Int J Clin Exp Med 2020;13(8):5772-5779
www.ijcem.com /ISSN:1940-5901/IJCEM0112898

*Original Article*

# Effects of microwave ablation combined with a targeted drug on the short- and long-term efficacies of advanced NSCLC patients

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Received April 20, 2020; Accepted June 2, 2020; Epub August 15, 2020; Published August 30, 2020

**Abstract:** Objective: The aim of this study was to analyze the effects of microwave ablation combined with a targeted drug on advanced non-small-cell lung cancer (NSCLC) patients. Methods: 92 patients clinically diagnosed with advanced NSCLC in our hospital were retrospectively analyzed and randomized into the control group (CG, n = 45, CG, treated by a targeted drug) and the observation group (OG, n = 47, treated by microwave ablation and a targeted drug) by the random number table. Disease control rates (DCR), progress-free survival (PFS), 1-year and 2-year survival rates, incidences of complications, and quality of life (QOL) were compared between the two groups. Results: The DCR, PFS, 1-year and 2-year survival rates were 85.11%, 16.85±2.28 months, 85.11% and 44.68% in the OG, 66.67%, 12.34±1.87 months, 57.78%, and 28.89% in the CG (P<0.05); (2) At the end of and at 1 month after treatment, the Zubrod-ECOG-WHO scores of OG were lower than those of the CG (P<0.05); (3) No statistical difference was found between the two groups in terms of the incidences of acneiform miliaris, xerosis cutis, diarrhea, nausea, and liver dysfunction after treatment (P>0.05). Conclusion: Treated by microwave ablation and the targeted drug, advanced NSCLC patients managed to effectively control their disease, extend the PFS, and improve the long-term survival rate and quality of life in a safe manner.

**Keywords:** NSCLC, advanced, microwave ablation, targeted drug, short term, long term, efficacy

## Introduction

Lung cancer is a type of malignant tumor with the highest and increasingly rising incidence in China as more people smoke, more pollution is caused to environment, and our living surroundings grow worse [1]. According to statistics, lung cancer tops other cancer types in terms of incidence and fatality rate in China, and as its main type, NSCLC accounts for almost 80% [2].

If NSCLC is identified in the early stage, a surgery may be feasible with good prognosis. However, the fact is that NSCLC seldom manifests itself in the early stage, and its rate of being diagnosed is low as most patients have entered the progressive or advanced stage when the disease is found. At this moment, a radical surgery is impossible, and patients have to choose radiotherapy or chemotherapy [3]. Chemotherapy is more extensively applied in advanced NSCLC patients based on platinum-containing dual-drug first-line treatment program. After chemotherapy, about 35% of the patients claimed comparatively higher short-term efficacy, and 10-15% of the patients managed to live for more than 2 years if they receive thermotherapy on a regular basis [4]. However, chemotherapy is associated with obvious toxic reactions that some low-tolerant patients quitted in the process [5]. As the study goes further, targeted treatment gradually becomes a new therapy, and Gefitinib, Erlotinib, Icotinib and Afatinib are approved as the first-line targeted drugs [6]. In addition, ablation also works in advanced NSCLC patients, including percutaneous radiofrequency ablation and microwave ablation which have a larger scope of application. Microwave ablation bases on high-frequency electromagnetic wave to raise the local temperature to about 80°C in a short period of time, in order to deactivate and hydrate tumor cells to make tumor tissues coagulated and necrotic. Microwave ablation

can not only deactivate lung cancer cells in situ, but also improve our immunity [7].

According to a number of studies, the combination of chemotherapy and microwave ablation can achieve good effects in advanced NSCLC patients, but there are few studies focusing on the combination of microwave ablation and targeted drug. In this study, 92 advanced NSCLC patients were included to specifically analyze the values of microwave ablation and targeted drug in treatment.

## Materials and methods

### *Materials*

92 advanced NSCLC patients in our hospital were retrospectively analyzed and divided into the CG (n = 45) and the OG (n = 47) by the random number table. Patients in the CG aged from 46 to 75 with BM between 57 and 72 kg and tumor diameter between 2.0 and 5.0 cm. In 20 cases, the tumor was on the left lung, and in 25 cases, it was on the right lung; patients in the OG had an age between 48 and 78, BM between 56 and 73 kg, and tumor diameter between 2.0 and 5.0 cm. 23 cases reported tumor on the left lung and 24 on the right lung. (1) Inclusion criteria: compliance with the NSCLC diagnosis criteria [8]; in the stages IIIB and IV according to the TNM staging system [9]; 1 measurable primary tumor; age under 80; ECOG score [10] between 0 and 2; direct sequencing showed EGFR gene status; after the failure in the first radiotherapy or chemotherapy, targeted therapy was used, or switch to targeted therapy due to intolerance of radiotherapy and chemotherapy; expected survival time over 3 months; informed consent received from patients or their guardians. (2) Exclusion criteria: distal metastasis; previous history of radiotherapy, chemotherapy, targeted treatment and immunotherapy; complication of severe organ dysfunctions, coagulation disorders and contradictions of minimally invasive surgeries. The study was approved by the ethics committee of Shantou Central Hospital.

### *Methods*

Patients in the OG received combined treatment of microwave ablation with a targeted drug. (1) Microwave ablation: patients were prohibited from food and water 6 h before operation, and were subcutaneously injected with 10 mg morphine half an hour before operation. During the operation, slow intravenous drip of 500 ml 0.5% sodium chloride solution and one piece of Sauteralgyl was conducted, along with ECG monitoring, oxygen inhalation and dynamic blood pressure level monitoring. The general surface projection site of the tumor was fixed with lead wires to maintain stability. The lesion site was canned by double-helix CT to determine the tumor size, the point, distance and direction of needle inserting. The puncturing point was marked on the skin with a marker, and the surgical area was disinfected and covered by a towel. Anesthesia was done by lidocaine injection. As patients were anesthetized, puncturing was performed according to the scheduled pathway with the coaxial puncture system and 15 G coaxial bushing. The bushing tip was positioned by CT. A 17 G microwave ablation needle was inserted into the tumor at a depth of 0.5-1.0 cm outside its distal end through the coaxial system, and secured for microwave ablation. As the treatment instrument, microwave ablation needle and water cooling pump were connected, and the lesion site punctured was thoroughly ablated. The ablation effects were confirmed by CT. After then, the needle path ablation began, and the coaxial bushing was retreated until the ablation needle was totally removed. Next operations included local disinfection, dressing, double-helix lung CT scanning to observe any change in tumor density and seepage. Special conditions were handled immediately. Patients were transferred to general wards after their vital signs returned to the normal level following 4 h ECG monitoring. (2) Targeted drug: Gefitinib tablets (GYZZ H20163465, manufacturer: Qilu Pharmaceutical (Hainan) Co., Ltd., specification: 0.25 g × 10 s) were selected and taken orally on the day when the ablation was performed for targeted treatment. The dose was 250 mg each time, once a day. During treatment, the drug was withdrawn in case of patients showing intolerable adverse reactions, but recovered in 2 weeks.

Patients in CG were treated by the same targeted drug according to the same processes.

### *Observation indexes*

Short-term efficacy [11]: Complete response (CR): all targeted lesions disappear and the short axis of all pathological lymph nodes is less than 10 mm; partial response (PR): on the

**Table 1.** Intergroup comparison of general materials ($\bar{x}$ ± sd)/[n (%)]

| Material | | OG (n = 47) | CG (n = 45) | $t/X^2$ | *P* |
|---|---|---|---|---|---|
| Gender | Male | 25 (53.19) | 26 (57.78) | 0.196 | 0.658 |
| | Female | 22 (46.81) | 19 (42.22) | | |
| Age (y) | | 64.59±12.41 | 63.28±11.19 | 0.531 | 0.597 |
| Weight (kg) | | 64.33±5.80 | 65.26±5.84 | 0.552 | 0.582 |
| Tumor diameter (cm) | | 3.45±1.08 | 3.50±1.12 | 0.218 | 0.828 |
| Tumor location | Left lung | 23 (48.94) | 20 (44.44) | 0.186 | 0.666 |
| | Right lung | 24 (51.06) | 25 (55.56) | | |
| Pathological type | Glandular | 40 (85.11) | 38 (84.44) | 0.008 | 0.930 |
| | Non-glandular | 7 (14.89) | 7 (15.56) | | |
| Clinical staging | III | 31 (65.96) | 30 (66.67) | 0.005 | 0.943 |
| | IV | 16 (34.04) | 15 (33.33) | | |

**Table 2.** Intergroup comparison of DCR after treatment [n (%)]

| Group | CR | PR | SD | PD | DCR |
|---|---|---|---|---|---|
| OG (n = 47) | 15 (31.91) | 15 (31.91) | 10 (21.28) | 7 (14.89) | 40 (85.11) |
| CG (n = 45) | 10 (22.22) | 12 (26.67) | 8 (17.78) | 15 (33.33) | 30 (66.67) |
| $X^2$ | | | | | 4.296 |
| *P* | | | | | 0.038 |

basis of sum of critical radiuses, the sum of radiuses of all targeted lesions reduce by at least 30%; stable disease (SD): the conditions of patients stay between PR and PD; progressive disease (PD): on the basis of minimum sum of critical radiuses, the sum of radiuses of all targeted lesions increase by 20%, and the absolute total increase of radiuses exceeds 5 mm, or new lesions develop. DCR is the sum of CR, PR and SD.

Long-term efficacy: Progression-Free-Survival (PFS), 1-year and 2-year survival rates after treatment were recorded and compared between the two groups.

Quality of life: Zubrod-ECOG-WHO 5-point method [12] was used to evaluate patients' quality of life before and after treatment. The scale consists of 0-5 grades, of which, 0 stands for complete recovery of capacity for action to the level before the disease, 1 for free walking and light physical activity, 2 for free walking and independence in life but incapable of working, and 1/2 of the daytime for activities, 3 for partial independence in life and 1/2 of the daytime for lying in bed, 4 for lying in bed and dependence in daily life, and 5 for death. Where the grade ascends by 2 points, the QOL is improved; if the increase is limited to 1 point or no change is found, the patients have a stable QOL, and if the score reduces, patients' QOL reduces. The Improvement rate of QOL = Improvement rate + Stability rate.

Safety: The incidences of acneiform miliaris, xerosis cutis, diarrhea, nausea, and liver dysfunction were compared between the two groups before and after treatment.

*Statistical analysis*

Statistical analysis was performed with SPSS22.0. In case of numerical data expressed as mean ± standard deviation, comparison studies were carried out through independent-samples *t* test; in case of nominal data expressed as [n (%)], comparison studies were carried out through $X^2$ test for intergroup and intragroup comparison. For all statistical comparisons, significance was defined as $P<0.05$.

## Results

*Intergroup comparison of general materials*

Statistical difference was not found between the two groups in terms of proportions of male and female patients, average age, average tumor diameter, average weight, tumor location, pathological type and clinical staging ($P>0.05$) (**Table 1**).

*Intergroup comparison of short-term efficacy*

The number of patients with CR, PR, SD and 7 were 15, 15, 10 and 7 in the OG (DCR = 85.11%), 10, 12, 8 and 15 in the CG (DCR = 66.67%) ($P<0.05$) (**Table 2**).

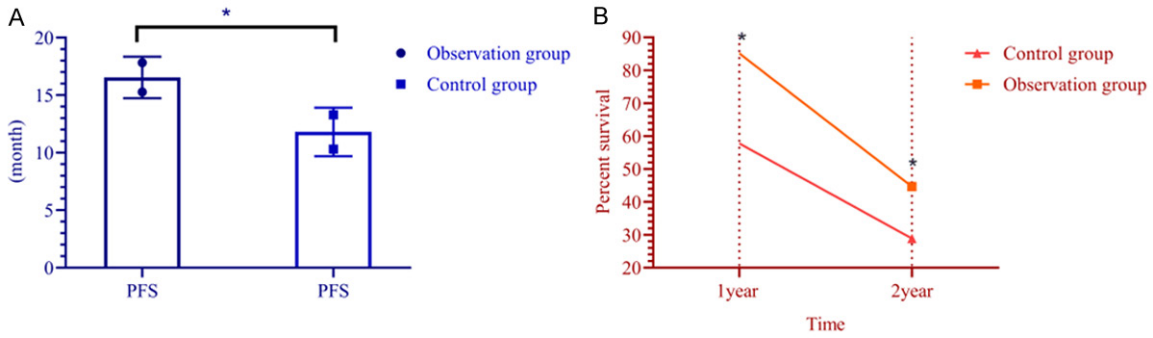


**Figure 1.** Intergroup comparison of survival rate and time. The OG had longer PFS (A) and higher 1-year and 2-year survival rates (B) as compared with the CG (P<0.05). * indicates P<0.05 for comparison between the two groups.

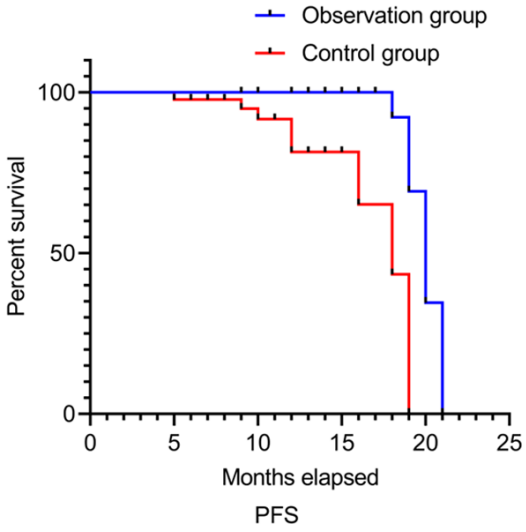


**Figure 2.** Intergroup comparison of PFS survival curve.

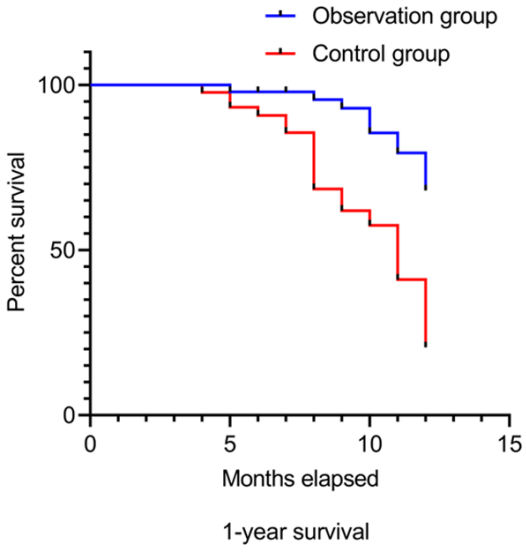


**Figure 3.** Intergroup comparison of 1-year survival curve.

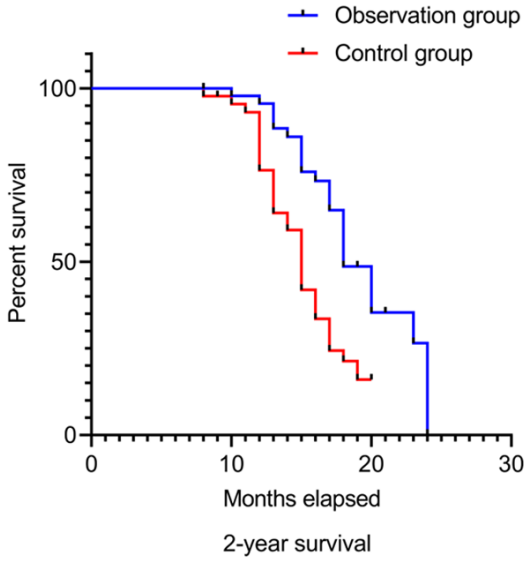


**Figure 4.** Intergroup comparison of 2-year survival curve.

*Intergroup comparison of long-term efficacy*

The PFS was 16.85±2.28 months in the OG and 12.34±1.87 in the CG; 40 (85.11%) patients in the OG and 26 (57.78%) patients in the CG survived at 1 year after treatment; at 2 years after treatment, the survival rate was 44.68% in the OG with 21 patients alive, and 28.89% in the CG with 13 patients alive. The PFS in the OG was significantly longer than that in the CG, with the 1-year and 2-year survival rates after treatment higher than those in the CG, showing statistically significant difference (P<0.05) (**Figures 1-4**).

*Intergroup comparison of QOL improvement rate*

17 patients in the OG and 12 in the CG experienced QOL improvements after treatment. 23

**Table 3.** Intergroup comparison of QOL improvement rates

| Group | Improved | Stable | Compromised | Total |
|---|---|---|---|---|
| OG (n = 47) | 17 (36.17) | 23 (48.94) | 7 (14.89) | 40 (85.11) |
| CG (n = 45) | 12 (26.67) | 18 (40.00) | 15 (33.33) | 30 (66.67) |
| $X^2$ | | | | 4.296 |
| *P* | | | | 0.038 |

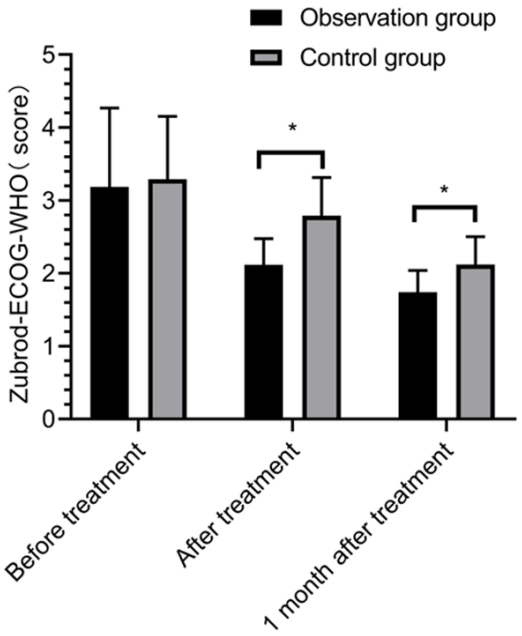


**Figure 5.** Intergroup comparison of Zubrod-ECOG-WHO score. There was no significant difference in the Zubrod-ECOG-WHO score between the two groups before treatment (P>0.05). The scores at the end of treatment and 1 month after treatment were significantly lower in the OG compared with those in the CG (P<0.05). * indicates P<0.05 for comparison between the two groups.

patients in the OG and 18 patients in the CG claimed stable QOL; 7 patients in the OG and 15 patients in the CG were compromised in QOL. Accordingly, the QOL improvement rate was 85.11% in the OG and 66.67% in the CG (P<0.05) (**Table 3**).

*Intergroup comparison of zubrod-ECOG-WHO score*

The Zubrod-ECOG-WHO scores of the two groups were not significantly different before treatment (P>0.05); at the end of and at 1 month after treatment, the Zubrod-ECOG-WHO scores were reduced in both groups (P<0.05), and were far lower in the OG (P<0.05) (**Figure 5**).

*Intergroup comparison of safety*

After treatment, the case numbers of acneiform miliaris, xerosis cutis, diarrhea, nausea and liver dysfunction were 15, 7, 12, 3, and 1 in the OG, and 16, 9, 10, 4, 2 in the CG. There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05) (**Table 4**).

## Discussion

Lung cancer is not only characterized by a high incidence and a high mortality, but also a high reoccurrence rate after treatment, and poor prognosis in most cases, threatening the life of patients severely [13]. Upon diagnosis, patients with lung cancer have entered the advanced stage when the disease progresses rapidly along the lymph and blood, producing difficulties in treatment and affecting patients' prognosis [14]. Previously chemotherapy was the major tool against lung cancer patients in the middle and advanced stages, but failed to show satisfactory efficacy. With studies on lung cancer going further, new tumor drugs and lung cancer treatment methods emerge now [15, 16].

Targeted drug treatment is a principal means of accurately treating tumors, especially, NSCLC, with patients' survival time and QOL obviously improved according to many evidences [17, 18]. Along with the further development in medical devices, microwave ablation is also effective for advanced lung cancer. As a local treatment method, it is highly capable of coagulating blood in a short period of time with high heating efficiency, which means that the impacts on blood circulation is minimized [19]. Microwave ablation is performed with only a 2-3 mm needle path when patients are locally anaesthetized to protect their lung functions. It is prominently minimally invasive and safe [20]. In this study, patients of the OG were treated with microwave ablation and a targeted drug to treat patients in the OG, and the results showed that DCR was 85.11%, which was higher than that of 66.67% in patients of the CG treated with a targeted drug. Besides, the PFS, 1-year and 2-year survival rates were also significantly higher in the OG (P<0.05), indicating that the combination

**Table 4.** Intergroup comparison of safety

| Group | Acneiform miliaris | Xerosis cutis | Diarrhea | Nausea | Liver dysfunction |
|---|---|---|---|---|---|
| OG (n = 47) | 15 (31.91) | 7 (14.89) | 12 (25.53) | 3 (6.38) | 1 (2.13) |
| CG (n = 45) | 16 (35.56) | 9 (20.00) | 10 (22.22) | 4 (8.89) | 2 (4.44) |
| $X^2$ | 0.136 | 0.417 | 0.138 | 0.205 | 0.391 |
| *P* | 0.712 | 0.518 | 0.710 | 0.650 | 0.532 |

of microwave ablation and the targeted drug in the treatment of NSCLC patients could achieve not only better short-term efficacies but also ideal long-term efficacies, with longer survival time and higher survival rates. To analyze the reason, it was because microwave ablation directly damages the integrity of internal vessels and blood supply microvessels in the tumor, occludes the blood vessels, and blocks the supply of tumor tissue nutrition, which promotes the gradual apoptosis of tumor tissue [21]. Botsa et al. [22] established that microwave ablation can improve the transparency of tumor vessels, promote drug penetration and their absorption in our body for better efficacy. Lung tissues around the tumor are weakly conductive of heat and electricity. By covering the local ablation area of the lesion, sufficient heat can accumulate to fully inactivate the tumor tissues while normal lung tissues remain intact [23].

The results in this study showed that the QOL improvement rate of patients in the OG was 85.11%, higher than that of 66.67% in the CG ($P<0.05$). At the end of the treatment and at 1 month after treatment, the Zubrod-ECOG-WHO score of QOL in the OG was significantly lower than that in the CG ($P<0.05$), suggesting that the combination of microwave ablation and the targeted drug can improve patients' quality of life on the basis of enhancing long-term efficacy. In addition, no statistical difference was found between the two groups in terms of the incidences of acneiform miliaris, xerosis cutis, diarrhea, nausea, and liver dysfunction ($P>0.05$), indicating that the microwave ablation is highly adaptive and will not affect the safety of treatment with the targeted drug. The combination of microwave ablation and the targeted drug can enhance the clinical effects. This should be attributed to their different mechanisms of action. More specifically, microwave ablation can directly kill the primary tumors and activate its own immunological effect on tumors, while the targeted drug can effectively inhibit the angiogenesis in tumor tissues and control tumor metastasis. The synergistic effect of the two methods can play a good role in controlling the effects over the progression of NSCLC [24]. According to Du et al. [25], for elderly lung cancer patients with poor heart and lung functions, or intolerable in a surgery, microwave ablation could achieve basically the same effects. More than 95% of the patients could achieve clinical mitigation and a low severity of postoperative complications. Ni et al. [26] also showed in their study that after microwave ablation, the reoccurrence interval of tumor in lung cancer patients was up to 16 months, and the 3-year survival rate was around 50%, indicating the good treatment value of microwave ablation. A comparative study conducted by Wan et al. [27] showed that compared with lung cancer patients who received chemotherapy alone, lung cancer patients treated by chemotherapy and microwave ablation had higher short-term efficacy and long-term survival rate.

In conclusion, the combination of microwave ablation and targeted drug is highly safe and effective in advanced NSCLC patients by controlling the disease, extending the PFS, improving the long-term survival rate and patients' QOL. However, as a retrospective study, the subjects were not screened in advance and were limited in number. The results were not comprehensively analyzed and sufficiently representative. Future studies shall focus on larger-sample sizes and more aspects, and be forward-looking to yield more scientific and representative conclusions for the reference of treating advanced NSCLC patients.

## Disclosure of conflict of interest

None.

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