procedure. The test was two-sided and a p value of <0.05 was considered as statistically significant.

Results

Pain control

MWA combined with osteoplasty was performed on 33 bone lesions in 26 lung cancer patients with painful extraspinal bone metastases. The procedures were technically successful in all bone lesions. The pre-procedure mean VAS score was 7.4±1.6 (range, 5–10). The post-procedure VAS scores were as follows: 48 h, 1.7±1.2 ($p<0.001$); 7 days, 1.9±1.7

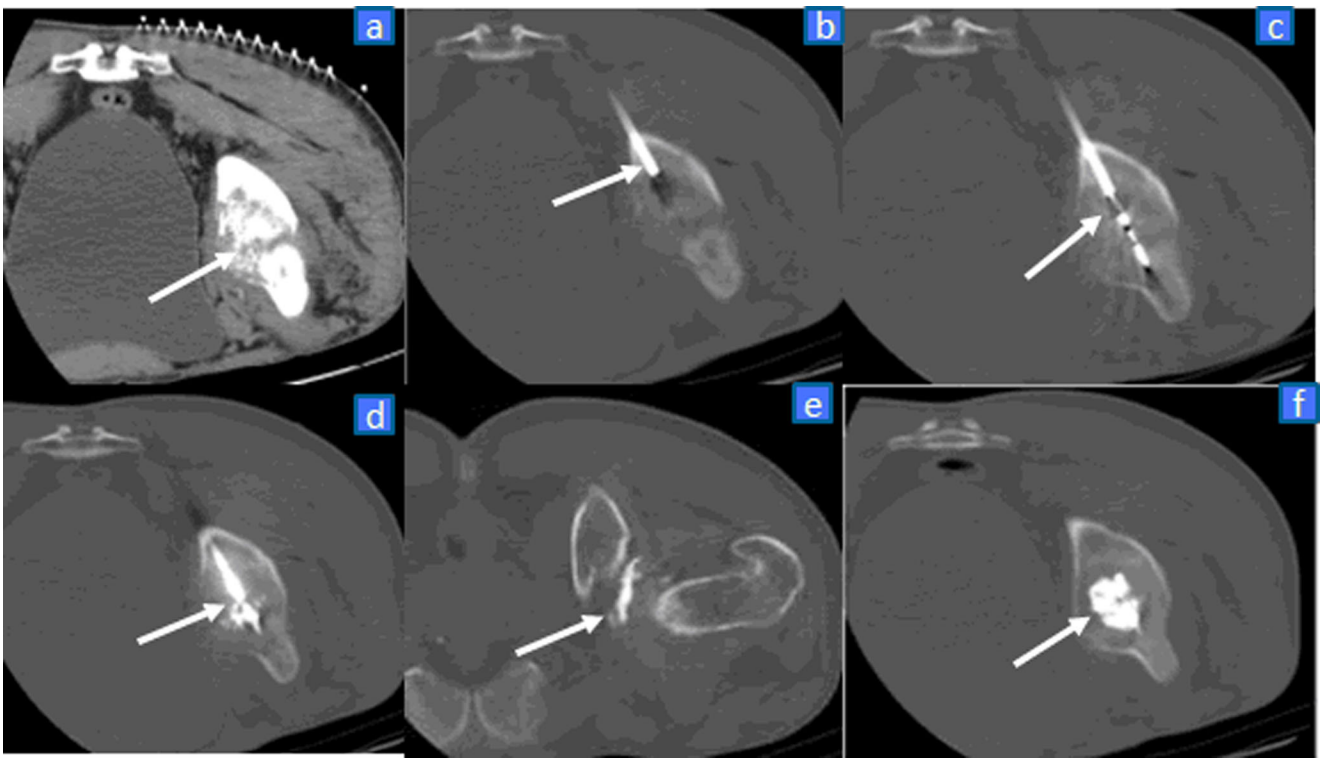

Fig. 1 The procedure of MWA plus osteoplasty for a 51-year-old male of metastatic adenocarcinoma of the lung with bone metastasis. **a** Metastatic lesion (*arrow*) in the *right* ilium. **b** A 13-gauge bone needle (*arrow*) was inserted to establish a "working channel". **c** The microwave antenna (*arrow*) was inserted through the "working channel" into the lesion. **d** Mixed bone cement (*arrow*) was injected into the lesion through the "working channel". **e** A small amount of cement (<0.5 ml; arrow) leaked into the surrounding soft tissue. **f** Bone cement uniformly distributed to the metastatic lesion (*arrow*)

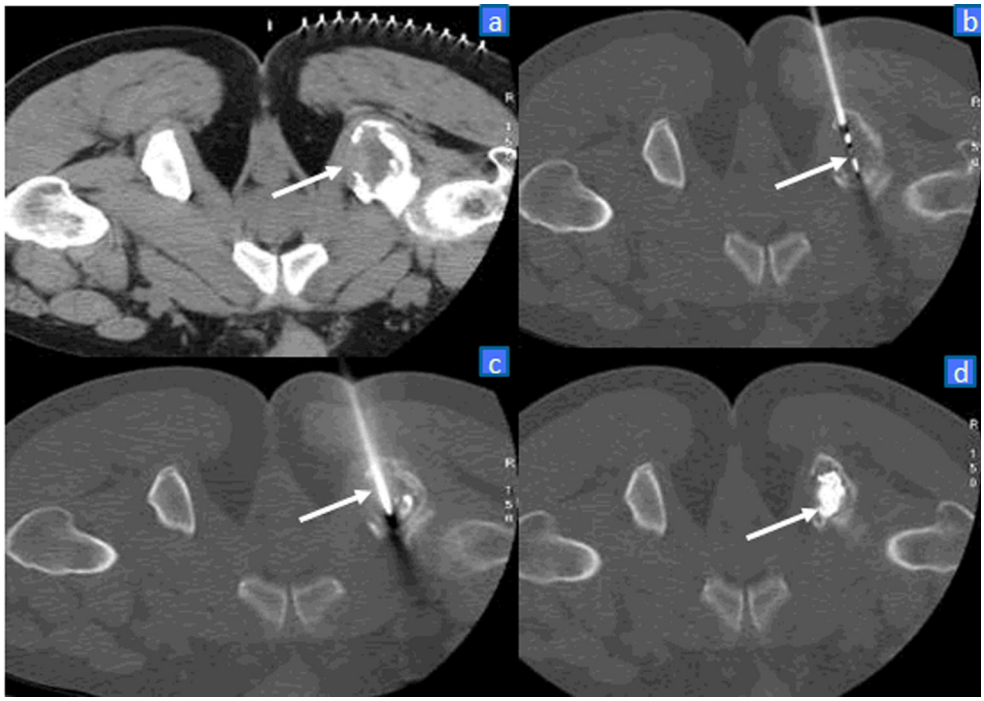

Fig. 2 The procedure of MWA plus osteoplasty for a 60-year-old female of metastatic squamous cell carcinoma of the lung with bone metastasis. **a** Metastatic lesion (*arrow*) in the *right* ischium. **b** The microwave antenna (*arrow*) was inserted along the "working channel" into the lesion. **c** Mixed bone cement (*arrow*) was injected into the lesion through the "working channel". **d** Bone cement evenly distributed (*arrow*) to the ablative lesion

($p<0.001$); 1 month, 1.5±0.9 ($p<0.001$); 3 months, 0.9±0.7 ($p<0.001$); and 6 months, 1.2±0.8 ($p<0.001$) (Fig. 4). Localized infection occurred in one patient with clavicle metastasis at 8 days post-procedure and the pain worsened, whereas two patients had developed new bone metastases by 5 months post-procedure and the pain had worsened. These two patients received repeat MWA combination with osteoplasty and achieved pain relief.

Morphine dose

Before the procedures were carried out, all patients had taken morphine. The pre-procedure mean daily morphine dose was 47.7±30.1 mg (range, 20–120 mg). The mean daily morphine doses post-procedure were as follows: 48 h, 29.6±16.1 mg ($p=0$ .003); 7 days, 16.1±12.0 mg ($p<0.001$); 1 month, 10.8±10.9

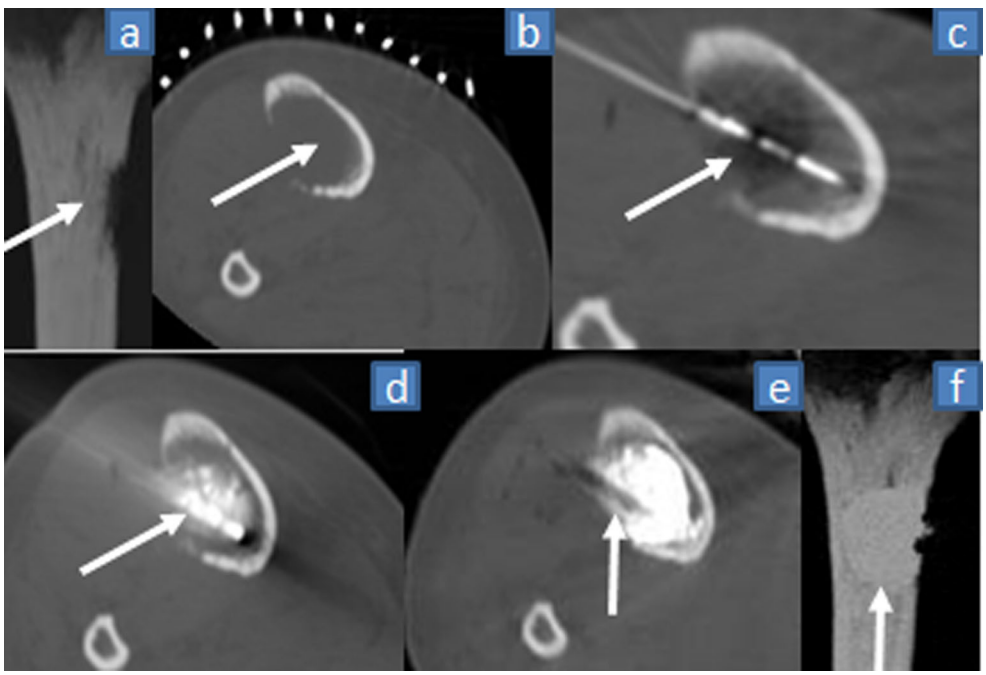

Fig. 3 The procedure of MWA plus osteoplasty for a 57-year-old male of metastatic adenocarcinoma of the lung with bone metastasis. **a**–**b** Metastatic lesion (*arrow*) in the *right* tibia (x-ray; CT scan). **c** A microwave antenna (*arrow*) was inserted into the lesion. **d** Mixed bone cement (*arrow*) was injected into the lesion. **e**, **f** Bone cement uniformly distributed (*arrow*) to the lesion

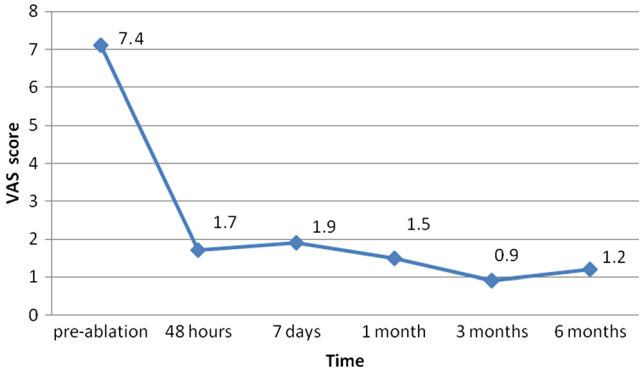

Fig. 4 VAS score before and after microwave ablation

($p<0.001$); 3 months, 8.4±9.2 mg ($p<0.001$); 6 months, 9.2±12.3 mg ($p<0.001$) (Fig. 5).

Side effects and complications

Side effects

Pain was the most common side effect during the procedures and procedure was completed after the pain. Patients experienced moderate pain in 26 sessions and severe pain in 6 sessions. When severe pain occurred, the procedure was stopped and patients were treated with morphine injection and midazolam. Other side effects mainly involved post-ablation syndromes, which were exhibited in 11 patients.

Complications

No peri-procedural death was observed. Major complications were observed in two patients (7.7 %); one patient experienced left clavicle purulent infection at 8 days after the procedure, and the other had a bone fracture at 20 days after the procedure. Surgical incision and drainage were conducted; meanwhile, antibiotics were also administrated for the patient with infection. One month post-procedure, the infection was controlled. The bone fracture occurred in the left ilium; however, no surgery was conducted due to the fact that the fracture was an incomplete fracture, which had no effect on the bone stability and the patient did not suffer pain. With a follow up of 4 months, the fracture healed. Six patients (23.1 %) had minor complications—small amounts of bone cement (<0.5 ml) leaked into the surrounding soft tissue in these patients, resulting in no associated symptoms.

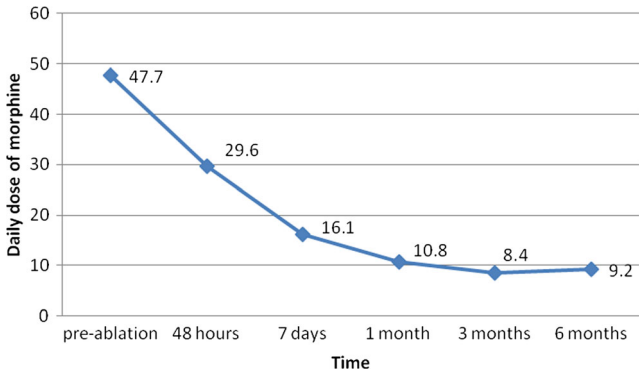

Fig. 5 Daily dose of morphine before and after the microwave ablation

Discussion

For lung cancer patients with bone metastases, the most common symptom is intractable pain. The physiopathological mechanisms involving pain include the release of chemical agents or cytokines, which result in stimulation of sensory nerves, activation of osteoclast activity, periosteal stretching, pathological fractures, as well as infiltration and compression of nerves and surrounding tissues [27–29]. In general, patients with bone metastases have a short life expectancy and poor quality of life. Palliation and improvement of quality of life is the aim of treatment for those patients. Thermal ablation has been applied for the therapy of pulmonary bone metastases. The possible mechanisms of pain relief after ablation are as follows: destruction of the sensory fibers; shrinkage of the tumor leading to reduced stimulation of the nerve plexus; inhibition of osteoclastic activity; and reduction in certain cytokines secondary to central sensitization and pain upregulation [22]. Although thermal ablation could relieve pain, it can not improve the stability of the bone metastases, and may even cause fractures [30, 31]; however, osteoplasty can stabilize bones by means of the exothermic polymerization of the cement [22]. In theory, thermal ablation combined with osteoplasty could decrease tumor cell spread either mechanically through the formation of an ablation-shell barrier or through embolization of necrotic tumor cells; in addition, it could improve the stability of the bone.

To date, few studies have focused on the combination of thermal ablation and osteoplasty in the treatment of bone metastases and verified the efficacy of combination [23, 32, 33]. In our study, 26 patients had intractable pain and had taken morphine; pre-procedure VAS scores and the dose of morphine were decreased significantly post-procedure. These results suggested that lung cancer patients with painful bone metastases could quickly benefit from treatment with MWA plus osteoplasty, which was in accordance with previous reports [23, 32, 33]. Because of the occurrence of additional bone metastases, two patients experienced pain aggravation at 5 months after the procedure. These two patients received repeat MWA combination with osteoplasty and achieved pain relief.

Regarding the safety of this combination treatment, no peri-procedural death was observed. The common complications in the present study were pain and post-ablation

syndrome. Major and minor complications were observed in 7.7 and 23.1 % patients, respectively.

In conclusion, our study showed that MWA combination with osteoplasty could be an efficacious and safe treatment for pulmonary, primary extraspinal bone metastases. However, the small sample size limited statistical confidence. Further large-scale studies are needed to verify our conclusion.

Conflict of interest The study was supported by Shandong Province Medical and Health Science and Technology Development projects (2014WS0346).

References

1. Berrettoni BA, Carter JR. Mechanisms of cancer metastasis to bone. J Bone Joint Surg Am. 1986;68(2):308–12.
2. Coleman RE. Clinical features of metastatic bone disease and risk of skeletal morbidity. Clin Cancer Res. 2006;12(20):6243s–9.
3. Jemal A, Thun MJ, Ries LA, et al. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. J Natl Cancer Inst. 2008;100: 1672–94.
4. Harris K, Chow E, Zhang L, et al. Patients' and health care professionals' evaluation of health-related quality of life issues in bone metastases. Eur J Cancer. 2009;45:2510–8.
5. Dorrepaal KL, Aaronson NK, van Dam FS. Pain experience and pain management amongst hospitalized cancer patients: a clinical study. Cancer. 1989;63:593–8.
6. van der Linden YM, Dijkstra SP, Vonk EJ, et al. Prediction of survival in patients with metastases in the spinal column: results based on a randomized trial of radiotherapy. Cancer. 2005;103: 320–8.
7. Smith HS. Painful osseous metastases. Pain Physician. 2011;14: 373–403.
8. Gösling T, Becker-Schiebe M. Surgical treatment of skeletal metastases. Unfallchirurg. 2015;118(4):347–63.
9. Johnstone C, Lutz ST. External beam radiotherapy and bone metastases. Ann Palliat Med. 2014;3(2):114–22.
10. Pusceddu C, Sotgia B, Fele RM, et al. Treatment of bone metastases with microwave thermal ablation. J Vasc Interv Radiol. 2013;24(2): 229–33.
11. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. Radiographics. 2005;25 Suppl 1:S69–83.
12. Kurup AN, Callstrom MR. Ablation of musculoskeletal metastases: pain palliation, fracture risk reduction, and oligometastatic disease. Tech Vasc Interv Radiol. 2013;16(4):253–61.
13. Lam MK, Huisman M, Nijenhuis RJ, et al. Quality of MR thermometry during palliative MR-guided high-intensity focused ultrasound (MR-HIFU) treatment of bone metastases. J Ther Ultrasound. 2015;3:5.
14. Dupuy DE, Liu D, Hartfeil D, et al. Percutaneous radiofrequency ablation of painful osseous metastases: a multicenter American College of Radiology imaging network trial. Cancer. 2010;116(4): 989–97.
15. Carrafiello G, Laganà D, Ianniello A, et al. Radiofrequency thermal ablation for pain control in patients with single painful bone metastasis from hepatocellular carcinoma. Eur J Radiol. 2009;71(2):363–8.
16. Masala S, Schillaci O, Bartolucci AD, et al. Metabolic and clinical assessment of efficacy of cryoablation therapy on skeletal masses by 18F-FDG positron emission tomography/computed tomography (PET/CT) and visual analogue scale (VAS): initial experience. Skelet Radiol. 2010;40:159–65.
17. Carrafiello G, Laganà D, Pellegrino C, et al. Percutaneous imaging-guided ablation therapies in the treatment of symptomatic bone metastases: preliminary experience. Radiol Med. 2009;114:608–25.
18. Simon CJ, Dupuy DE. Percutaneous minimally invasive therapies in the treatment of bone tumors: thermal ablation. Semin Musculoskelet Radiol. 2006;10(2):137–44.
19. Basile A, Giuliano G, Scuderi V, et al. Cementoplasty in the management of painful extraspinal bone metastases: our experience. Radiol Med. 2008;113:1018–28.
20. Xie L, Chen Y, Zhang Y, et al. Status and prospects of percutaneous vertebroplasty combined with ^{125}I seed implantation for the treatment of spinal metastases. World J Surg Oncol. 2015;13(1):119.
21. Clarecon F, Jean B, Pham HP, et al. Value of percutaneous radiofrequency ablation with or without percutaneous vertebroplasty for pain relief and functional recovery in painful bone metastases. Skelet Radiol. 2013;42:25–36.
22. Halpin RJ, Bendok BR, Sat KT, et al. Combination treatment of vertebral metastases using image guided percutaneous radiofrequency ablation and vertebroplasty: a case report. Surg Neurol. 2005;63:469–74.
23. Tian QH, Wu CG, Gu YF, et al. Combination radiofrequency ablation and percutaneous osteoplasty for palliative treatment of painful extraspinal bone metastasis: a single-center experience. J Vasc Interv Radiol. 2014;25(7):1094–100.
24. Wei Z, Ye X, Yang X, et al. Microwave ablation in combination with chemotherapy for the treatment of advanced non-small cell lung cancer. Cardiovasc Intervent Radiol. 2015;38(1):135–42.
25. Yang X, Ye X, Zheng A, et al. Percutaneous microwave ablation of stage I medically inoperable non-small cell lung cancer: clinical evaluation of 47 cases. J Surg Oncol. 2014;110(6):758–63.
26. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. Radiology. 2005;235(3):728–39.
27. Mantyh PW, Clohisy DR, Koltzenburg M, et al. Molecular mechanisms of cancer pain. Nat Rev Cancer. 2002;2:201–9.
28. Mannion RJ, Woolf CJ. Pain mechanisms and management: a central perspective. Clin J Pain. 2000;16(3 Suppl):S144–56.
29. Goblirsch MJ, Zwolak PP, Clohisy DR. Biology of bone cancer pain. Clin Cancer Res. 2006;12(20Pt):6231s–5.
30. Alexander ES, Hankins CA, Machan JT, et al. Rib fractures after percutaneous radiofrequency and microwave ablation of lung tumors: incidence and relevance. Radiology. 2013;266(3):971–8.
31. Lannessi A, Garnon J, Cormier É, et al. Interventional radiology for bone metastases. Bull Cancer. 2013;100(11):1163–73.
32. Jakanani GC, Jaiveer S, Ashford R, et al. Computed tomography-guided coblation and cementoplasty of a painful acetabular metastasis: an effective palliative treatment. J Palliat Med. 2010;13(1): 83–5.
33. Lane MD, Le HB, Lee S, et al. Combination radiofrequency ablation and cementoplasty for palliative treatment of painful neoplastic bone metastasis: experience with 53 treated lesions in 36 patients. Skelet Radiol. 2011;40:25–32.