Long-Term Results of Radiofrequency Ablation Treatment of Stage I Non-small Cell Lung Cancer

A Prospective Intention-to-Treat Study

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Introduction: About one-fifth of patients with resectable non-small cell lung cancer (NSCLC) are unsuitable for surgical treatment. Radiofrequency ablation offers an alternative minimally invasive option. We report the result of an intention-to-treat study with long-term follow-up.

Methods: From 2001 to 2009, we performed 80 percutaneous radiofrequency ablations of 59 stage I NSCLC in 57 inoperable patients. Two patients were treated for two separate lesions. The study group consisted of 45 males and 12 females, with mean age of 74 years (range, 40–88 years). All patients had pathological evidence of NSCLC, which was in stage IA in 44 cases and in stage IB in the other 15 cases. The mean size of the lesions was 2.6 cm (range, 1.1–5 cm). Fourteen lesions were retreated up to five times. The procedure was always performed under local anesthesia and conscious sedation. Most of the procedures were performed under computed tomography guidance, with nine under ultrasonography guidance.

Results: In all cases, the procedure was technically successful. No mortality was recorded, and major morbidity consisted of four cases of pneumothorax requiring pleural drainage. At a mean follow-up of 47 months, the complete response rate was 59.3% (stage Ia 65.9%, stage Ib 40%, $p = 0.01$), with a mean local recurrence interval of 25.9 months. Median overall survival and cancer-specific survival were 33.4 and 41.4 months, respectively. Cancer-specific actuarial survival was 89% at 1 year, 59% at 3 years, and 40% at 5 years.

Conclusions: Radiofrequency ablation treatment of early-stage NSCLC seems to be a effective minimally invasive therapy even in the long-term period, particularly for stage Ia tumors.

Key Words: NSCLC, Early stage, Radiofrequency ablation, Percutaneous thermal ablation, Minimally invasive treatment.

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Surgical resection remains the cornerstone of therapy for early-stage non-small cell lung cancer (NSCLC). Lobectomy with hilar and mediastinal lymphadenectomy is the standard surgical treatment for stage I and II disease and offers the best chance for cure. Five-year survival rates are reported between 57 to 85% for stage I and 39 to 55% for stage II disease.[1,2] The extent of pulmonary resection required to achieve complete eradication of the malignancy has been a hotly debated issue. Recently, some studies evaluate the role of sublobar resections such as segmentectomy for early-stage NSCLC, showing functional advantage,[3–6] but doubts about disease control still persist.[1] However, many patients with resectable early-stage disease are unable to tolerate pulmonary resection, even sublobar resection, because of compromised cardiopulmonary functions or other comorbidities. El-Sherif et al.[1] estimate that more than 20% of patients who are diagnosed with early-stage NSCLC do not undergo operation because of comorbidity health factors. Traditionally, patients deemed medically inoperable have been treated by external-beam radiation. Even if this therapy generally increases survival in patients with early-stage NSCLC, the results were poor, with a mean survival of 20 months and a 5-year survival rate of 12%.[7,8]

In this scenario, it is not surprising if we have been witness to a strong drive to develop other nonsurgical local therapies. On one hand, there has been an evolution of the same radiation therapy which led to the stereotactic technique with interesting preliminary results.[9–11] On the other hand, since the early 1990s, image-guided percutaneous ablation procedures have been developed to treat solid tumors, both primary and secondary, starting from that of the liver and then being transferred also to the lung tumors.[12–16] Today, many authors describe percutaneous radiofrequency ablation

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(RFA) as a minimally invasive technique with promising oncological results and a relative degree of safety for treatment of NSCLC.[17–21] But few data are available about its efficacy with a reasonable follow-up. Herein, we report the outcomes of a prospective single-center study in the RFA treatment of stage I NSCLC.

MATERIALS AND METHODS

This study received approval from the local ethical committee for human research care. The primary end points of the study were technical success, safety, and complete ablation (CA) of the target tumor (evaluated at a minimum follow-up of 1 year). Secondary end points were overall and cancer-specific survival.

Patients were required to sign a written informed consent, after adequate explanation of risks and possible benefits of the procedure.

Preoperative Assessment and Selection Criteria

All patients underwent preoperative assessment as for major pulmonary resection: chest radiograph, computed tomography (CT) scan of the chest and upper abdomen, lung function test, and cardiovascular evaluation. Additional exams (e.g., brain CT scan, bone scintigraphy, and positron emission tomography [PET]) were used in selected cases, when clinical/radiological criteria raised the suspect of distant metastases. Patients with mediastinal nodes greater than 1 cm in short axis diameter on CT scan underwent transbronchial needle aspiration and/or PET scan to exclude N2 disease.

The first selection criteria was a contraindication: contraindication to surgical treatment. A thoracic surgeon, together with an experienced anesthesiologist, evaluated the patients as not suitable for lung resection. Main contraindications to surgery were presence of significant comorbidity and poor lung function that makes the patient unable to tolerate even a limited lung resection. Comorbidity was evaluated prospectively according to the Adult Comorbidity Evaluation-27 (ACE-27) scoring system. Moreover, three patients refused surgery. Other main selection criteria were lesions $\leq$5 cm; a distance from large vessels and airways more than 1 cm; preoperative pathological proof of malignancy; and a platelet count greater than $50 \times 10^3/\mu$l.

Devices and Technique

We used a radiofrequency generator able to provide monopolar energy to perform coagulation and ablation of soft tissue (RITA Model 1500 and 1500X, AngioDynamics, Latham, NY). This is an automatic device with a maximum power output of 150 to 250 W operating at 460 MHz. The generator has a display where temperatures, impedance, and power are continuously monitored. The energy was transferred into the lesion by a deployable array (StarBurst XL, AngioDynamics). It consists of a 14-gauge needle cannula with nine deployable electrodes that open flower-like up to 5 cm. Five electrodes have a thermocouple on the tip which allows continuous measurement of treatment temperature. Two grounding pads were applied to each shaved leg to ground the current and to reduce risks of heat injuries to the skin.

All the procedures were performed with the patients under conscious sedation (usually achieved with administration of ketorolac 0.5–0.8 mg/kg, propofol 1–2 mg/kg/h, and remifentanil 0.1 mg/kg/min) and local anesthesia (subcutaneous 1% lidocaine). Vital signs of the patient were noninvasively monitored continuously. We used CT guidance in the most of cases while, more recently, lesions in contact with parietal pleura underwent RFA by ultrasonography guidance. In all cases, the target temperature was 90°C. It was maintained, according to the protocol, for a time which ranged from 15 to 27 minutes according to the size of the tumor, which also determined the deployment of the electrodes (Table 1). These electrodes were deployed gradually, starting from 2 cm and then 1 cm for each step. Since 2007, we used a new deployable array (StarBurst Talon, AngioDynamics) with a perfusion system (Intelliflow pump, AngioDynamics) that operates at 105°C, reducing the time at target temperature to 5 to 9 minutes, again according to the size of the tumor (Table 1). In all cases, when technically possible, the objective of the lung RFA protocol was to encompass the tumor with an ablation zone around the tumor of at least 1 cm thickness. At the end of the procedure, after the automatic cooling down of the radiofrequency system, the expandable tines were retracted and the generator shifted to "track ablation mode" which allows ablation of the pathway from the tumor to the subcutaneous tissue to prevent bleeding or tumor cell dissemination. After the procedure, all patients were transferred to the recovery room for a 24-hour observation period. Then, after a chest radiograph to exclude complications, they were discharged.

Follow-Up and Evaluation Criteria

Radiological follow-up included contrast-enhanced CT at 1, 3, and 6 months and then at 6-month intervals. CT scans were evaluated by two physicians, the same who performed the procedure and another experienced thoracic surgeon or radiologist. First evaluation was done just after RFA with a postprocedural CT enhanced with contrast material. Technical success was defined as correct placement of the ablation device into all target tumors with completion of the planned ablation protocol (maintenance of the target temperature for the required time according to tumor size).

The safety assessment included identification of treatment-related complications and changes in pulmonary function. Pulmonary function testing, obtained before and after RFA, included measurement of forced expiratory volume in the first second (FEV1), FEV1% of that predicted, forced vital capacity (FVC), and FVC percentage of that predicted.

TABLE 1. RFA Protocols According to the Device and the Size of the Lesion

Tumor Diameter	Electrodes Deployment/Time at Target Temperature	
	StarBurst XL	StarBurst Talon
<2 cm	3 cm/15 min	3 cm/5 min
2–3 cm	4 cm/20 min	3.5 cm/7 min
>3 cm	5 cm/27 min	4 cm/9 min