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Original Article

Results of Radiofrequency Ablation Treatment for Patients with Inoperable Non-Small Cell Lung Cancer at Nghe an Provincial Oncology Hospital, Vietnam

Pham Vinh Hung[1]*, Nguyen Van Hieu[2] and Nguyen Quang Trung[3]

1. Nghe An Oncology Hospital, Vietnam
2. Hanoi Medical University, Vietnam
3. Hue University of Medicine and Pharmacy, Vietnam

Abstract

Background: To evaluate the results of Radiofrequency Ablation (RFA) treatment for patients with inoperable Non-Small Cell Lung Cancer (NSCLC) at Nghe An Provincial Oncology Hospital.

Methods: An uncontrolled clinical intervention study, comparing before-and-after results on 63 inoperable NSCLC patients who were treated with radiofrequency ablation at Nghe An Provincial Oncology Hospital from January 2014 to August 2022.

Results: In the 63 patients studied, the average age was 64.8±7.9 *yrs*. Men accounted for 82.5%. The average tumor size was 4.45±1.86 *cm*. The group of tumors with a size of 5 *cm* accounted for 39.7%, from 3 *cm* to less than 5 *cm*, and tumors <3 *cm* all had a rate of 30.2%. There were 34 cases of partial response (54.0%), 31.7% of intact disease, and 14.3% of progressive disease. There was no complete response. The results of multivariate Cox regression analysis showed that tumor size <3 *cm* (HR=0.258; 95%CI:0.094-0.703), mild disease stage (Stage I/II/III) (HR=0.263; 95%CI: 0.099-0.696) and having a treatment response after RFA (HR=0.332; 95%CI: 0.160-0.690) were factors that affect the patient's overall survival time.

Conclusion: RFA is a minimally invasive treatment method that is effective in local tumor control and survival time.

Keywords: Non-small cell lung cancer, Radiofrequency ablation, Survival, Vietnam

*** Corresponding author**

Pham Vinh Hung, PhD
Nghe An Oncology Hospital, Vietnam
Email: nguyenthithi19699@gmail.com

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Introduction

Primary lung cancer has become one of the most prevalent malignancies worldwide over the past few decades. According to GLOBOCAN 2022 data, lung cancer was the most frequently diagnosed cancer, approximately 2.5 million new cases and 1.796 million deaths were reported globally, accounting for 18% of all cancer-related fatalities (1). In Vietnam, preliminary data from population-based cancer registries indicate a high incidence of primary lung cancer in both men and women, with over 20,000 new cases diagnosed annually (2). While smoking remains the primary etiological factor, environmental exposures such as air pollution, secondhand smoke, radon gas, and occupational carcinogens significantly contribute to lung cancer development. The increasing levels of air pollution, particularly fine Particulate Matter (PM 2.5) from vehicle emissions, industrial activities, and wildfires, are a major risk factor, especially in urban areas (3). These environmental factors, exacerbated by modern pollution trends, drive genetic mutations associated with lung cancer, underscoring the critical need for early detection and intervention, particularly for Non-Small Cell Lung Cancer (NSCLC), the most common subtype (4).

NSCLC accounts for 75-80% of all lung cancer cases (5). It is a heterogeneous group of cancers, including adenocarcinoma, squamous cell carcinoma, and large cell carcinoma (6). For NSCLC patients with early-stage disease who are unsuitable for surgical intervention or for those with locally advanced stages, radiotherapy serves as the preferred treatment option. Radiotherapy plays a crucial role in local disease control and overall survival improvement. However, this approach may not be suitable for patients with comorbidities, particularly those with functional lung ventilation impairment (7,8)

Radiofrequency ablation (RFA) is a minimally invasive technique that utilizes heat to destroy localized tumors. This method is currently under investigation and being applied in the treatment of NSCLC (5,6). To date, there have been limited studies conducted in Vietnam exploring the application of RFA in NSCLC treatment, and initial observations have been restricted due to time constraints and patient numbers. This study aims to assess the efficacy and safety of RFA in the treatment of inoperable early-stage NSCLC patients in Vietnam.

Materials and Methods

Participants

Between January 2014 and August 2022, 63 inoperable NSCLC patients were treated with RFA at Nghe An Provincial Oncology Hospital. Patients included in the study were required to have a confirmed diagnosis of NSCLC based on histopathological examination and to have undergone staging using the Tumor-Node-Metastasis (TNM) cancer staging system (11,12).

They were considered inoperable due to various factors, including medical comorbidities and functional status limitations [*e.g.*, Eastern Cooperative Oncology Group (ECOG) ≥2, cardiovascular disease, or respiratory insufficiency] (13). Tumor-related contraindications such as proximity to major airways, blood vessels, or the heart, as well as tumor-associated lung collapse or multiple primary cancers, also rendered them unsuitable for surgery or chemoradiotherapy. Additionally, patients with significant coagulation disorders, defined as a prothrombin ratio <60% or platelet count <50 *G/L*, were excluded from surgical interventions. Some patients declined surgery or chemoradiotherapy due to personal, financial, or logistical reasons, opting for RFA as a less invasive alternative.

In select Stage IV patients, the primary lung tumor was ablated for palliative purposes, primarily to relieve symptoms such as hemoptysis, cough, dyspnea, or pain. In some cases, RFA was performed to achieve local tumor control and prevent complications such as airway obstruction or tumor invasion into adjacent structures. All treatment decisions were made following multidisciplinary case discussions, with RFA pursued only when clinically justified.

Data collection

Conduct RFA technique: The *RFA* was meticulously conducted to ensure precision and effectiveness. Initially, a Computed Tomography (CT) scan was performed to determine the cross-sectional view of the target area, the exact location for needle insertion, and the angle required to guide the needle to the center of the tumor. An electrode was placed on the patient's thigh, positioned perpendicularly to the direction of the needle. The high-frequency

generator was prepared with precise settings, and the patient was administered pre-anesthesia, provided with continuous oxygen ventilation, and closely monitored using a medical monitor. To maintain sterile conditions, the skin at the puncture site was disinfected, and a sterile surgical cloth was carefully draped around the area (14,15).

Local anesthesia

Local anesthesia was administered before the needle was inserted according to the pre-determined guide. CT imaging was then used to confirm the correct positioning of the guide needle. Once confirmed, the RFA machine was activated to burn the lung tumor according to its automatic parameters. The procedure commonly employed the standard ablation mode, in which the system automatically adjusted impedance and power levels to effectively burn different tissue types. The duration of the burning process varied based on the tumor size. For tumors with a diameter within the heat radiating range of the needle, the procedure typically lasted 8 *min*. Larger tumors were addressed in segments, with each burning session taking no more than 30 *min*. In cases of multiple tumors, each block was treated sequentially to ensure maximum effectiveness (16) (Appendix 1).

Assess overall condition according to ECOG

The ECOG Performance Status Scale, which assessed a patient's overall condition based on their functional ability was outlined (13). It ranged from Grade 0, indicating full activity without restrictions, to Grade 5, representing death. Intermediate grades described varying levels of impairment: Grade 1 reflected limited strenuous activity but the ability to perform light tasks; Grade 2 indicated self-care capability but an inability to work, with over 50% of waking hours active; Grade 3 described limited self-care and confinement to a bed or chair for more than half the day; and Grade 4 represented complete disability and total confinement to bed or a chair. The scale provided a concise and systematic method for evaluating patient functionality (Appendix 2).

Criteria for evaluating solid tumor response according to RECIST (Response Evaluation Criteria in Solod Tumors)

RECIST 2009 standards are based on target lesions, assessed by clinical examination and imaging tests (ultrasound, CT-scanner, endoscopy) (17). Target lesions are measurable lesions, take a maximum of 5 lesions (maximum 2 lesions per organ), take the sum of the largest diameters of the lesions selected as the target lesion as the basis for evaluation response (Appendix 3).

Data analysis

Data were entered into EpiData and verified for accuracy before analysis using Stata 13.0. Descriptive statistical methods, including frequency, rate, percentage, mean, and Standard Deviation (SD), were used. The Chi-square (χ^2) test and Cox regression analysis were performed to identify factors associated with ANC utilization, with statistical significance set at $p<0.05$.

Ethical approval

This study was approved by the Institutional Review Board of Hanoi Medical University (Approval No. QĐ 224/HĐĐĐĐHYHN, dated December 30, 2016). All participants received detailed information about the study, and written informed consent was obtained from each individual prior to participation. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Results

According to table 1, 63 patients with prostate cancer had an average age of 64.8 *yrs*, predominantly male (82.5%), with an average weight of 51.6 *kg* and a high smoking prevalence (77.8%). Over half of the patients had ECOG PS scores of 1 or 2, with an average tumor size of 4.45 *cm*. Most tumors were classified as stage T2, N2, and M1, with stage IV being the predominant disease stage. Partial response to treatment was observed in 54.0% of patients.

Eastern Cooperative Oncology Group: ECOG

Table 2 summarized the treatment responses observed in 63 patients. Among them, 54.0% had demonstrated a partial response, while 31.7% had shown no response, and 14.3% had experienced disease progression. Notably, no patients had achieved a full response to the treatment.

Table 1. General characteristics of participants

Characteristics			Frequency (n = 63)	Percentage %
Age (yrs)	<50		2	3.2
	50-59		15	23.8
	60-69		30	47.6
	≥70		16	25.4
	$\overline{X}$ ± SD (Min-Max)		64.8±7.9 (46-85)	
Gender	Male		52	82.5
	Female		11	17.5
Height (*cm*)	$\overline{X}$ ± SD (Min-Max)		161.1±5.2(150-176)	
Weight (*kg*)	$\overline{X}$ ± SD (Min-Max)		51.6±7.7 (38-72)	
Body Mass Index (BMI, kg/m^2)	Underweight		24	38.1
	Healthy weight		30	47.6
	Overweight		9	14.3
	$\overline{X}$ ± SD (Min-Max)		19.9±3.1 (15.2-27.6)	
Smoking	Yes		49	77.8
	No		14	22.2
ECOG scale	0		5	7.9
	1		34	54.0
	2		24	38.1
	3-4		0	0
Tumor size (*cm*)	<3		19	30.2
	3-5		19	30.2
	≥5		25	39.7
	$\overline{X}$ ± SD (Min-Max)		4.45±1.86 (1.5-8.7)	
Cancer stage	T	T1	17	27.0
		T2	22	34.9
		T3	16	25.4
		T4	8	12.7
	N	N0	9	14.3
		N1	16	25.4
		N2	22	34.9
		N3	16	25.4
	M	M0	29	46.0
		M1	34	54.0
	General stage	Stage I	9	14.3
		Stage II	11	17.4
		Stage III	9	14.3
		Stage IV	34	54.0

Table 2. Treatment response outcomes in patients (n=63)

Treatment response	Frequency (n=63)	Percentage %
Fully response	0	0
Partly response	34	54.0
No response	20	31.7
Progressive disease	9	14.3

Table 3 presents a multivariate Cox regression analysis of factors affecting overall survival time, identifying several significant findings. Tumor size smaller than 3 *cm* was associated with improved survival (HR=0.258, 95% CI:0.094–0.703, p=0.008), as was earlier cancer stage, with patients in stages I–III showing better outcomes than those in stage IV (HR=0.263, 95% CI:0.099–0.696, p=0.007). Positive response to RFA also significantly improved survival (HR=0.332, 95% CI 0.160–0.690, p=0.003). In contrast, gender, age, Body Mass Index (BMI), smoking status, and ECOG performance scale were not significantly associated with survival. These results highlight the critical role of tumor size, cancer stage, and RFA response in survival outcomes.

Discussion

The American College of Chest Physicians (ACCP) evidence-based clinical practice guidelines had suggested that RFA could be considered a treatment option for inoperable patients with stage I NSCLC, particularly for peripheral tumors smaller than 3 *cm* (18). Similarly, the 2017 clinical practice guidelines from the European Society for Medical Oncology had highlighted RFA as a viable alternative for managing stage I NSCLC (19). Furthermore, the National Comprehensive Cancer Network (NCCN) guidelines version 1.2020 had recommended definitive radiation therapy, including Stereotactic Body Radiation Therapy (SBRT), for medically inoperable patients with stage IA NSCLC, and had acknowledged

Table 3. Multivariate analysis of factors affecting overall survival time

Indicators		Cox regression analysis		
		HR	95%CI	p-value
Gender	Female		ref	
	Male	0.574	0.229-1.436	0.236
Age (*yrs*) group	≥60		ref	
	<60	0.635	0.303-1.332	0.230
BMI (kg/m^2)	Healthy weight		ref	
	Underweight	1.625	0.789-3.347	0.188
	Overweight	1.361	0.560-3.308	0.496
Smoking	No		ref	
	Yes	0.785	0.352-1.752	0.555
ECOG Scale	2		ref	
	0-1	1.040	0.540-2.003	0.907
Tumor size (*cm*)	≥3		ref	
	<3	0.258	0.094-0.703	0.008
Cancer stage	Stage IV		ref	
	Stage I. II. III	0.263	0.099-0.696	0.007
RFA response	No		ref	
	Yes	0.332	0.160-0.690	0.003

image-guided thermal ablation as an option for carefully selected cases (20).

In this study of 63 patients, age was identified as a significant risk factor for cancer, with the majority of patients falling within the over-50 age group. The most common age range was 60-69 years old, accounting for 47.6% of the patients. The average age was 64.8±7.9 *yrs*. These findings are consistent with previous studies by Picchi *et al* (21) and Simon, who reported average ages of 67.7±8.7 years and 75.5± 7.52 years, respectively (10). The lower average age in this study may be attributed to the lower life expectancy in Vietnam compared to European countries. Additionally, the study found a high smoking prevalence of 77.8%, comparable to rates reported in other studies of Scagliotti (22) ,Ciuleanu (23).

In the present study, the PS 1 patient group accounted for the largest proportion with 54.0%, the PS 2 patient group accounted for a lower proportion with 38.1%, the PS 0 patient group had only 5 patients accounting for 7.9%. Research by Seyer Safi and colleagues (24) on 25 patients treated with RFA showed that 16% of patients had a general status index of PS 0; 84% of patients had a general status index of PS 1 (13). According to Semiha Elmaci Urvay studied on 148 patients in stage III, at the time of diagnosis ECOG PS=0-1 accounted for the majority (81%) (14). In PARAMOUNT study, author Ciuleanu T and CS studied on 663 patients, 39.4% of patients had PS = 0 and 60.3% of patients had PS=1 (12). According to Scagliotti GV and CS (2008) (1,725 patients), the proportion of patients with PS=1 is 64.3%, PS=0 is 35.7% (11). We believe that there is a difference partly due to the geographical differences in patient populations in the studies, partly because our study population included both stage III and IV patients with more severe conditions than the above authors.

The present study revealed an average tumor size of 4.45±1.86 *cm*. The tumor size distribution was as follows: >=5 *cm* (39.7%), 3-5 *cm* (30.2%), and <3 *cm* (30.2%). These findings are consistent with the observation that the present study population primarily comprised stage III and IV patients, typically associated with larger tumor sizes. In comparison, Lee's study of 31 patients with primary and metastatic lung cancer reported an average tumor size of 5.2±2.4 *cm*, suggesting larger tumor dimensions in their patient cohort (15).

Overall survival time serves as a crucial metric for assessing the efficacy of treatment modalities, including RFA therapy. In the present study, 58 patients succumbed during follow-up, while two were lost to contact. Notably, three patients remained alive after five years, yielding a median overall survival of 20.5 months. The shortest survival period was four months, whereas the maximum was 60 months. The overall survival rate progressively diminished over time, reaching only 6.3% by the fifth year.

Lee *et al* conducted a study on a group of NSCLC patients treated with radiofrequency ablation and reported an overall survival time of 15.2±5.1 months (15). Notably, patients treated with curative intent demonstrated a significantly longer survival time of 21.1 months compared to the 8.7 months observed in the palliative treatment group. This study further revealed that patients with complete tumor necrosis following treatment exhibited a superior overall survival time of 19.7 months compared to those with partial necrosis (8.7 months). Additionally, patients with tumor sizes smaller than 3 *cm* displayed a longer overall survival time (18.6 months) compared to those with tumor sizes greater than 3 *cm* (11.7 months).

This study also shows that overall survival time is different in treatment groups with different goals. However, this study had a lower overall survival time in both groups of patients than the present study, which is explained by the increasingly advanced radiotherapy techniques and equipment, in addition to the increasing number of patients. More and more new chemical drug groups are being researched such as pemetrexet, anti-angiogenesis drugs, targeted therapy drugs and immunotherapy drugs, thereby increasing survival time for lung cancer patients (16-18).

According to the study of Shuhui Du and colleagues (10) on 77 patients with late stage NSCLC (III, IV) divided into 2 groups. Group 1 includes patients receiving chemotherapy combined with RFA, group 2 includes patients receiving chemotherapy alone. The study results showed that group 1 had an average overall survival of 22.1 months, with 1-year and 2-year survival rates of 70.74 and 39.31%, respectively. Group 2 had a lower average overall survival time

of 18.1 months (6). It can be seen that this author's results are similar to the present study both in terms of average survival time as well as survival rate.

After incorporating various factors into the multivariable Cox regression analysis, only three were found to significantly impact overall survival time: tumor size, disease stage, and treatment response following RFA. Similar findings were reported in a study by T.D. Yan and colleagues, which indicated that RFA was less effective for tumors larger than 3 *cm*, with over 70% of such patients dying within 14 months (19). Dupuy DE also highlighted that smaller tumor sizes, early-stage disease, and solitary lung lesions positively influenced local disease progression (20). Matsui *et al* reported survival rates after RFA treatment for stage I NSCLC to range from 83-96% at one year, 40-74% at three years, and 23-61% at five years (14). Similarly, Lam *et al* (32) found survival rates for early-stage NSCLC patients treated with RFA to be 89.8% at one year, 51.2% at three years, and 27.7% at five years (32). A comparative analysis by Jiachang Chi and colleagues between RFA and microwave ablation showed similar survival durations: 33 months (95% CI: 27.070–38.930) for RFA and 30 months (95% CI: 18.482–41.518) for microwave ablation (21). These findings suggest that the effectiveness of the two modalities is comparable (34). Similarly, Zemlyak et al (2010) found that the three-year survival rates of RFA and cryotherapy were similar (87.5 *vs*. 77%), although higher than in this study, as their subjects were limited to stage I patients with less severe disease (22). These results reinforce the potential benefits of RF ablation for early-stage NSCLC patients and suggest that regionalized lung cancer management could improve overall survival outcomes (36,37).

The present study highlighted the potential of RFA as a minimally invasive treatment option for inoperable NSCLC, contributing valuable clinical insights into patient outcomes and survival factors. By identifying key prognostic indicators such as tumor size, disease stage, and treatment response, present findings helped refine patient selection criteria and improve treatment strategies in the field of interventional oncology.

Conclusion

RFA is a minimally invasive treatment method that is effective in local tumor control and survival time. In the future, more studies should be done with larger sample sizes to have more solid evidence of the effectiveness of the method.

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Conflict of Interest

The author team declares no potential conflicts of interest with respect to the authorship and/or publication of this manuscript.

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