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Original Article

Radiofrequency Ablation for Lung Carcinomas: A Retrospective Review of a High-Risk Patient Population at a Community Hospital

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Abstract

Purpose: The purpose of this study is to retrospectively evaluate the technical efficacy, safety, and treatment outcomes of percutaneous radiofrequency ablation (RFA) of lung tumors in patients not amenable to surgery at an urban community hospital. **Materials and Methods:** Informed consent and IRB approval was obtained. Eligible tumors were defined as those in patients deemed poor surgical candidates by multidisciplinary consensus or those refusing surgery. Response to treatment was assessed by computed tomography (CT) performed immediately postprocedure and regular intervals up to 36 months later. Complete response was measured as a 30% decrease in mean tumor diameter without evidence of contrast enhancement or tumor growth within the ablation zone as defined by the response evaluation in solid tumors. Patient demographics, technical success, postprocedure complications, and survival were assessed and compared with data available in literature. **Results:** Twenty-four patients with a total of 29 tumors underwent percutaneous CT guided RFA for biopsy-proven lung malignancies between 2010 and 2016. Complete response was achieved in 82% (14/17) of treated tumors in patients who complied with postprocedure imaging recommendations. Immediate postprocedure complications occurred following 27.6% (8/29) ablations with pneumothorax being the most common, 17.2% (6/29). Mean survival is 28.5 months (95% confidence interval: 19.7–37.3). Progressive disease was seen in 18% (3/17) patients. No immediate treatment mortality was found. No significant difference was found in survival in patients with multiple comorbidities as measured by the Charlson Comorbidity Index. **Conclusions:** RFA of lung tumors is a well-tolerated procedure with low incidence of minor complications, a good tumor response and survival benefit in selected patients in the community setting. This is a positive endorsement of the potential success of tumor RFA programs outside of the academic setting. In addition, patients with multiple comorbidities should still be considered candidates for RFA as no difference was seen in survival in patients with multiple medical comorbidities.

Keywords: *Interventional oncology, lung carcinoma, percutaneous radiofrequency ablation*

Introduction

Primary lung cancer is the number one cause of cancer-related death in the United States and is responsible for over 160,000 deaths annually.[1] In addition, the lungs are the second-most common sites of metastatic disease occurring in up to 40% of all other malignancies.[2] While surgical management with adjunctive chemotherapy is the standard of care for early-stage primary lung cancer, there remains a sizable cohort of patients ineligible for this management strategy. Over 15% of all patients diagnosed with early-stage lung cancer and over 30% of those over the age of 75 years are not surgical candidates because of locally advanced disease or unsafe comorbidities.[2] For these patients, the standard available option is often limited to external beam irradiation with best-reported 2-year survival of 51%.[1] Radiofrequency ablation (RFA) represents an increasingly popular minimally invasive and lung sparing therapy for treating patients with primary and secondary lung tumors.

Currently, RFA is approved for use in patients for whom treatment is expected to produce a survival benefit and possibly improved quality of life. Typically, eligible patients include those with early Stage I or II non-small cell lung cancer (NSCLC) in patients who are not surgical candidates. Patients with local recurrence of tumor following surgical resection as well as patients with metastatic tumors to the lung who are deemed poor surgical candidates

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can also receive RFA.[3] A generally accepted criterion is that there should be fewer than 5 lesions in each hemithorax with tumors <5 cm (ideally <3.5 cm) and >1 cm from the trachea, main bronchus, esophagus, or large central vessel.[4] However, palliative RFA may also be utilized for larger lesions in select patients to alleviate pain, numbness or motor function disorders.[5]

Previous investigations have demonstrated survival in patients with early-stage NSCLC following RFA to be between 57% and 78% in small series studies.[6] Specifically, median 1-, 2-, and 3-year survival rates between 63%–85%, 48%–83%, and 15%–46% have been established in the literature.[3,7] Despite this positive endorsement of RFA technique, there is yet no clearly defined a place for RFA in the treatment algorithm of both primary and secondary lung tumors. The selection of patients for RFA is often dependent on independent institutional practices and departmental culture, in addition to well-accepted technical criteria.

Urban community hospitals represent a unique platform for demonstrating the effectiveness of RFA for lung tumors as patients often present at a later disease stage with fewer established resources and worse comorbidities. Therefore, finding technical success rates, survival and complication rates comparable with or better than those found in the literature is a positive endorsement of tumor RF ablation programs in the community at-large, outside of the academic setting.

Materials and Methods

This study was designed as a retrospective analysis of patients treated at a single institution from September 2010 to June 2016 for lung tumor by RFA. Informed consent was waived with the approval of the Institutional Review Board. Candidates were selected for RFA after achieving consensus within a multidisciplinary team, which included interventional radiologists, oncologists, and thoracic surgeons. Malignancy was confirmed through biopsy before ablation in all but one patient. The main selection criteria for RFA for this study were patients who were not candidates for curative surgical resection because of cardiorespiratory comorbidity, poor pulmonary function as measured by forced expiratory volume in 1 s (FEV_1) or forced vital capacity (FVC), other comorbidities, or older age. In addition, patients who refused surgical resection had a failure of previous surgical resection, or who had metastases were deemed eligible. Electronic and paper medical records were reviewed for patient demographic information, clinical information, pathologic findings, and outcomes. Databases from the department of interventional radiology were reviewed, and additional clinical data were gathered from the department of thoracic surgery and pulmonology. All patients treated had a tumor size <3 cm.

RF ablation was performed under computed tomography (CT) guidance utilizing sterile technique. The necessity of sedation or general anesthesia was determined by the anesthesiologist in private consultation with respect to the patient and tumor characteristics. The anesthesiologist was present during each procedure and vital signs, pulse oximetry, and electrocardiography were monitored continuously throughout the procedure. The most common protocols used for intravenous sedation was administering a bolus of ketorolac (0.5–0.8 mg/kg) followed by infusion of propofol (0.5–2.0 mg/kg/h) or remifentanil (0.05–0.15 μg/kg/min). The grounding pads were attached to the patients' thigh, and the skin of the planned insertion site prepped. A single RITA Starburst XL electrode (AngioDynamics Inc., Latham, NY, USA) was inserted under CT guidance and directed towards the center of each target lesion using a path to avoid vessels, bronchi blebs, or fissures. Electrodes were 15 or 25 cm in length with an outer diameter of 14 gauge/6.4 French. The alternating electrical current was applied with a model × 1500 RF generator with the goal of heating tissues to a target temperature between 60°C and 100°C. The ablation algorithm consisted of initial power setting of 35 W, gradually increased to 150 W. Treatment times ranged from 4 to 12 min (mean 7 min) with goal of obtaining at least a 0.5 cm-ablation margin. CT was performed every 1–3 min during the procedure and immediately after the procedure to exclude procedure-related complications. Patients were transferred to the recovery room for a 24-h observation period. Then, after two negative chest radiographs to exclude complications the patients were discharged home. Extended admission was determined by the occurrence of postprocedural complications and the patient's subsequent clinical status.

The technical success was defined as correct placement of the ablation device into all tumor targets with the completion of the planned ablation protocol. Chest CT scans were acquired preprocedure, within 24 h postprocedure and at follow-up visits approximately 3, 6, 12, 18, 24, and 36 months after ablation with varying patient compliance. Size of each lesion was measured in 3 dimensions and then used to determine tumor response. Medical records were also reviewed to determine survival or disease progression. In accordance with Response evaluation criteria in solid tumors criteria, a 30% decrease in longest tumor diameter at follow-up in reference to immediate postprocedure follow-up scan, no evidence of tumor growth from the zone of ablation, and no evidence of contrast enhancement were criteria to assume a tumor underwent complete ablation.[8] Similarly, tumors which demonstrated at least 20% increase in longest tumor diameter or evidence of tumor growth outside of the zone of ablation were categorized as having progressive disease (PD).[8] The assessment of tumor outcomes was performed by CT analysis with/without contrast depending on the patient's renal function status [Figure 1]. Complications were assessed by use of the Society

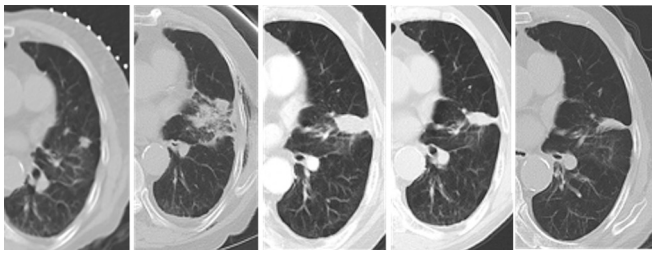

Figure 1: Patient with biopsy proven primary squamous cell carcinoma. At 1 and 2 years postprocedure, complete response maintained without evidence of recurrence. 85% decrease in longest diameter at 2.5 years when compared with initial postprocedure computed tomography. From left to right: Preradiofrequency ablation, immediate postprocedure, 3 months, 12 months, 2.5 years

of Interventional Radiology Classification System for Complication by Outcome.[9]

For patients with at least 3 months of follow-up imaging, overall survival, disease-specific survival, and progression-free survival curves were calculated from the time of the first postablation study with the use of the Kaplan–Meier survival plots method and univariate analysis. Changes in mean diameter of the ablated lesions were measured and analyzed.

Results

CT-guided RFA of 29 tumors was performed in a total of 24 patients (age range, 52–87 years; mean 72.4 years) between June 2010 and September 2016. There were 15 men (age range, 52–87 years) and 9 women. The median Charlson Comorbidity Index (CCI) of sampled patients fell between 3 and 4 (CCI range 2–11). Mean FEV_1 was 1.4 and mean FVC was 2.5 for the group.

Technical success was achieved in all patients for treatment of biopsy-proven primary or secondary lung tumors with intent to cure or for palliation. The initial diagnoses included NSCLC in 23 patients and metastatic disease from primary colon cancer in one patient. Of those with NSCLC, further histological assessment revealed adenocarcinoma (n = 12) and squamous cell carcinoma (n = 4). Three of the 24 patients underwent RF ablation of multiple lung tumors concurrently. One patient with metastatic lung disease had undergone systemic chemotherapy and/or external irradiation before RF ablation. Tumor size on preprocedure imaging ranged between 0.6 and 3.4 cm with a mean diameter of 1.6 cm [Table 1].

No procedure-related deaths occurred. The most common major procedural complication was pneumothorax, which occurred in 6 patients, 3 of whom required chest tube placement (SIR Class C). In one patient, a small volume pneumothorax (SIR Class A) was noted immediately following the initial biopsy portion of the procedure but did not preclude ablation because the patient remained asymptomatic (note that this was the only patient who had a concurrent biopsy and ablation at the request of the patient and referring provider). All other pneumothoraces were noted on final CT scan performed at the end of the procedure. Minor complications (SIR Class A, B) included the development of a pleural effusion not requiring drainage (n = 1) and self-limited blood-tinged sputum (n = 1). The median length of hospital stay was 1 day (range 1–21). Those patients with longer hospital stays were due to either procedure-related complications or to independent comorbidities or medical complications.

Table 1: Baseline characteristics for 24 patients with malignant lung tumors who were analyzed in this study

Variable	Data
Patients, *n*	24
Sex, *n*	
Female	9
Male	15
Age, mean (SD)	72.4 (9)
Number of tumors, *n*	29
Tumor size, cm	
Mean (SD)	1.73 (0.77)
Median (range)	1.55 (0.61-3.35)
Histological tumor type	
Adenocarcinoma, *n*	10
Squamous, *n*	8
Other, *n*	6
Median follow up, months	24.4

SD: Standard deviation

Fourteen of the initially treated 24 patients have at least 3 months of follow-up imaging available for analysis. Those patients for whom adequate follow-up imaging is not available because of noncompliance were not included in the final analysis. Of these patients with adequate follow-up and with a total 17 tumors, 82% demonstrated complete tumor response (n = 14/17). PD was found in 18% of treated tumors (n = 3) with evidence of tumor recurrence on follow-up imaging [Table 2]. There was no significant difference in tumor response when stratified by histology.

At the time of this retrospective analysis, 14 patients were alive and 10 had expired. Four patients with squamous cell cancer and four patients with adenocarcinoma died from cancer-related causes. Two patients died of nonmalignancy related causes including heart disease. Both overall survival and cancer-specific survival were 79% (confidence interval [CI]) at 1 year and 46% (CI) at 2 years' postprocedure. Overall survival in patients with adenocarcinoma was 90% at years 1 and 2 postprocedure and 60% at 3 years' postprocedure. Overall survival in patients with squamous cell carcinoma was 100% at 1 year and 38% at 2 years' postprocedure [Figures 2-5]. The mean days of survival in patients with high CCI (≥5) was 1177.2 days as compared to 1316.7 days in patients with CCI <5 (P = 0.33).

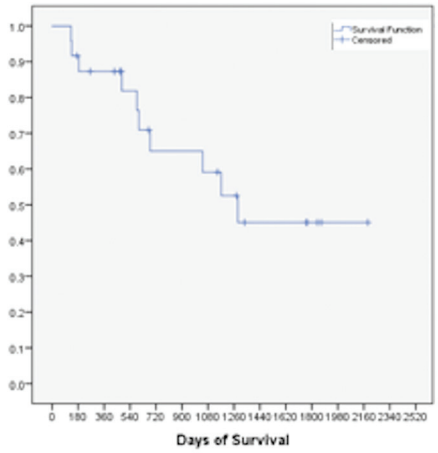

Figure 2: Overall patient survival curve for patients with inoperable primary or secondary pulmonary malignancy following percutaneous radiofrequency ablation

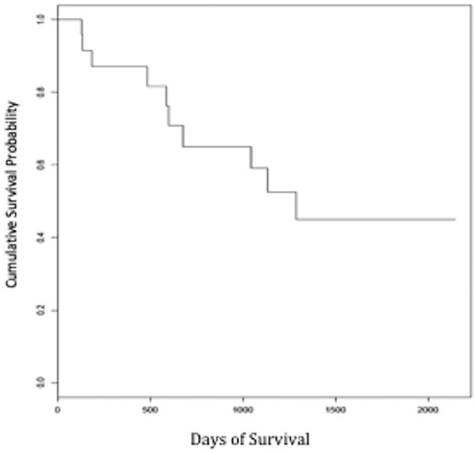

Figure 3: Cancer-specific patient survival curve for patients with inoperable primary or secondary pulmonary malignancy following percutaneous radiofrequency ablation

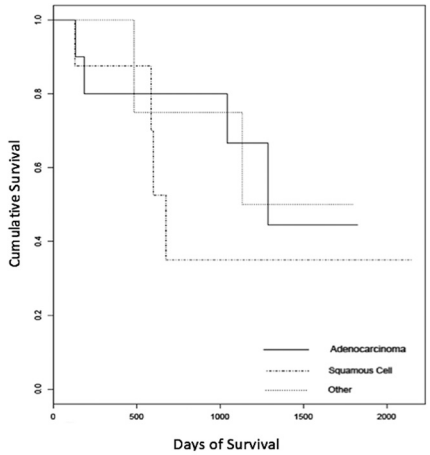

Figure 4: Overall survival curves for 24 patients with inoperable pulmonary malignancy following percutaneous radiofrequency ablation stratified by tumor histology

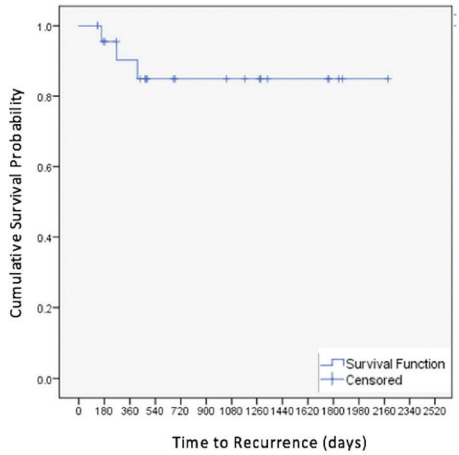

Figure 5: Disease free progression of 24 patients with primary or secondary pulmonary malignancy following percutaneous radiofrequency ablation

Discussion

Multiple prior prospective and retrospective reports have demonstrated the efficacy of RFA in controlling lung tumors with low associated morbidity. In this study, the effectiveness of RFA is demonstrated in a different setting, the urban community hospital. Patients were categorized according to the CCI in an effort to stratify their level of risk. For our cohort of patients, the median CCI was between 3 and 4 (range 2–11). Studies have shown that high CCI scores are associated with impaired survival and increased risk of death. In a study by Simon *et al*. a CCI score ≥5 was associated with overall survival of 10.43 months as compared to a CCI of 1–2 (overall survival 55.5 months) or CCI of 3–4 (overall survival 36.62 months).[7,10] The median CCI of the patients in this study qualifies them as moderate risk due to their comorbid conditions. Although the length of survival in this study was greater in patients with lower CCI (1316.7 vs. 1177.2 days), the difference between the groups was not statistically significant (P = 0.33). Therefore, RFA should not be avoided in patients with higher CCI with significant comorbidities and survival is similar to patients with lower CCI.

Table 2: Outcome of radiofrequency ablation in 14 patients (17 total tumors) with malignant pulmonary disease who were assessed for the primary efficacy endpoint of target tumor response

	Overall (*n*=17)	Adenocarcinoma (*n*=8)	Squamous cell (*n*=7)	Other (*n*=2)
Confirmed CR, *n* (%)*	14 (82)	7 (87)	5 (71)	2 (100)
PD/recurrence, *n*	3	1	2	0

*Defined as 30% decrease in tumor diameter between immediate postprocedure and last available follow-up evaluation without evidence of enhancement or tumor growth in the ablation zone. PD: Progressive disease, CR: Complete response

This retrospective analysis demonstrates overall survival in patients deemed nonsurgical candidates with lung tumors following RFA similar to that found in the literature. In the RAPTURE study by Lencioni *et al*. in 106 patients with a mean tumor size of 1.7 cm, the overall survival was 70% at 1 year and 48% at 2 years in patients with NSCLC.[11] Cancer-specific survival was 92% at 1 year and 73% at 2 years in patients with NSCLC.[11] Likewise, Simon *et al*. reported a 1-year overall survival of 78%- and 2-year overall survival of 57% on a mean tumor diameter of 3.0 cm.[3] This is comparable to overall survival and cancer-specific survival in this study, which was 79% (CI) at 1 year and 46% (CI) at 2 years' postprocedure, respectively.

This study confirmed that carefully selected patients experience adequate tumor response with low morbidity. About 82% of patients in this study demonstrated complete tumor response (n = 14/17). The RAPTURE study, for comparison, demonstrated an 80% complete response.[11]

Furthermore, the results in our study show that patients experience minor complications (SIR Class A, B) at a similar frequency as reported in the literature. The most frequent complication of RFA was pneumothorax (seen in 20.7% of patients). No patients died as a result of this procedure and 92% (13/14) of patients were deemed stable following the procedure to be discharged within 24 h after the procedure. One patient remained in house for an extended stay secondary to unrelated medical problems. In comparison, in the RAPTURE study pneumothorax was seen in 27/137 procedures (19.7%) with a median hospital stay of 3 days, which was longer than 1 day reported in this study.[11]

The biggest challenge, we faced during this analysis was its retrospective technique. We were limited in our ability to obtain pre/postpulmonary function testing and to direct imaging follow-up protocols and frequency of our treated patients because they were primarily managed by the thoracic surgery team. An additional limitation was cohort size; over the course of 6 years, we treated 24 eligible patients. With a larger sample population, additional analyses of patients could have been pursued including survival when stratified by tumor histology, tumor size or lesion location.

The National Institute for Health and Clinical Excellence guidelines state that RFA is a safe and effective treatment option for those patients with inoperable lung tumors as well as carefully selected patients with small, early-stage tumors.[12] While our findings and those found in the literature support this assessment, greater work needs to be done at the referral level based on additional research to encourage utilization of this technique to a broader range of patients.

Although the mainstay of treatment of low-risk patients remains surgery because of its high success rate, the algorithm of treating inoperable and otherwise high-risk patients presents a greater challenge and includes stereotactic radiotherapy (SBRT) and percutaneous ablation techniques. Further investigation and direct comparison are required to delineate the efficacy of these treatment options. One recent analysis demonstrated overall survival rates of 66% and 39% at 3 and 5 years, respectively, following SBRT in patients with inoperable Stage I lung tumors.[13] The results in this study are in a similar range with 3-year overall survival at approximately 60% in patients with mostly early stage inoperable lung tumors and therefore supports ablation as an alternative to SBRT. Evidence suggests that ablation may be safer than SBRT. SBRT has been reported to have significant complications. In a study done by Timmerman *et al*. 82.9% of patients reported Grade 1–2 toxicity to SBRT; 11.4% reported grade 3–4 toxicities; and 6 patients died (from Grade 5 toxicities). It is believed the SBRT treatment may have contributed to the events leading to their death.[14]

In addition, the comparison between sublobar resection and ablation therapy in Stage I lung cancer patients demonstrated similar overall survival rates (87.1% sublobar resection vs. 87.5% RFA) in a recent study.[15] Therefore, pursuing primary RFA of stage I lung tumors with curative intent in carefully selected patients is a possibility that should be explored more exhaustively.

Conclusions

As an urban community center where patients often present at a later disease stage with fewer resources and worse comorbidities, finding technical success rates, positive patient outcomes, and complication rates comparable with or better than found in the literature is a positive endorsement of the potential success of tumor RFA programs outside of the academic setting. RFA should be considered a valuable treatment option for patients with medically inoperable lung malignancies.

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Conflicts of interest

There are no conflicts of interest.

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