A Sequential Meta-Analysis on the Effects of Microwave Ablation on Three-Year Survival of Non-Small Cell Lung Cancer

Qian Chen a, Yuanmen Ren b, Ying Zhang a, Aiming Hu a and Jinhong Xu c,*

a College of Medicine, Jishou University
Jishou, Hunan 416000, P.R. China

b Zunyi Medical University
Zunyi, Guizhou province 563000, P.R. China

c Department of Oncology, Tongren City People's Hospital
Tongren Guizhou province 554300, P.R. China

* Corresponding author

Abstract

Objectives: To systematically evaluate the efficacy of microwave ablation in the treatment of non-small cell lung cancer (NSCLC), and to calculate the required sample size by sequential trial analysis (TSA), so as to provide objective evidence-based basis for the diagnosis and treatment of lung cancer.

Methods: Chinese and English databases were used to search the randomized controlled trials of microwave ablation for lung cancer. Two researchers evaluated the quality of the literature according to Jadad scale and then extracted the data. Review manager 5.1 was used to merge the data, and TSA software was used to calculate the sample size.

Results: A total of 7 studies with 1751 patients were included. The results showed that compared with radio-chemotherapy alone, microwave ablation combined with radio-chemotherapy could significantly improve the survival rate of patients with lung cancer (OR=3.27, 95%CI=2.45-4.36, Z=8.06, P < 0.00001). The results of sequential analysis showed that the three-year survival rate was stable and no further validation was needed. Conclusion: Microwave ablation combined with chemotherapy can significantly improve the three-year survival rate of patients.
compared with chemotherapy alone, and the results are reliable, which can provide reliable evidence for clinical treatment of lung cancer.

Keywords: non-small cell lung cancer; microwave ablation: partial response rate; complete response rate; total effective rate

1 Introduction

Lung cancer has attracted much attention due to its top morbidity and mortality. The onset of lung cancer is hidden, and many patients miss the opportunity of surgical treatment due to late stage at the first diagnosis. For tumors with large local tumor load, local treatment is a more appropriate treatment. In 2019, a study analyzed the short-term efficacy of microwave ablation, such as objective response rate, disease control rate, and half-year survival rate, without calculating the sample size. In addition, the impact of microwave ablation on the three-year survival rate of non-small cell lung cancer was still lacking in a systematic description. On the basis of previous studies, cumulative meta-analysis and TSA analysis were applied in this study, and dynamic analysis results and estimated effective sample size were used to evaluate the study results, so as to judge their authenticity and further clarify the application value of microwave ablation in the treatment of lung cancer, aiming to provide more accurate evidence-based evidence for the clinical diagnosis and treatment of lung cancer patients.

2 Materials and Methods

2.1 Retrieval strategy

All the literature on microwave ablation and lung cancer in Chinese and English were searched without language restriction. The databases were divided into Chinese and English databases. The Chinese databases included CNKI, WanFang Data and Vip. The English databases included the Cochrane Library, PubMed, MEDLINE and Web of Science. The search time limit is from database construction to 31 August 2022. The key words in English search were Lung Neoplasms, microwave ablation. The Chinese search terms were "lung cancer" and "microwave ablation", and the search methods were lung cancer and microwave ablation.

2.2 Inclusion criteria of literature inclusion and exclusion criteria

2.2.1 Literature inclusion criteria

(1) Study subjects: patients diagnosed with lung cancer by pathology; (2) Intervention measures: the control group received whole body radiotherapy or chemotherapy, and the experimental group received microwave ablation on the basis of whole-body chemotherapy or radiotherapy; (3) Outcome indicators: survival rate 3 years after treatment.

2.2.2 Literature exclusion criteria:

(1) randomized controlled trial (RCT); (2) Missing or incomplete data; (3) Literature on the use of surgery for treatment (3) Repeated publication of literature.
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(4) The quality of literature is low. (5) Reviews, case reports, opinions, animal experiments, conference papers.

2.3 Literature quality evaluation and data extraction

Meta-analysis was performed according to the entries in the Systematic Review Priority Report (PRISMA) statements, and the Jadad quality evaluation table was used to evaluate the literature quality separately. According to the Jadad scoring standard, high-quality literature is 4 to 7 points, low-quality literature is not 1 to 3 points, and 0 points are excluded. Excel 2007 table was used to extract the basic information of the literature. All eligible literature was reviewed by two researchers. And record the basic information of each article. The data extraction table includes outcome metrics, namely OR and 95% CI. The evaluation process was completed independently by two researchers and cross-checked. In case of differences, they were discussed and resolved or decided by a third party to reach a consensus.

3 Results

3.1 Literature search results and their characteristics

In this study, 7 papers were included, including 6 Chinese and 1 English, including 364 patients who underwent microwave ablation alone or in combination with radiotherapy and chemotherapy, and 363 patients who underwent radiotherapy and chemotherapy alone. The flow chart of literature retrieval is shown in Figure 1, and the basic information and Jadad scores of the included literatures are shown in Table 1.

<table>
<thead>
<tr>
<th>The First author</th>
<th>Year</th>
<th>Intervention</th>
<th>Sample size</th>
<th>Male/Female</th>
<th>Age</th>
<th>Jadad score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hui Chen[3]</td>
<td>2018</td>
<td>Ablation and chemotherapy</td>
<td>Intervention</td>
<td>Sample size</td>
<td>Male/Female</td>
<td>Age</td>
</tr>
<tr>
<td>Jiangrong Liao[4]</td>
<td>2018</td>
<td>Ablation</td>
<td>E group 64</td>
<td>C group 50</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Xia Yang[5]</td>
<td>2012</td>
<td>Ablation and chemotherapy</td>
<td>E group 55</td>
<td>C group 47</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dongwen Rong[6]</td>
<td>2017</td>
<td>Ablation and chemotherapy</td>
<td>E group 25</td>
<td>C group 25</td>
<td>11/14</td>
<td>10/15</td>
</tr>
<tr>
<td>YingQing Zhang[7]</td>
<td>2020</td>
<td>Ablation and chemotherapy</td>
<td>E group 52</td>
<td>C group 48</td>
<td>56/44</td>
<td>-</td>
</tr>
<tr>
<td>Shouzhong Wang[8]</td>
<td>2021</td>
<td>Ablation and chemotherapy</td>
<td>E group 93</td>
<td>C group 98</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Abbreviations: E group: Experimental group; C group: Control group
3.2 Cumulative effect evaluation

According to 7 reports [2-8], Q and I² tests showed no heterogeneity among the literatures (I²=0%, P=0.63). Therefore, a fixed-effect model was adopted, which suggested that microwave ablation combined with chemoradiotherapy was better than other conventional chemoradiotherapy alone. The survival rate of patients was higher (OR=3.27, 95%CI=2.45-4.36, Z=8.06, P < 0.00001), and the difference was statistically significant, as shown in Figure 2.

![Figure 1. Flow chart of document retrieval](image1)

**Figure 1. Flow chart of document retrieval**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>microwave ablation</th>
<th>chemotherapy</th>
<th>Odds Ratio</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Dongwen Xu2017</td>
<td>15</td>
<td>25</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Hui Chen2018</td>
<td>22</td>
<td>37</td>
<td>23</td>
<td>37</td>
</tr>
<tr>
<td>Shuosheng Wang2021</td>
<td>101</td>
<td>175</td>
<td>52</td>
<td>175</td>
</tr>
<tr>
<td>Tinghong Pan2016</td>
<td>11</td>
<td>30</td>
<td>3</td>
<td>30</td>
</tr>
<tr>
<td>Xia Yang2012</td>
<td>14</td>
<td>65</td>
<td>8</td>
<td>66</td>
</tr>
<tr>
<td>Yinglin Zhang2020</td>
<td>16</td>
<td>52</td>
<td>6</td>
<td>48</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>496</td>
<td>484</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>261</td>
<td>159</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Ch² = 2.59, df=6 (P=0.89); I²=0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z=0.08 (P=0.99999)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

**Figure 2 Forest map of three-year survival rate after microwave ablation combined with chemoradiotherapy**
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3.3 Bias analysis

Figure 3A Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

A total of 7 RCTS were included, all of which were described as randomized controlled experiments. Among them, 2 literatures described the randomization method as using random number table method for randomization, while the other 5 literatures did not specify the specific method. None of the seven literatures described whether the allocation scheme was hidden or not, so the risk was not unknown. Two of the literatures adopted blind method, and the outcomes of all cases were tracked and reported in all the above seven literatures, with no data missing. No selective results were reported in all the seven literatures, and other biases may be unknown. The results can be seen in Figure 3A and Figure 3B.

Figure 3B Risk of bias summary: review authors' judgements about each risk of bias item for each included study.
3.4 TSA result analysis

The sequential analysis results of the trials showed that the Z-curve intersected the threshold value, and the current total sample size had reached RIS(N=401), indicating that the results had been stable and the possibility of false positives was small. The subsequent study data had little impact on the results, and future studies could stop paying excessive attention to the three-year survival rate, as shown in Figure 4.

![Sequential analysis results of three-year survival rate trials after microwave ablation](image)

**Figure 4** Sequential analysis results of three-year survival rate trials after microwave ablation

4 Discussion

Studies on microwave ablation combined with radiotherapy or chemotherapy or on non-small cell lung cancer alone are not uncommon, but there are differences in sample size, different study regions, dispersed study factors and inconsistent study results among different studies. Therefore, this study conducted a meta-analysis of each study and analyzed the literature on case-control studies related to microwave ablation of lung cancer in the past 10 years. After literature screening according to the inclusion criteria, a total of 7 literatures[2-4][5][2-16][7-10][11-16] randomized controlled trials were selected. According to the uniformity of included indicators, we analyzed the effect of microwave ablation alone or combined with chemoradiotherapy on the three-year survival rate of patients compared with chemoradiotherapy alone.

It was found that 7 studies were included in this meta-analysis, and there was no heterogeneity among the included literatures. Therefore, the fixed-effect model was used for analysis. The results of the meta-analysis suggested that compared
A sequential meta-analysis on the effects of microwave ablation on non-small cell lung cancer, the survival rate of patients was higher, which was consistent with the results reported in the literature. Combined with the TSA results, it can be seen that the possibility of false positives is small, and the subsequent research data has little impact on the result, so we can stop paying attention to this indicator.

Limitations: There are some shortcomings in this meta-analysis, such as: This study only analyzed the three-year survival rate, and did not analyze the short-term effect evaluation indicators such as one-year survival rate, two-year survival rate, OS, PFS, etc. In addition, there were few randomized double-blind control studies in the included studies, most of the included literatures were domestic, and foreign studies were rare, so there was insufficient evidence-based evidence for microwave ablation abroad.

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References


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