RESEARCH ARTICLE

Ablation techniques in non-small cell lung cancer patients: experience of a single center

Botsa E[1], Thanou I[2], Tavernaraki K[2], Thanos L[2]

[1]First Pediatric Clinic, National and Kapodistrian University of Athens, Agia Sofia Children's Hospital
[2]Department of Medical Imaging and Interventional Radiology, Sotiria General Hospital for Chest Diseases Athens, Greece

Abstract

Background: Percutaneous radiofrequency ablation (RFA) and microwave ablation (MWA) are well-established treatments for patients with non-small cell lung cancer (NSCLC). This study assessed the efficacy and safety of RFA and MWA performed on NSCLC patients.

Material and Methods: This retrospective study included one hundred twenty-four patients with NSCLC who underwent percutaneous ablation from November 2014 to November 2020 in the Department of Medical Imaging and Interventional Radiology of Sotiria General Hospital for Chest Diseases in Athens, Greece. Forty (stage IA) were treated with RFA, while 84 were treated with MWA (stages IA, IB, and IIA). All procedures were performed using the AMICA GEN radiofrequency and microwave generator. As a follow-up method, computed tomography was performed immediately after the procedure to evaluate the lesion's response and complications and one, three, six, and twelve months after the ablation.

Results: All ablations were technically successful. The first-month follow-up revealed stage IIA residual tumors in eight patients. Local recurrence was detected one year after RFA in two of the 40 patients and thirteen of the 84 patients after MWA. Overall survival (OS) rates at one, two, and three years for stage IA NSCLC patients treated with ablation were 94 %, 73 %, 57 % for RFA, and 96 %, 75 %, and 62 % for MWA, respectively. In contrast, the OS for stages IB and IIA patients treated with MWA was 90 %, 66 %, and 51 % for the IB stage and 82 %, 62 %, and 48 % for the IIA stage, respectively. Fifteen percent of patients after RFA and 9.5 % after MWA experienced minor complications. Pneumothorax was documented in three patients after RFA and four after MWA. Post-ablation syndrome occurred in 15 % of RFA patients and 8.3 % of MWA patients. There were no major complications.

Conclusion: RFA and MWA have comparable efficacy and safety for patients in stage IA. MWA is an effective alternative treatment option for non-resectable IB or IIA stages NSCLC patients. HIPPOKRATIA 2022, 26 (3):105-109.

Keywords: Lung, non-small cell lung cancer, NSCLC, radiofrequency, microwave, ablation

Corresponding author: Evanthia Botsa, First Pediatric Clinic, National and Kapodistrian University of Athens, Agia Sofia Children's Hospital, Thivon & Levadias, Goudi, Athens, Greece, tel: +306945559966, e-mail: evanthiabotsa@gmail.com

Introduction

Lung cancer is the most prevalent malignancy worldwide and the leading cause of cancer-related mortality[1]. Around 95 % of lung cancers are histopathologically either small cell lung cancers (SCLC) or non-small cell lung cancers (NSCLC). This differentiation is essential for accurate staging, therapy, and prognosis. The initial treatment of patients with NSCLC is determined by disease staging. Surgical resection is the gold standard of treatment for patients with early-stage disease; however, only one-third of patients are eligible for surgery[2]. Chemotherapy or radiotherapy administered concurrently is favored for patients with extensive intrathoracic disease. In contrast, advanced disease patients are managed palliatively with systemic and/or regional treatment modalities[3]. For the removal of tumors in patients with primary NSCLC, percutaneous ablation appears to be a viable alternative to surgery or radiation therapy[4]. Compared to chemotherapy and radiation therapy, there are fewer side effects, which may aid in reducing morbidity, mortality, and survival rates[5,6]. In patients with stage IA disease, thermal ablation may be curative, but surgery remains the preferred treatment option.

Radiofrequency ablation (RFA) and microwave ablation (MWA) rely on thermal tissue injury in a similar fashion[5]. MWA causes cell death via an electromagnetic field, unlike RFA's use of an electrical current. A more predictable ablation zone is achieved by MWA permitting multiple lesion treatments simultaneously and generates, in less time than RFA, larger volumes of coagulation[7]. Major complications are uncommon and comparable with both methods[8]. However, no convincing evidence

exists of differences regarding clinical outcomes, such as survival and local recurrence rates. This study aimed to conduct a retrospective analysis concerning the safety and efficacy of RFA and MWA procedures performed on NSCLC patients with varying disease stages.

Materials and methods

An analysis of retrospectively collected data was conducted, selecting NSCLC patients who underwent RFA or MWA percutaneous ablation from November 2014 to November 2020 in the Department of Interventional Radiology of Sotiria General Hospital for Chest Diseases in Athens. During hospitalization, patients received the standards of care according to institutionally approved protocols, and all human procedures were conducted in accordance with Helsinki's ethical guidelines. The hospital's Scientific Committee approved the retrospective collection and analysis of clinical data (decision No 18416, date: 15/11/2021).

Inclusion - Exclusion criteria

All patients included in this study met the following inclusion criteria: all lesions were histologically confirmed after a biopsy; all patients were not surgical candidates; they either refused surgery or could not undergo surgery due to anatomic or technical contraindications; all ablated lesions were less than five cm; patients had no more than two lesions; patients had a good Eastern Cooperative Oncology Group (ECOG) performance status (ECOG: 0 to 2); and all were referred to the interventionalist. According to the WHO classification of non-small cell carcinoma lung tumors, cases were classified as squamous cell carcinoma, large cell carcinoma, adenocarcinoma, and undifferentiated carcinoma.

The pre-procedural tests included platelet enumeration, the international normalized ratio (INR), and partial thromboplastin time. Coagulopathy (INR >1.5) or a <60,000 /mm^3 platelet count were exclusion criteria.

Patient characteristics

According to institutional protocols, patients were divided into two treatment-method-based groups. Depending on the method's availability, IA patients were treated with RFA or MWA, while IB and IIA patients were treated with MWA. Forty patients with stage IA NSCLC underwent RFA (23 males and 17 females, age range 48-78 years, median age 65.3 years). MWA was utilized in 84 NSCLC patients (52 males and 32 females, ages 47-82, median age 66.3 years). The MWA patient group included 46 patients in stage IA (29 males and 17 females), 24 patients in stage IB (13 males and 11 females), and 14 patients in stage IIA (10 males and 4 females). All patients were submitted to adjuvant therapies according to established oncology protocols. The characteristics of patients and tumors are detailed in Table 1.

Treatment protocol

All patients were informed before the procedure and provided written consent. We administered bromazepam (3 mg orally) and pethidine hydrochloride (50 mg intramuscularly) to all patients one hour before the procedure. Every ablation was carried out under local anesthesia with a lidocaine injection[9], utilizing spiral computed tomography (CT) guidance (Somatom Emotion Duo System, Siemens, Erlangen, Germany). Depending on the location of the lesion, patients were positioned either supine or laterally. All procedures were performed by an experienced interventional radiologist who opted for a safe, direct electrode insertion route (Figure 1). We monitored patients' pulse, blood pressure, and oxygen saturation during the entire procedure. All ablations were performed utilizing an AMICA-GEN programmable RF (450 kHz/200 W @ 50 Ohm) and MW (2450 MHz/190 W) generator (NH Hospital Service, Rome, Italy) coupled to a 17G and 16G antenna, respectively[10]. The energy consumed was 100 W. The duration of ablation varied based on lesion size, type, and location. Ablation was intended to result in coagulation necrosis of the radial region surrounding the lesion. During electrode retrieval, each tract was ablated. When the lesion was accurately punctured and the entire tumor was ablated, ablation was considered technically successful. We utilized dual-phase contrast-enhanced spiral CT to assess the patient's immediate ablation response and screen for complications. All patients were monitored for 24 hours for complications before being discharged if none occurred. CT follow-up examinations were planned and performed at one, three, six, and twelve months after ablation and every six months after that. Local recurrence rates and overall survival (OS) estimations were employed to evaluate the outcome[11].

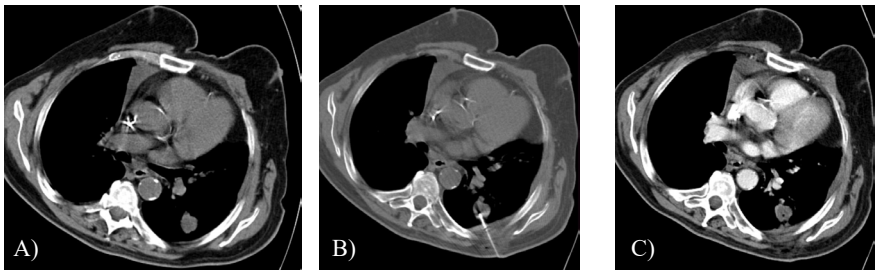

Figure 1: Axial computed tomography images of a male patient with non-small cell lung cancer of the inferior lobe of the left lung, treated with microwave ablation (MWA). A) Tumor lesion on computed tomography before MWA; B) the microwave antenna punctured the lesion; C) follow-up computed tomography immediately after MWA reveals imaging of the lesion as hypodense without contrast enhancement.

Table 1. Demographical, histology, disease stage profile, and follow-up of our series of 124 patients with non-small cell lung cancer patients grouped based on ablation method.

	Total	RFA	MWA		
Stage descriptors		**IA**	**IA**	**IB**	**IIA**
Number of cases	124	40	46	24	14
Age (years)	48-82	48-78	50-78	47-81	49-82
Males	75	23	29	13	10
ECOG Performance Status Scale					
0	58	21	24	8	5
1	50	17	18	10	5
2	13	2	4	3	4
Histology					
Squamous cell	37 (29.8 %)	10 (25 %)	12 (26 %)	10 (41.6 %)	5 (35.7 %)
ADC and large cell	77 (62.09 %)	27 (67.5 %)	30 (65.2 %)	12 (50 %)	8 (57.1 %)
NSCLC-Undiff	10 (8.06 %)	3 (7.5 %)	4 (8.6 %)	2 (8.3 %)	1 (7.1 %)
Lesion size (cm)		1.2-3	1.5-3	3-4	4-5
Ablation time (min)		8-14	4-6	5-7	5-7
Follow up					
Residual tumor - 1m follow-up		none	none	none	8
Tumor recurrence - 1y follow-up		2	2	5	6
Complications - minor	14	6 (15 %)		8 (9.5 %)	
Pleural effusion	4	2 (5 %)		2 (2.3 %)	
Minimal hemoptysis	10	4 (10 %)		6 (7.1 %)	
Pneumothorax	7	4 (10 %)		3 (2.8 %)	
Post ablation syndrome	13	6 (15 %)		7 (8.6 %)	

Data is presented as numbers and percentage in brackets. ECOG: Eastern Cooperative Oncology Group, RFA: radiofrequency ablation, MWA: microwave ablation, ADC: adenocarcinoma, NSCLC-Undiff: undifferentiated non-small cell lung cancer.

Complications

Complications were evaluated according to the Cirse Classification System of Complications Reporting[8]. Minor complications are defined as those that can be treated during the same procedure, while major complications require hospitalization or cause mild or severe sequelae or even death.

Statistical analysis

The data were analyzed using the statistical software IBM SPSS Statistics for Windows, Version 20.0. (IBM Corp., Armonk, NY, USA). All the data were entered and analyzed using descriptive statistics such as mean, median, and percentages.

Results

From November 2014 to November 2020, a total of 147 ablations were performed on 124 NSCLC patients. The median lesion size was estimated to be 2.22 cm (range: 1.2-3 cm) for RFA-ablated lesions and 3.77 cm (range: 1.5-3 cm) for MWA-ablated lesions. Regardless of tumor size, one needle position was used to perform ablations. The median ablation time for RFA was 11 minutes (range: 8-14 minutes), whereas the median ablation time for MWA was 4.6 minutes (range: 4-7). In eight of the fourteen stage IIA patients who underwent MWA, post-ablation imaging one month after ablation revealed a viable residual tumor. Every one of them had an effective second MWA session. Local recurrence was observed in 2/40 stage IA patients one year after RFA and 13/84 patients after MWA. Local recurrence was observed one year after MWA in 2 % of stage IA patients, 20 % of stage IB patients, and 42 % of stage IIA patients (Table 1). A second ablation was successfully performed on all those patients. According to our data, patients with a tumor diameter >3 cm (stage IB or IIA) had a higher rate of local recurrence. The median duration of follow-up was 38 months. In patients with stage IA NSCLC, the one, two, and three-year OS rates for RFA and MWA were 94 %, 73 %, and 57 %, respectively. One, two, and three-year OS rates following MWA were 90 %, 66 %, and 51 % for stage IB NSCLC patients and 82 %, 66 %, and 48 % for stage IIA patients, respectively.

Six out of forty (15 %) and eight out of 84 (9.5 %) patients experienced grade 1 minor complications after RFA and MWA, respectively. Five percent of patients who underwent RFA and 2.3 % who underwent MWA experienced minimal asymptomatic pleural effusion. Four out of forty (10 %) and 6/84 (7.1 %) patients treated respectively with RFA and MWA reported minimal hemoptysis. Pneumothorax occurred in seven patients, three after RFA and four after MWA; five cases were self-limiting, and the interventional radiologist immediately inserted a Heimlich catheter in two patients. Post-ablation syndrome was reported in 15 % of RFA patients and 8.3 % of MWA patients. Acute pulmonary bleeding, pneumothorax necessitating tube insertion, pulmonary embolism, excessive non-target tissue necrosis, bronchopulmonary fistulas, or death did not occur in our series.

Discussion

Depending on their size, NSCLC tumors without lymph nodes or other distant metastases are classified as stages IA, IB, or IIA, IIB. Thus, stage IA tumors are up to three cm in diameter, stage IB tumors are 3-4 cm in diameter, stage IIA tumors are 4-5 cm in diameter, and stage IIB tumors are 5-7 cm in diameter. Even though surgical resection is considered the treatment of choice for primary and metastatic lung cancer, many patients cannot undergo surgery due to advanced age, comorbidities, or insufficient pulmonary reserves to undergo pneumonectomy or lobectomy[12].

As traditional radiotherapy and chemotherapy offer limited benefits to patients with unresectable lung cancer, many new local treatment methods, including percutaneous ablation therapy, have emerged[13]. RFA is the most studied thermal ablation technique for lung lesions; consequently, numerous researchers have emphasized RFA as a treatment option for inoperable NSCLC[14]. The American College of Chest Physicians (ACCP) guidelines include percutaneous ablation as a therapeutic option for stage I NSCLC patients who are inoperable. The RAPTURE study and the American College of Surgeons Oncology Group Z4033 trial (51 patients with IA NSCLC) reported one-year OS rates of 86.3 % and two-year OS rates of 69.8 %, with two-year survival rates increasing to 83 % for patients with lesions less than two cm and better performance status[15,16]. Our study indicates that stage IA patients' one, two, and three-year OS rates are 94 %, 73 %, and 57 %, respectively.

MWA is increasingly utilized, either alone or as an adjunct to chemotherapy, radiotherapy, and limited pulmonary resection, with promising results regarding technical feasibility, therapeutic response, short- and long-term survival, and a low incidence of complications when performed by an experienced interventional radiologist[17]. MWA demonstrates similar efficacy to RFA but also allows for a larger and more uniform necrosis volume, a shorter treatment duration, and better lung tissue penetration[18]. The randomized, controlled LUMIRA study of lung RFA versus MWA in 52 patients with stage IA disease revealed no difference in survival. Still, MWA was associated with less pain and a more significant reduction in tumor size[19]. Local control rates of 96 % and 48 % at one and five years after MWA were reported by Yang et al, while OS rates at one, two, three, and five years were respectively 89 %, 63 %, 44 %, and 16 %, with significantly improved survival in patients with smaller than 3.5 cm^2 lesions[20]. Our study displays comparable, if not more promising, results than previous publications. The median duration of overall survival was 38 months. OS rates at one, two, and three years were 96 %, 75 %, and 62 % for stage IA; 90 %, 66 %, and 51 % for stage IB; and 82 %, 62 %, and 48 % for stage IIA, respectively. OS for stage IA patients after MWA is marginally better than after RFA (one, two, and three-year OS were 94 %, 73 %, and 57 %, respectively); therefore, these two ablation techniques have comparable efficacy. In addition, these results suggest that MWA improves the survival of NSCLC patients in stages IB and IIA.

The average lesion diameter in the RFA group was 2.22 cm, whereas 3.77 cm in the MWA group, constituting the primary factor that led us to choose MWA over RFA. Local recurrence was observed one year after MWA in 4.3 % of patients with stage IA, 20.8% with stage IB, and 42 % with stage IIA. Greater local recurrence rates were observed in patients with tumor diameters exceeding three cm (stages IB and IIA); thus, our data confirm literature evidence that tumor size is an independent predictor of local tumor recurrence after ablation, with three cm being the most frequently reported threshold for statistical significance[16,21]. In the case of larger tumors, combination therapy may be utilized. According to Wei et al, combining chemotherapy and MWA in patients with advanced NSCLC increased progression-free survival compared to chemotherapy alone without increasing the adverse effects of chemotherapy[6].

There are a few complications reported after thermal ablation[8,14]. Pneumothorax, the most frequent complication, is reported between 8 % and 63 %[5,13]. In our series, the incidence of pneumothorax was 5.6 % (7.5 % after RFA and 4.7 % after MWA), 71.4 % being self-limiting, and 28.5 % treated by interventional radiology with immediate insertion of a Heimlich catheter. As mentioned by Rothman et al, we also observed that chronic obstructive airway disease and the central location of the lesion were associated with an increased incidence of pneumothorax[22]. Fifteen percent and 9.5 % of patients experienced minor complications such as minimal pleural effusion and minimal hemoptysis following RFA and MWA, respectively. The incidence of post-ablation syndrome was 15 % after RFA and 8.3 % after MWA. The fact that in our series, no major complications occurred and the rate of minor complications was relatively low was likely due to the fact that an experienced interventional radiologist performed all procedures. Practically, treatment response to RFA and MWA can only be determined through radiological follow-up[11,23]. On a post-treatment CT scan, the ablation zone appears as a ground glass opacity surrounding the targeted tumor. Immediately after the ablation and even one month later, the ablation zone appears as a region surrounding the original lesion area with specific radiological characteristics (size and density), whereas for the three-month follow-up, dimensional criteria are used. Our patients were evaluated with both criteria in every follow-up for persistent or recurrent disease.

Our study confirms the efficacy and safety of RFA and MWA in treating patients with stage IA NSCLC, with comparable rates of overall survival, local recurrence, and complications. Positive outcomes were observed in patients with NSCLC stages IB and IIA, demonstrating the efficacy of MWA even in this patient population. The findings of this study must be considered in light of existing limitations that could be addressed in future studies. Firstly, only a small number of patients in stages IB and IIA were included in the study. Secondly, the group deter-

mination was made retroactively. Nevertheless, the study provides valuable insights into the early stages of cancer. It serves as a springboard for further investigation, especially for patients with stage IB, IIA. Future research should employ a larger sample size and a prospective group determination to avoid retrospective bias.

Conflict of interest

The authors declare that they have no conflict of interest.

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