Is radiofrequency thermal ablation a safe and effective procedure in the treatment of pulmonary malignancies?

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Abstract

Objective: Radiofrequency ablation (RFA) has been recently applied as an alternative option of pulmonary surgery in the treatment of pulmonary malignancies. In this study, we assessed the risk associated with percutaneous RFA, and discussed its safety and efficacy. Methods: The clinical data of 329 consecutive patients with primary (n = 237) and metastatic (n = 92) lung tumor treated with RFA from 1999 to 2006 in this hospital were considered for this study, and the character and clinical data of these patients were analyzed. Complications, local progression, and overall survival at 1, 2 and 5 years of these patients were evaluated. Results: Following the procedure 63 (19.1%) patients presented with pneumothorax, 14 (4.2%) with hemoptysis (one death), 10 (3.0%) hemothorax, 15 (4.5%) pneumonia, and three (0.9%) pericardial tamponade (one death); the 30-day mortality after the procedure was 0.6%. Needle-track implantation was observed in six (1.8%) patients. Median progression-free interval was 21.6 months. The overall survival at 1, 2 and 5 years was 68.2%, 35.3%, and 20.1%, respectively. A total of 78 (23.7%) patients developed local progression during the follow-up. Significant difference in the risk of local progression was found in tumors more than 4 cm; however, no significant difference was found in tumors less than 3 cm and 3—4 cm in our group. Conclusion: RAF is a safe and well-tolerated procedure with satisfied efficacy in the treatment of malignant lung nodules. To avoid complications with potential fatal outcome, adequate training and careful patient selection by a multidisciplinary team might be helpful.

Keywords: Percutaneous radiofrequency thermal ablation; Pulmonary carcinoma; Pulmonary metastases

1. Introduction

Surgical resection is the standard treatment in resectable primary pulmonary cancer and offers the best chance of cure [1]. Unfortunately, many patients with primary malignant lung nodules or pulmonary metastases tumors are considered medically inoperable for various reasons. During the past few years, radiofrequency ablation (RFA) has emerged as an alternative treatment option for these nonsurgical lung tumor candidates. The main advantage of image-guided lung RFA is its short hospital stay and less injury to the patients. Published data indicate low mortality and complication rates associated with RFA [2]. However, fatal complications have been reported [3], and the clinical safety and efficacy of RFA are still under discussion, especially in large number of patients. With our result, the purpose of this study was to assess the incidence of complications of RFA for lung tumors, and evaluate the efficacy of RFA.

2. Patients and methods

Between October 1999 and July 2006, 329 consecutive patients (208 males and 121 females, mean age 62.1 years (standard deviation (SD) 7.8; range, 20—82 years) were treated by RFA at our institution. Written informed consent was obtained from all patients before the treatment. Ethical guidelines of the local ethical committee were followed.

A total of 237 patients were treated for non-small-cell lung cancer (NSCLC), and 92 for metastases of other tumors. A total of 483 nodules were detected by computed tomography (CT) and 436 of them were treated by RFA under CT guidance. The mean number of passes required per patient was 1.85. Diameters of the tumors treated by RFA were less than 3 cm for 253, 3—4 cm for 102, while the others were larger than 4 cm. Mean tumor diameter was 23.1 ± 1.7 mm (range from 9 to 58 mm). For patient characteristics, see Tables 1 (NSCLC) and 2 (pulmonary metastasis tumor).
2.1. Patient selection

Selection of patients to undergo lung RFA was often multifactorial. Specific inclusion criteria consisted of: (1) age between 18 and 80 years; (2) patients with relatively early-stage NSCLC, however, were precluded from surgery because of poor pulmonary function with forced expiratory volume in 1 s (FEV1) < 1 L, FEV1% < 50%; maximum voluntary ventilation (MVV) < 50% and/or high cardiac risk; and (3) patient refusing to undergo surgery.

2.2. Technique of percutaneous RFA

RFA was performed by thoracic surgeons. Under local anesthesia and sedation, a 0.5-cm incision (subcostal or intercostal) was performed and the needle was inserted into the center of the nodule under CT scan guidance if the diameter of the nodule was less than 3 cm (an expandable needle with seven or nine tines connected to a 50 or 90 W radiofrequency (RF) generator was used). As the diameter of the nodule was more than 3 cm or the shape was irregular, the point of the needle was inserted into the deepest part of the nodule. The tines of the needle were deployed and the generator switched on. The tines were deployed once every 2 cm. Every cycle time of the procedure was controlled by the RFA machine’s computer system. When a satisfactory CT scan image pattern was obtained (a low-consistency image, 1 cm in diameter greater than the previous image of the nodule), the tines were retracted and the needle was removed.

2.3. Complications evaluation

Treatment-related complications being counted are only within 30 days after this procedure. Minor complications were defined as those resulting in no sequelae or needing nominal treatment or a short hospital stay for observation. Major complications were defined as those resulting in re-admission to the hospital for treatment, an unplanned increase in the level of care, extended hospitalization, permanent adverse sequelae, or death. Patients were then followed up after 1 month, then every 3 months for 2 years with CT scan. Median follow-up was 24 months.

Local progression was quantified according to Response Evaluation Criteria in Solid Tumors (RECIST).

2.4. Statistical methods

Statistical analysis was performed by $\chi^2$ test. Statistical Package for the Social Sciences program (SPSS) 16.0 (SPSS Inc., Chicago, IL, USA) was used for all data analysis and statistical significance was set at $P < 0.05$.

3. Results

The median hospital stay was 4.5 days (range, 3–38 days). There were totally 113 out of 329 (34.3%) patients with complications following this procedure, including 63 (19.1%) pneumothorax, 14 (4.2%) hemoptysis (one death) and 10 (3.0%) hemothorax and 15 (4.5%) pneumonia, three (0.9%) pericardial tamponade (one death), and the 30-day mortality was 0.6%.

Needle-track implantation was observed in six (1.8%) patients, 4–6 months after RFA. Chest pain was complained by 97 patients 1–2 h after RFA, which lasted for 2–4 h and needed no peculiar treatment. Postoperative fever was observed in 128 patients, most of whose temperature was lower than 38.5 °C and could be easily controlled by physiotherapy or antipyretic drugs.

Median progression-free interval was 21.6 months. The overall survival at 1, 2, and 5 years was 68.2%, 35.3%, and 20.1%, respectively. For patients with NSCLC, the survival at 1, 2, and 5 years was 80.1%, 45.8%, and 24.3%, respectively. For patients with pulmonary metastasis tumor, the survival at 1, 2, and 5 years was 50.6%, 30.1%, and 17.3%, respectively. A total of 78 (23.7%) patients developed local progression...
The use of RFA suggested in 1990 for the treatment of hepatic tumors has virtually replaced percutaneous ethanol injection and is now used throughout the world as the most-favored ablative technique [4]. From then on, radiofrequency thermal ablation had also been used to treat lung lesions, and the clinical safety and efficacy of RFA has become the main concern due to its wide application. Reports from Caroline et al. showed that 30-day mortality related to the procedure was 0.4—2.6% [5,6]. In our series, it was 0.6% (2/329). All these results demonstrate that RFA is a safe procedure in practice. On the other hand, the results demonstrated that RFA was not free from fatal complications. Therefore, RFA should only be performed under suitable patient selection criteria and following adequate guidance and training. In our group, one patient who died of uncontrolled hemoptysis had an obvious cavity (diameter 0.8 cm) in the nodule, which was enlarged by RFA and lead to irresistible hemorrhage. This fact indicated that it should be prudential when we decide to treat an empty lesion with RAF. The other patient died of pericardial tamponade, and the tumor was located in the central area adjacent to hilum of the lung. The tines of the needle were found inserted in the pericardium by reviewing the CT scan photograph afterward. Almost all cases of hemoptysis in our group occurred in patients with the center nodule near the lobe bronchus. Hence, we believe that the exclusion criteria of RAF should include the central lesion that is immediately adjacent to major pulmonary vessels or the pulmonary hilum of the lung.

The most common complication after percutaneous RFA was pneumothorax, the incidence of which was reported to be about 40—50% [7,8]; in our cases, it was 19.1%. Most of the pneumothorax events were encountered in elderly patients, all of whom were easily handled with thoracentesis or closed pleural cavity drainage. The median duration of the chest-tube drainage was less than 24 h (range, 1—16 days); however, prolonged air leak was rare. Less common complications after RFA include hemorrhage, hemoptysis, and pericardial tamponade. Most of these complications developed in the patients with much longer treated time (over 3 h); hence, the RFA treatment period should be shortened as far as possible, especially in patients with poor physical condition. Other complications included chest pain and postoperative fever. Chest pain might result from thermal injury to the pleural nerve. Postoperative fever was probably due to the absorption of necrotic products and, in most cases, it was for a short duration of time. Based on our result, we consider RFA a safe and well-tolerated procedure in the treatment of malignant lung nodules.

The median progression-free interval and survival ratio at 1, 2, and 5 years and the risk of developing local progression in our group show that RFA is effective in the treatment of malignant lung nodules, especially in patients with NSCLC. The efficiency of RFA for patients with pulmonary metastasis tumor was poorer, which may be caused by the later stage. Local progression of the tumor, even after successful ablation of lung malignancy using RFA, is an important but unresolved issue. Local progression rates after RFA of lung carcinoma vary from 3% to 38.1% [9]. Of the 329 patients in this study, 78% showed local progression with intrapulmonary tumor after RFA treatment. It must be acknowledged that local progression seen in this series most likely represents incomplete tumor treatment. These failures were detected both locally at the primary ablation site and regionally in the lung. Beside technical issues, one possible factor contributing to this high recurrence rate might be related to the size of the tumor. In our group, of all the 436 tumors ablated, 34 with local progression had lesions larger than 4 cm before treatment; hence, the patients with tumor larger than 4 cm might have a higher ratio of local progression and it seems they should be ablated for a greater number of times. Wolf also observed that tumor size was a predictor of recurrence after RFA. The best results in terms of complete tumor ablation are achieved in patients with lesions no larger than 3 cm in diameter; patients with an index tumor size of larger than 3 cm were significantly more likely to have recurrent disease at the ablation site [10]. However, no significant difference was found in tumors less than 3 cm and 3—4 cm in our group (Table 3).

### 4. Discussion

Table 3. The relation between sizes of tumor and local progression.

<table>
<thead>
<tr>
<th>Tumor diameter</th>
<th>n</th>
<th>No local progression</th>
<th>Local progression</th>
</tr>
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<tbody>
<tr>
<td>&lt;3 cm</td>
<td>253</td>
<td>185</td>
<td>68</td>
</tr>
<tr>
<td>3—4 cm</td>
<td>102</td>
<td>74</td>
<td>28</td>
</tr>
<tr>
<td>&gt;4 cm</td>
<td>81</td>
<td>47</td>
<td>34</td>
</tr>
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<3 cm versus 3—4 cm, x² = 0.12, P = 0.912; <3 cm versus >4 cm, x² = 6.593, P = 0.039; 3—4 cm versus >4 cm, x² = 4.253, P = 0.039.

During the follow-up. Of the 436 nodules treated by RFA, 253 nodule diameters were lesser than 3 cm, 102 were 3—4 cm, while the others were larger than 4 cm in diameter. Significant difference in risk of local progression was found in tumors larger than 4 cm; however, no significant difference was found in tumors less than 3 cm and 3—4 cm in our group (Table 3).

Malignant seeding is a well-known complication of both diagnostic and therapeutic procedures in patients with lung malignancies. Akebohi et al.‘s review of the literature determined that there were six cases of tumor seeding following lung biopsy in 9738 patients [11]. He estimated that the relative risk of tumor seeding per patient was about 0.061%. From the results of our survey, the incidence of track implantation after RFA is approximately 1.8%. It seems that RFA of lung malignancies confers a higher risk of seeding compared with percutaneous local biopsy alone. This small seeding risk is random and well tolerated, and might be lessened by reducing the frequency of puncture during RFA.

An advantage of this study was that the sample size of patients was large. Based on our result, we consider RAF a safe and well-tolerated procedure with satisfied efficacy in the treatment of malignant lung nodules. To avoid complications with potential fatal outcome, adequate training and careful patient selection by a multidisciplinary team might be helpful.
Acknowledgment

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References