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Note

Therapeutic effects of computerized tomography (CT)-guided percutaneous microwave ablation on malignant lung tumors

Yuanzhi Gao[1], Xu Jiang[2], Haitao Tang[3] & Guanghai Mei[4]*

[1]Disinfection Supply Center; [2]Department of Radiology; [3]Department of Thoracic Surgery, First Hospital of Changsha, Changsha 410005, Hunan Province, China
[4]Department of Psychiatry, The Seventh Affiliated Hospital of Nanhua University, Changsha 410 000, Hunan Province, China

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Lung cancer is a common clinical malignancy. In this study, we aimed to evaluate the therapeutic effects of computerized tomography (CT)-guided percutaneous microwave ablation (MWA) on malignant lung tumors. Sixty patients in our hospital enrolled between January 2015 and January 2017 were picked up as subjects. They were allocated into control group (30 malignant lung cancer patients underwent chemotherapy) and observation group (thirty patients received CT-guided percutaneous MWA). Later, comparisons of the objective response rate, tumor markers in serum, prevalence rate of untoward effects, long-term survival rate, relapse rate and quality-of-life (QoL) score were implemented. MWA patients showed an objective response rate of 66.7% (the rate was 40.00% in chemotherapy group; P <0.05). Serum carcinoembryonic antigen (CEA), cancer antigen 125 (CA125) and CA153 had lower levels after MWA in both groups than those before MWA (P <0.05) (this tendency was especially striking in observation group; P <0.05). In MWA patients, totally 10.00% of patients showed untoward effects (this was 33.33% in chemotherapy patients; P <0.05). The QoL scores were higher after MWA in both groups than those before MWA (P <0.05), especially in the observation group (P <0.05). For patients with malignant lung tumors, CT-guided percutaneous MWA may augment the short-term efficacy, control the tumor progression, relieve the adverse reactions and long-term local recurrence, increase the survival rate for a long term and improve the QoL during survival.

Keywords: Chemotherapy, CT guidance, Lung cancer, Lung tumor, Microwave ablation

Lung cancer is a common clinical malignancy, dominating all malignancies in regard of its prevalence and death rates[1,2]. At present, surgical resection is still a well-accepted method for treating lung cancer in clinical practice, but most patients have already in the middle and advanced stages upon diagnosis, and the efficacy of radiotherapy and chemotherapy is limited. Besides, surgery is not applicable to the patients complicated with cardiac or liver dysfunction[3]. As a minimally invasive technique, local ablation has been applied to treat early lung cancer[4], mainly including radiofrequency ablation (RFA) and microwave ablation (MWA). MWA has larger ablation volume, shorter time and lower recurrence rate than those of RFA[5-8], but the efficacy and safety of MWA still need further validation[9].

Computerized tomography (CT)-guided percutaneous MWA can promote the shrinkage of lung tumors[10]. In this context, here, we assessed the therapeutic effects of CT-guided percutaneous MWA on malignant lung tumors.

Materials and Methods

Baseline clinical data

This is a retrospective cross-sectional study which has been approved by the ethics committee of our hospital (No. 201412892209). Sixty patients admitted to the hospital between January 2015 and January 2017 were picked up as subjects. They were allocated into control group (30 malignant lung tumor patients underwent chemotherapy) and observation group (30 patients received CT-guided percutaneous MWA). Indications for chemotherapy and CT-guided percutaneous MWA: Patients who cannot tolerate surgical resection due to poor cardiopulmonary function or older age; those who refused surgical resection; those with postoperative recurrence of lung tumors; those with recurrence of single lesions after other local treatments; those with single lungs (absence of one lung due to various reasons).

The sample size was estimated based on our pre-experiments. Control group was composed of 22 males and 8 females at the age of 30-85 (56.67±13.24) years old. In terms of TNM stage, stage II lung cancer appeared in 7 patients, stage III in 14 patients, and stage IV in 9 patients. As to the pathological type, there were 18 squamous cell carcinoma (SCC) patients, 10 adenocarcinoma (AC) patients, 1 small cell lung cancer (SCLC) patient and 1 neuroendocrine carcinoma (NEC) patient. Their tumor sizes were 2.1-4.6 (3.4±0.5) cm. Observation

*Correspondence:
E-Mail: unmietaticpi@gmx.de

group comprised 23 males and 7 females at the age of 29-86 (56.23±12.47) years old. As with TNM stage, stage II lung cancer appeared in 6 patients, stage III in 16 patients, and stage IV in 8 patients. Pathologically classified, this group incorporated 19 SCC patients, 9 AC patients, 1 SCLC patients and 1 NEC patient. Their tumor sizes were 2.2-4.7 (3.5±0.4) cm. Both groups had similar gender ratio, age, TNM stage, tumor size, pathological type, lesion location and pathological diagnosis (P >0.05) (Table I).

Inclusion criteria were as follows: Patients with malignant lung tumors diagnosed by imaging examination, observation of clinical symptoms, and pathological test; those with indications for chemotherapy or MWA; those who were acknowledged of the therapeutic regimen and given the informed consent before treatment; those with a survival time of >3 months; those with complete clinical data.

Exclusion criteria were as follows: Patients complicated with severe infection; those with other malignancies; those who had undergone thoracic surgery; those with incomplete clinical data; or tumors adjacent to great vessels.

Methods

All patients had contraindication for surgery. All examinations were conducted by the same group of doctors, including 2 radiologists and 3 interventionists, all of whom had more than 5 years of experience in lung cancer treatment. Single-blinded CT scan was performed.

For control group, the following chemotherapy regimen was employed: 1,000 mg/m^2 gemcitabine (Nanjing Chia-Tai Tianqing Pharmaceutical Co., Ltd., China; batch No. H20093404; specification: 1.0 g) was intravenously infused on the 1st d and 8th days, and 40 mg/m^2 cisplatin (Qilu Pharmaceutical Co., Ltd., China; batch No. H37021357; specification: 20 mg×5) was intravenously infused on the 1st-3rd days. The chemotherapy lasted for 3 consecutive cycles, with 21 day as a cycle.

For observation group, CT-guided percutaneous MWA was performed. The patients' lungs were scanned using Lightspeed VCT 64-slice CT scanner (GE, USA). After the size, number and distribution of lung tumors were determined, the MWA plan was developed. The patients were kept fasting for 6 h before MWA, and 10 mg of morphine was intramuscularly injected and 30 mg of codeine phosphate was orally taken 30 min before operation. During operation, the venous access was established for patients in a supine position, an electrocardiogram monitor was connected, and the puncture point was determined according to CT images. After local infiltration anesthesia using 5 mL of lidocaine, the patients were instructed to hold their breath, and the microwave antenna was punctured to the site of lung tumors through the puncture point. After the antenna was punctured in place, KY-2000 MWA system (Nanjing Echem Pharmaceutical Co., Ltd., China; frequency: 2450 MHz, power: 60 W) was connected for 8-16 min of ablation based on tumor size, and the scope of ablation was controlled within 0.5 cm beyond the edge of tumor. Then the patients were instructed to hold their breath again, the power was adjusted to 35 W, and the antenna was slowly pulled out. The ablation time was determined according to tumor location and size.

Table 1 — Baseline clinical data of all patients (n=30)

Data	Control	Observation	t/χ^2	P
Gender			χ^2=0.089	0.766
Male	22	23		
Female	8	7		
Age (year)	56.67±13.24	56.23±12.47	t=0.133	0.895
Tumor stage			χ^2=0.269	0.874
II	7	6		
III	14	16		
IV	9	8		
Pathological type			χ^2=0.080	0.994
Squamous cell carcinoma	18	19		
Adenocarcinoma	10	9		
Small cell lung cancer	1	1		
Neuroendocrine carcinoma	1	1		
Tumor diameter (cm)	3.4±0.5	3.5±0.4	t=0.855	0.396
Lesion location			χ^2=0.098	0.754
Left lung	23	24		
Right lung	7	6		
Pathological diagnosis			χ^2=0.111	0.739
Primary lung cancer	25	24		
Metastatic lung cancer	5	6		

Observation indices

The objective response rate, tumor markers in serum, prevalence rate of untoward effects, long-term survival rate, relapse rate and quality-of-life (QoL) score were compared. (References for each parameter). The patients were followed up for 36 months. In the first 12 months, they were admitted to the hospital for re-examination once a month. In the next 24 months, they were re-examined every 3 months. CT scan was performed in the 3rd month.

Evaluation criteria for short-term efficacy

For evaluation of short-term efficacy we followed the earlier study[11]. Tumor lesions were observed by CT scan after surgery. (i) Complete response (CR): Tumor lesions completely disappear, and there are no

new lesions; (ii) Partial response (PR): Tumor volume decreases by ≥50%; (iii) Stable disease (SD): 25%≤ tumor volume reduction <50%; and (iv) Progressive disease (PD): Tumor volume reduction <25%, or there are new lesions. Objective response rate = CR + PR. The slice thickness of CT scan was 3-5 mm. The tumor length was calculated according to the number of CT slices, and the tumor volume was calculated according to the following formula: TV=(W×D×L×π)/6, where TV is the tumor volume, W is the width, D is the vertical diameter of width, and L is the tumor length. The assessment was performed by the same physician.

Carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), CA153 and other tumor markers in serum were detected by chemiluminescence assay using an automatic chemiluminescence detector and related reagents (Bayer, Germany).

Long-term survival rate and recurrence rate

The survival and local tumor recurrence during 1 year and 3 years of follow-up after the MWA were recorded. Local recurrence was confirmed with biopsy, imaging and subsequent clinical outcomes.

QoL score

The WHOQOL-BREF (Chinese translation version) developed by WHO was used[12], including 4 items (fitness, mental health, social relationships, and environmental support). Each item is scored 0-100 points, and the higher score meant the higher QoL. This score was evaluated during 1 year and 3 years of follow-up.

Statistical analysis

SPSS 22.0 software (IBM Inc., USA) was employed. All measurement data were tested for homogeneity of variance and normal distribution. The normally distributed measurement data were expressed as (mean ± SD). Intergroup comparisons were performed by the *t* test, and intragroup comparisons before and after treatment were conducted with the paired t test. The count data (n) were subjected to the χ^2 test. Survival analysis was carried out using the Kaplan-Meier method, and the log-rank test was used for comparison. P-value under 0.05 suggested a significant difference.

Results and Discussion

Objective response rate

MWA patients showed an objective response rate of 66.7% (the rate was 40.00% in chemotherapy group; P <0.05) (Table 2).

Levels of serum tumor markers

Serum carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125) and CA153 had lower levels after MWA in both groups than those before MWA (P <0.05) (this tendency was especially striking in observation group; P <0.05) (Table 3).

Prevalence rates of untoward effects

In observation group, there were 2 cases of pneumothorax and 1 case of pleural effusion, who were cured after postoperative thoracic drainage. In control group, nausea and vomiting, myelosuppression and inappetence occurred in 5 cases, 2 cases and 3 cases, respectively, which were all relieved after symptomatic treatment. In MWA patients, totally 10.00% of patients showed untoward

Table 2 — Objective response rates of all patients [n (%) (n=30)]

	Control	Observation	χ^2	P
CR	1 (3.33%)	4 (13.33%)		
PR	11 (36.67%)	16 (53.33%)		
SD	14 (46.67%)	9 (30.00%)		
PD	4 (13.33%)	1 (3.33%)		
ORR	12 (40.00%)	20 (66.67%)	4.286	0.038

[CR, Complete response; PR, Partial response; SD, Stable disease; PD, Progressive disease; and ORR, Objective response rate]

Table 3 — Levels of tumor markers in the serum of all patients ($\bar{x} \pm s$)

Group	Time	CEA (ng/mL)	CA125 (U/mL)	CA153 (U/mL)
Control (n=30)	Before treatment	32.45±6.23	85.06±16.74	53.76±12.37
	After treatment	25.19±4.51#	67.48±12.13#	39.53±9.64#
	t	5.170	4.658	4.970
	P	<0.001	<0.001	<0.001
Observation (n=30)	Before treatment	32.17±6.29	84.61±16.87	53.42±12.83
	After treatment	20.38±3.95	43.15±9.56	29.27±7.05
	t	8.694	11.711	9.036
	P	<0.001	<0.001	<0.001
t (intergroup comparison before treatment)		0.173	0.104	0.104
P (intergroup comparison before treatment)		0.863	0.918	0.917
t (intergroup comparison after treatment)		4.394	8.628	4.705
P (intergroup comparison after treatment)		<0.001	<0.001	<0.001

[CA, Carbohydrate antigen; CEA, Carcinoembryonic antigen]

effects (this was 33.33% in chemotherapy patients; *P* <0.05) (Table 4).

Long-term survival and recurrence rates

Subsequent to three years of follow-up, it appeared that as opposed to those in control group, higher 1- and 3-year survival rates and lower 1- and 3-year relapse rates were observed in observation group (log rank P=0.011) (Table 5 and Fig. 1).

Long-term QoL scores

The QoL scores were higher after MWA in both groups than those before MWA (*P* <0.05) (this tendency was also especially striking in observation group; *P* <0.05) (Table 6).

Lung cancer is a common clinical malignancy, exhibiting high prevalence and death rates[13]. Owing to the absence of early typical symptoms, the onset of lung cancer is often ignored. Tumor has often developed to the mid-late stage when diagnosed, so patients have missed the opportunity of radical surgery[14,15].

Clinically, chemotherapy is recommended for lung cancer patients who cannot undergo radical surgery. As a method of palliative treatment, chemotherapy limit cancer cell proliferation and trigger their apoptosis in patients through drugs, thereby suppressing tumor progression and prolonging survival time[16]. During chemotherapy, however, patients are prone to toxic and side effects induced by drugs, which are markedly harmful to their prognosis. As an important local treatment method, radiotherapy has satisfactory palliative effects. Nevertheless, it exerts toxic and side effects while killing tumor cells and prolonging the survival time of patients. In severe cases, patients may become intolerable and give up treatment after suffering from immunity damage, loss of appetite and fatigue. Particularly, radiation-induced bone marrow suppression, pulmonary fibrosis, esophagitis and pneumonitis are bound to undermine the QoL of patients.

Interventional treatment has been recently extensively accepted as a therapy of malignant tumors. For example, MWA is used to oscillate tumors mainly through emitted microwave currents, so tumor tissues excite heat by friction[17]. Tumor tissues usually have lower resistance to heat than normal tissues. When the temperature rises to a certain level, tumor tissues are gradually ablated, which gives rise to the impairment and then apoptosis of mitochondria and lysosomes in cancer cells, achieving an antitumor effect[18,19]. Besides, CT-guided percutaneous MWA is based on CT for navigation, which allows accurate puncture and protects great vessels[20,21]. In this study, the outcomes of CT-guided percutaneous MWA and chemotherapy for malignant lung tumors were retrospectively compared. We

Table 4 — Prevalence rates of untoward effects of all patients [n (%)]

	Control (n=30)	Observation (n=30)	χ^2	P
Pneumothorax	0 (0.00)	2 (6.67)		
Pleural effusion	0 (0.00)	1 (3.33)		
Nausea and vomiting	5 (16.67)	0 (0.00)		
Myelosuppression	2 (6.67)	0 (0.00)		
Inappetence	3 (10.00)	0 (0.00)	4.812	0.028
Incidence rate of adverse reactions	10 (33.33)	3 (10.00)		

Table 5 — Long-term survival rates and relapse rates of all patients [n (%) (n=30)]

	Control	Observation	χ^2	P
Survival rate				
1-year	24 (83.33%)	29 (96.67%)	4.043	0.044
3-year	18 (60.00%)	25 (83.33%)	4.022	0.045
Recurrence rate				
1-year	7 (23.33%)	1 (3.33%)	5.192	0.023
3-year	9 (30.00%)	2 (6.67%)	5.455	0.020

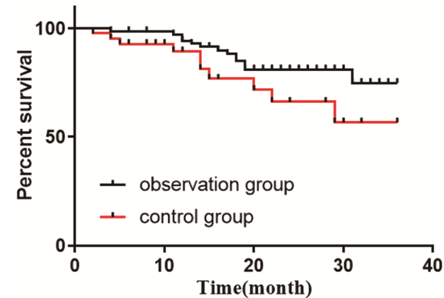

Fig. 1 — Survival curves of all patients

Table 6 — Long-term QOL scores of all patients ($\bar{x} \pm s$, point)

Group	Time (n)	Physiology	Psychology	Environment	Social relations
Control	1 year (n=24)	79.81±5.20	79.23±5.14	78.34±4.91	78.95±5.09
Observation	1 year (n=29)	85.96±5.37	85.45±5.43	84.68±5.29	84.70±5.56
	t	4.210	4.252	4.485	3.892
	P	<0.001	<0.001	<0.001	<0.001
Control	3 years (n=18)	77.34±6.42	77.82±6.17	76.46±5.23	76.63±5.40
Observation	3 years (n=25)	84.05±6.59	84.39±6.28	82.47±5.38	83.62±5.71
	t	3.329	3.409	3.656	4.050
	P	0.002	0.001	0.001	<0.001

found that observation group (66.67%) exceeded control group (40.00%) in objective response rate (P <0.05), and the serum CEA, CA125 and CA153 levels were lower in observation group after the MWA (P <0.05). Hence, CT-guided percutaneous MWA had evident short-term effects on malignant lung tumors by effectively promoting the shrinkage of tumor lesions and controlling their progression. In addition, observation group had less cases with untoward effects relative to control group (10.00% *vs.* 33.33%) (P <0.05), indicating that CT-guided percutaneous MWA is safer than chemotherapy. Probably, cytotoxic drugs were not used during CT-guided percutaneous MWA. Moreover, the operation was accurate under CT guidance, and the damage to surrounding tissues such as great vessels was mild. There were 2 cases of pneumothorax and 1 case of pleural effusion in the observation group. Pneumothorax is the most common complication after MWA. Although the incidence rate of pneumothorax is high, the symptoms are relatively mild and do not require clinical treatment. Other common complications, such as pleural effusion, can be effectively controlled with symptomatic and effective antibiotic therapy. Zheng et al. reported that emphysema was one of the risk factors for pneumothorax requiring drainage after MWA[22].

Furthermore, as opposed to those in control group, higher 1- and 3-year survival rates and lower 1- and 3-year relapse rates were observed in observation group (P <0.05). As opposed to control group, observation group yielded relatively high QOL scores (P <0.05). After MWA, the tissues around the ablation electrode immediately undergo changes such as degeneration and thickening of collagen fibers[23]. Six months after treatment, the tumor lesions in the lung were replaced by fibrous scar tissues. The complete necrosis rate of lung cancer after treatment was 38%-97%, the complete destruction rate was mostly above 70%, and the recurrence rate was only 3%-38.1%, which are similar to the results of this study. Taken together, CT-guided percutaneous MWA lengthens the survival and improve the QOL more effectively, mainly because this therapy has a higher objective response rate and can well control the tumor progression.

Conclusion

Our observations in the present investigation demonstrate that for patients with malignant lung tumors, computerized tomography (CT)-guided percutaneous microwave ablation (MWA) may augment the short-term efficacy, control the tumor progression, reduce the prevalence rate of untoward effects and long-term local recurrence rate, increase the long-term survival rate, and threby improve the QoL during survival. Regardless, this study still has limitations. Firstly, this is a retrospective study. Secondly, there are heterogeneous type of cancers, and the tumor markers may not be appropriate for all of them. Thirdly, the confounding effects concerning statistical analysis were not explored. Further, multicenter prospective studies with larger sample sizes are ongoing in our group to validate the findings herein.

Conflict of interest

Authors declare no competing interests.

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