Radiofrequency Ablation of Lung Metastases from Adenoid Cystic Carcinoma of the Head and Neck: Retrospective Evaluation of Nine Patients

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ABSTRACT

Purpose: To retrospectively evaluate the outcomes of radiofrequency (RF) ablation of lung metastases from head and neck adenoid cystic carcinoma (ACC).

Materials and Methods: Nine patients (two men and seven women; mean age, 61.6 y) with 45 lung metastases (mean diameter, 1.1 cm; range, 0.4–2.7 cm) from head and neck ACC underwent RF ablation in 30 sessions. Primary endpoints were technical success, technique effectiveness, and procedural complications. Secondary endpoints included overall survival (OS).

Results: RF ablation was technically successful for all 45 metastases. The median tumor follow-up period was 37.1 months (range, 12.9–128.3 mo). Local progression occurred in six tumors, two of which were treated again and subsequently showed complete response. Major complications (pneumothorax requiring chest tube placement) occurred in five sessions (16.7%). The median patient follow-up period was 61.6 months (range, 20.5–134.5 mo). Two patients died of disease progression at 38.9 and 61.6 months after RF ablation, respectively, whereas the other seven remained alive at the end of the study. OS rates from the initial RF ablation were 100% at 3 years and 83.3% at 5 years (mean survival time, 106.4 mo). OS rates from the treatment of the primary site were 100% at 5 years and 62.5% at 10 years (mean survival time, 210.1 mo).

Conclusions: RF ablation is an acceptable and effective local treatment for lung metastases from head and neck ACC. However, further study is needed to evaluate its effect on patient survival.

ABBREVIATIONS

ACC = adenoid cystic carcinoma, OS = overall survival, PET = positron emission tomography, RF = radiofrequency

Adenoid cystic carcinoma (ACC) is a rare malignancy, accounting for 1% of all head and neck cancers (1). This type of tumor exhibits unique malignant characteristics, such as slow growth and a high rate of systemic metastases. The lungs are the most frequent site of metastasis, and the median time to disease recurrence in the lungs has been reported to be between 28.7 and 45.0 months (2–4). Although results of surgical and systemic chemotherapy treatments for lung metastases from head and neck ACC have been previously reported in the literature (4–10), a standard management protocol for the disease has not been established. In the present study, we retrospectively evaluated the outcomes of radiofrequency (RF) ablation in nine patients with lung metastases from head and neck ACC.

MATERIALS AND METHODS

Informed consent was obtained from all patients before RF ablation. Our institutional review board approved this retrospective study and waived the informed consent requirement for the use of medical data from these patients.

Patients and Tumors
The characteristics of the studied patients are summarized in the Table. From July 2001 to March 2013, 11
patients with 53 lung metastases from head and neck ACC received percutaneous RF ablation at our institution. Among these patients, two with eight ablated tumors were not available for follow-up visits after 3 and 9 months, respectively, and were excluded from the study. Nine patients (two men and seven women; mean age, 61.6 y ± 6.1 [standard deviation]; range, 54–74 y) with 45 lung metastases were included. For treatment of the primary site, all nine patients underwent surgical resection. In addition, four also received postoperative adjuvant radiation therapy. The mean and median intervals between the date of treatment of the primary lesion and the date of initial lung RF ablation were 49.2 and 34.9 months (range, 9.2–146.0 mo), respectively.

Three nodules in three patients were histologically confirmed to be metastases from head and neck ACC based on samples obtained from computed tomography (CT)-guided lung biopsy. Other pulmonary metastases were diagnosed based on the results of serial CT images in which newly detected and/or enlarging nodules were diagnosed as pulmonary metastases without histopathologic confirmation. One patient with a solitary lung metastasis underwent positron emission tomography (PET)/CT before RF ablation treatment. In this patient, [¹⁸F] fluorodeoxyglucose accumulation was observed in the single tumor for which RF ablation was performed. The mean tumor diameter was 1.1 cm ± 0.5 (range, 0.4–2.7 cm). Thirty ablation sessions were performed to treat these tumors, including two repeat sessions conducted in cases of local tumor progression. Of these, 18 ablation sessions were conducted for the treatment of one metastasis each, eight were conducted for two each, three were conducted for three each, and one was conducted for four lesions.

Among the included patients, three had received previous treatment for lung metastases, including surgical resection and/or chemotherapy. No extrapulmonary distant metastases were detected in any patient included in the study. In six patients, all lung tumors were ablated (ie, curative therapy group), whereas RF ablation was performed to reduce lung metastatic burden in the other three patients (ie, noncurative therapy group). Four of the nine patients have previously been included in another publication (11) that reported the results of 128 patients treated between June 2001 and April 2006.

**RF Ablation Technique**

Detailed technical aspects of the RF ablation procedure conducted at our institution have been described previously (12). Briefly, RF ablation was performed percutaneously with the use of CT fluoroscopy (Asteion or Aquilion; Toshiba, Tokyo, Japan) in all sessions.

After local anesthesia with lidocaine and conscious sedation had been achieved, an electrode, which was connected to a generator, was introduced into the tumor, and then ablation was started. The electrodes used for the ablation included a multitined expandable electrode (LeVeen; Boston Scientific, Natick, Massachusetts) with an array diameter of 2 cm (n = 28) or 3 cm (n = 8), and a single internally cooled electrode (Cool-tip; Covidien, Mansfield, Massachusetts) with a 1-cm (n = 2), 2-cm (n = 7), or 3-cm (n = 2) uninsulated tip. Although a multitined expandable electrode was preferred, an internally cooled electrode was employed when the use of multitined expandable electrodes was deemed hazardous (eg, in cases of apical or hilar lesions). The procedure aimed at ablation of the tumor and at least a 5-mm margin.

Chest CT with 5-mm and/or thinner slice thickness was performed immediately after each RF ablation procedure to evaluate the ablation zone and procedural complications. A chest radiograph was obtained 3 hours after the completion of RF ablation and in the following morning to assess the occurrence of complications.

**Table. Summary of Information on Patients, RF Ablation Procedures, and Follow-up Results**

<table>
<thead>
<tr>
<th>Pt. No./Age (y)/Sex</th>
<th>Primary Site</th>
<th>Therapy of Primary Lesion</th>
<th>RF Ablation Sessions/ Treated Tumors</th>
<th>Curative RF Ablation</th>
<th>From Initial RF Ablation</th>
<th>From Therapy of Primary Site</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/65/F</td>
<td>Ear canal</td>
<td>Surgery</td>
<td>1/1</td>
<td>Yes</td>
<td>86.8</td>
<td>176.2</td>
<td>Alive</td>
</tr>
<tr>
<td>2/54/F</td>
<td>Floor of mouth</td>
<td>Surgery</td>
<td>5*/6</td>
<td>Yes</td>
<td>134.5</td>
<td>280.5</td>
<td>Alive</td>
</tr>
<tr>
<td>3/59/F</td>
<td>Floor of mouth</td>
<td>Surgery</td>
<td>6/10</td>
<td>No</td>
<td>80.8</td>
<td>90.4</td>
<td>Alive</td>
</tr>
<tr>
<td>4/62/M</td>
<td>Oropharynx</td>
<td>Surgery, RT</td>
<td>4/10</td>
<td>No</td>
<td>38.9</td>
<td>73.8</td>
<td>Dead</td>
</tr>
<tr>
<td>5/74/F</td>
<td>Maxilla</td>
<td>Surgery, RT</td>
<td>3/3</td>
<td>No</td>
<td>61.6</td>
<td>107.8</td>
<td>Dead</td>
</tr>
<tr>
<td>6/54/F</td>
<td>Maxilla</td>
<td>Surgery, RT</td>
<td>5/8</td>
<td>Yes</td>
<td>77.6</td>
<td>147.0</td>
<td>Alive</td>
</tr>
<tr>
<td>7/60/F</td>
<td>Submandibular gland</td>
<td>Surgery</td>
<td>2/3</td>
<td>Yes</td>
<td>31.3</td>
<td>40.5</td>
<td>Alive</td>
</tr>
<tr>
<td>8/61/M</td>
<td>Floor of mouth</td>
<td>Surgery, RT</td>
<td>3/3</td>
<td>Yes</td>
<td>25.5</td>
<td>42.2</td>
<td>Alive</td>
</tr>
<tr>
<td>9/65/F</td>
<td>Tongue</td>
<td>Surgery</td>
<td>1/1</td>
<td>Yes</td>
<td>20.5</td>
<td>41.5</td>
<td>Alive</td>
</tr>
</tbody>
</table>

*Includes two repeat sessions.*
Follow-up Examinations
Chest CT images with 5-mm and/or thinner slice thickness were usually obtained before and after intravenous administration of a contrast agent to assess local efficacy at 1, 3, 6, 9, and 12 months and every 6 months thereafter. Two patients did not undergo contrast-enhanced CT because of a history of adverse reactions to iodinated contrast medium or because they refused.

Local efficacy was evaluated by comparing the size and geometry of the ablation zone with observations on previous CT images. Local tumor progression was indicated when the ablation zone exhibited a gradual increase in size. The appearance of an irregular, scattered, nodular, or eccentric enhancement focus in the ablation zone was also considered to indicate local progression (13). Although PET/CT was not included in routine follow-up, five patients underwent PET/CT examinations to evaluate the outcomes of RF ablation.

Definition of Study Endpoints
The primary endpoints of this study were technical success, technique effectiveness, and procedural complications. Secondary endpoints included overall survival (OS).

Statistical Analysis
The OS was calculated from the date of primary tumor treatment or initial lung RF ablation to the date of death or final follow-up. The OS rate was estimated by Kaplan–Meier analysis. Technique effectiveness was defined as the complete ablation of the macroscopic tumor by follow-up imaging studies (14). The primary and secondary technique effectiveness rates were calculated by Kaplan–Meier analysis. The primary effectiveness rate was defined as the percentage of successfully eradicated tumors after the initial procedure (14). Similarly, the secondary effectiveness rate was defined as the percentage of tumors that received successful repeat ablation after identification of local tumor progression (14). The diameters of completely treated tumors after the first or second RF ablation and incompletely treated tumors were compared by using the Mann–Whitney U test.

A P value of less than .05 was considered statistically significant. All statistical analyses were performed with the use of SPSS software (version 22.0; IBM, Armonk, New York).

RESULTS
Technical Success and Technique Effectiveness
RF ablation was technically successful (14) in all 45 metastases. The mean and median tumor follow-up periods were 50.2 and 38.1 months (range, 12.9–128.3 mo). Local progression was observed in six of 45 tumors (13.3%), two of which were treated again in a repeat session and showed a complete response. Among the other four tumors, one was surgically resected and one patient with one tumor received chemotherapy. The other two patients with recurrences refused additional treatment. PET/CT was performed in five patients a median of 28.2 months after the initial RF ablation, and no abnormal accumulation of [18F]fluorodeoxyglucose was observed in 21 ablated tumors. The primary and secondary technique effectiveness rates were 100% and 100% at 1 year, 88.5% and 93.1% at 2 years, and 88.5% and 93.1% at 3 years, respectively (Fig 1). The diameters of completely and incompletely treated tumors were not significantly different (mean, 1.1 cm ± 0.5 vs 1.1 cm ± 0.5; P = .98).

Procedural Complications
The definition of a major complication was an event that led to substantial morbidity and disability, an increase in the level of care, or hospital admission or substantially lengthened hospital stay; all other complications were considered minor (14). Major complications (pneumothorax requiring chest tube placement) occurred in five treatment sessions (16.7%). Asymptomatic pneumothorax occurred in 11 sessions (36.7%), minor pulmonary hemorrhage in one (3.3%), and high fever (> 38.0°C) in 11 (36.7%).

Figure 1. CT image from a 74-year-old woman with multiple lung metastases from ACC of the maxilla. (a) CT image before RF ablation shows a tumor 2.2 cm in diameter located in the lower left lung (arrow). (b) CT fluoroscopic image during RF ablation demonstrates an electrode being inserted in the tumor. (c) CT image 37.3 months after RF ablation shows an involution of the ablated tumor (arrow), indicating complete ablation.
Survival Outcomes
The follow-up results of RF ablation are summarized in the Table. By the conclusion of the study, seven patients remained alive and two had died. The mean and median patient follow-up periods were 61.9 and 61.6 months (range, 20.5–134.5 mo), respectively. OS rates from the initial lung RF ablation were 100% at 1 year, 100% at 3 years, and 83.3% at 5 years (mean survival time, 106.4 mo; Fig 2). OS rates from the treatment of the primary site were 100% at 5 years and 62.5% at 10 years (mean survival time, 210.1 mo).

All six patients in the curative therapy group survived, with a 54.5-month median follow-up. New pulmonary metastases with or without extrapulmonary lesions were discovered in five patients. Two patients with new pulmonary metastases underwent RF ablation; another had lung RF ablation and chemotherapy; one with new pulmonary and thyroid metastases underwent lung RF ablation, thyroidectomy, and chemotherapy; and one with new pulmonary and brain metastases received only radiation therapy for the brain lesion. The remaining patient had no new distant metastases.

In the noncurative therapy group, new pulmonary and bone metastases developed in one patient, and new pulmonary and extrapulmonary metastases in the liver and lymph nodes were discovered in another patient. These two patients died of progression of these metastases and other untreated pulmonary lesions at 38.9 and 61.6 months after RF ablation, respectively. The other patient in this group remained alive with progression of lung metastases and development of new pleural metastasis.

DISCUSSION
The OS rates in head and neck ACC treated with standard or traditional therapy is reported to be 90.3% at 5 years, 79.9% at 10 years, and 69.2% at 15 years (15), and the incidence of distant metastases in head and neck ACC ranges from 29.8% to 56.3% (2,3,16). The lungs are the preferred site for distant metastases from head and neck ACC, accounting for 72.2%–90% of all metastatic disease (2,3,16). Overall median survival times after the diagnosis of lung metastases are reported as 21.2–32.3 months (2,3). In such cases, surgery and/or systemic chemotherapy are usually performed.

In patients with head and neck ACC, chemotherapy is often indicated in case of inoperable locoregional disease or distant metastases, especially when the tumors are symptomatic or progressing, leading to patients’ anxiety (5). However, head and neck ACC responds poorly to traditional chemotherapies (8). Limited data from a phase II clinical trial of chemotherapy for head and neck ACC in a small patient cohort (5,8) have suggested that head and neck ACC is relatively chemotherapy resistant, with response rates ranging from 0% to 10% (9,10). In addition, there is no established systemic chemotherapy protocol for patients with lung metastases from head and neck ACC.

As very few studies have reported results of lung metastasectomy for head and neck ACC metastasis, the impact of metastatic tumor resection on the overall disease outcomes remains uncertain (4,6,7). Bobbio et al (6) reported a mean survival of 72 months after the diagnosis of distant metastases in nine patients who received lung metastasectomy. Locati et al (4) reported 5- and 10-year survival rates of 58% and 16%, respectively, after metastasectomy. They suggested that only patients potentially amenable to a complete resection (ie, no residual disease) should be considered for lung metastasectomy.

However, there could be different treatment indications for patients with lung metastases from head and neck ACC. If curative treatment is possible, therapy might be attempted locally and/or systemically. Conversely, for noncurative treatment, the therapeutic strategy is more difficult. Although systemic therapy is not established and might be ineffective, it is often

![Figure 2. Kaplan-Meier curve demonstrating OS from initial lung RF ablation.](image)
performed or no treatment is offered because these metastases usually grow slowly. In the present study, of the three patients in the noncurative therapy group, two died at 38.9 and 61.6 months after RF ablation, respectively, and one remained alive at 80.8 months after RF ablation. Such outcomes demonstrate the diverse and therefore challenging nature of therapeutic indications in the noncurative therapy group.

Recently, percutaneous RF ablation has been employed as a local therapy for primary and secondary lung cancers, mostly in patients deemed unfit for surgery (11,17). The reported midterm and long-term survival rates after RF ablation for various types of lung metastases seem to be promising. In patients with colorectal cancer, 3-year survival rates of 50% (18) and 56.1% (19) and a 5-year survival rate of 34.9% (19) have been reported. In another study (20), all 15 patients with renal cell carcinoma who received curative RF ablation treatment were reported to have survived at 5 years. Ten patients with nasopharyngeal carcinoma who underwent RF ablation of pulmonary metastases had better OS than the 10 who did not (77.1 mo vs 32.4 mo; P = .009) (21). These favorable results have encouraged the use of RF ablation to treat other types of pulmonary metastases.

Compared with other therapeutic options, RF ablation offers several potential advantages such as feasibility, safety, minimal invasiveness, and the possibility of repeat treatment. The associated mortality and major complication rates have been reported to be 0%–2.6% and 9.8%–22.6%, respectively (22–25). This procedure seems to have less impact on pulmonary function compared with pulmonary surgeries. In a prospective multicenter study that enrolled 79 patients (22), pulmonary function test results at 1, 3, 6, and 12 months after lung RF ablation did not indicate any significant worsening compared with baseline values. Additionally, repeat RF ablation is possible upon detection of local progression, and such a procedure has been reported to significantly improve overall local disease control outcomes (26). The technique effectiveness rate in the present study was also improved by repeat RF ablation, from 88.5% to 93.1% at 3 years.

It is possible to treat numerous lung tumors over time with RF ablation without impairing lung capacity in cases of chronic evolution of metastatic disease. Tochio et al (27) reported the case of a patient with 50 lung metastases from parathyroid carcinoma who survived 20 RF ablation sessions within 4 years. These patients with long-term survival and chronic metastatic disease seem to benefit from RF ablation and be favorable candidates for such a procedure. In patients with numerous lung metastases from head and neck ACC, sequential RF ablation for selected lung lesions of larger size that show rapid growth and an aggressive nature might be an appropriate therapeutic option when curative treatment is impossible. In addition, PET may be useful in deciding treatment priority in cases of multiple metastases. Although only one patient underwent PET before RF ablation in the present study, PET could provide clues to more aggressive lesions requiring prioritized treatment via abnormal accumulation of [18F] fluorodeoxyglucose.

Many investigators have reported clinical outcomes of RF ablation for lung tumors, with control rates greater than 90% for lesions smaller than 2 cm (28,29). The present results are slightly worse than those described in these series, possibly because of the relatively small RF electrodes used in the study, which might reduce the active zone and margin coverage. Therefore, it is possible that local recurrence could be reduced with the use of larger electrodes.

The present retrospective study has limitations. The study population was very small, and the follow-up period was not sufficiently long for the course of this cancer type. A majority of ablated lesions were diagnosed as pulmonary metastases based on the results of serial CT images without histopathologic confirmation. In addition, the study was not designed to directly compare the outcomes of RF ablation and those of other treatments, such as surgery or stereotactic radiation therapy. On the contrary, it remains uncertain whether the treatment of lung metastases prolongs the survival of patients with head and neck ACC. In a study in nine patients who underwent complete resection of lung metastases, Bobbio et al (6) reported a cumulative survival from the time of lung surgery that was not significantly different from that in 11 patients whose distant metastases were diagnosed but not extirpated (72 mo vs 62 mo). In view of the limitations of previous retrospective studies enrolling small numbers of patients, larger prospective studies are needed to evaluate the benefit of treatment for lung metastases.

In conclusion, RF ablation is an acceptable and effective local treatment for patients with small lung metastases from head and neck ACC. However, further study to evaluate its effect on patients’ survival is needed.

REFERENCES


