Radiofrequency Ablation of Inoperable Non-Small Cell Lung Cancer

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Radio frequency ablation (RFA) of lung tumors is a relatively new procedure allowing local treatment with minimal parenchymal damage. This technique is able to induce coagulative necrosis in a limited pulmonary area.1 This emerging technology is used to achieve local treatment of primary and secondary lung tumors in patients with poor clinical status or technical contraindications to surgical resection.2,3

MATERIALS AND METHODS

Preoperative patient assessment is the same methodology used for major pulmonary resection. The current election criteria include contraindication to surgical treatment; maximal diameter of the tumor less than or equal to 5 cm; lesions located more than 1 cm from major blood vessels or airways; patients with platelet count of more than 50 \(\times 10^3/\mu\text{L}\).

To produce monopolar radiofrequency energy, we used an automatic apparatus with maximal power output of 150 W operating at 460 Hz (Model 1500; RITA Medical System, Mountain View, CA). It has multiple temperature displays and impedance and power monitoring, and software is available to record and graphically represent all the data on a personal computer. The energy is transferred to the tissue by means of a multi-tined expandable array (Starburst XL; RITA Medical System). It consists of a 15-gauge needle cannula with nine deployable electrodes that open flower-like up to 5 cm. Five electrodes are equipped with thermocouples that allow continuous measurement of the temperature inside the tissue. Two grounding pads are applied to each shaved leg to ground the current and to reduce risks of skin thermal injury.

The procedure is performed with the patients under conscious sedation (ketorolac 0.5–0.8 mg/kg, propofol 1–2 mg/kg/h, and remifentanil 0.1mg/kg/min) and local anesthesia (subcutaneous 1% xylocaine). Vital signs are continuously, non-invasively monitored. Computed tomographic (CT) guidance is used in most cases; it is usually enhanced by the administration of contrast material before and after coagulation to obtain information about the real effectiveness of the procedure. In a selected group of patients with the tumor in contact with the thoracic wall, it is possible to work under ultrasound guidance. The needle electrode is inserted through an intercostal space after administration of local anesthesia. The correct placement is confirmed by CT or ultrasound before applying the radiofrequency energy. The target temperature of ablation is 90°C. It is maintained for 15 to 27 minutes according to the size of the tumor; this variable also determines the gradual deployment of the electrodes, starting from 2 cm and then 1 cm for each step. When technically feasible, the ablation zone should include the whole lesion and 1 cm of the surrounding lung parenchyma.

After RFA, the ablation zone is generally visible at CT scan as a ground glass opacity surrounding the target lesion. After the procedure, the patient is transferred to the recovery room for observation. Twenty-four hours later, after performing a chest radiograph to exclude the occurrence of any complication (e.g., pneumothorax), the patient is discharged. Radiological follow-up includes contrast-enhanced CT scan at 1, 3, and 6 months and then at 6-month intervals.

RESULTS

Since 2001, we have performed more than 100 RFA of lung tumors. In 50 cases, radiofrequency ablation was used for non-small cell lung cancer (NSCLC) for 42 men and 8 women with mean age of 73.7 years (range, 51–89 years). RFA was performed because of medical contraindication to surgery in 36 patients with stage I NSCLC and because of advanced disease in 14 cases, often with an integrated therapeutic approach.

All the procedures were well tolerated. We observed no mortality, and morbidity consisted of five cases of partial pneumothorax (10%), two of which required pleural drainage.

At a median follow-up period of 31 months, the overall radiological complete response rate was 59%, and median survival was 25 months (61% and 28.9 months, respectively, in stage I disease).

DISCUSSION

After the first percutaneous RFA of lung lesions reported by Dupuy et al. in 2000,4 a number of works have described the feasibility and safety of the procedure. In particular, an international survey with almost 500 RFA of lung tumors reported by Steinke and colleagues in 2004 stressed the low
invasiveness approach of this technique, negligible mortality, low morbidity, short hospital stay, and quality of life improvement.\(^5\)

Most of the reports address short-term results with encouraging data. Herrera et al.\(^3\) treated a mixed cohort of 18 patients (5 via thoracotomy and 13 percutaneously) with primary and metastatic lung tumors. They used a needle electrode with multiple tines deployable into the tumor for 2 or 4 cm. After a mean follow-up of 6 months, they reported a 55% complete or partial response rate and a 17% stable disease rate in lesions with a mean diameter of 5.3 cm. The response rates seemed to be better for smaller lesions (66% for lesions smaller than 5 cm vs 33% for lesions larger than 5 cm). Another important issue that arose in that study was the contraindication to treat central lesions because of the risk of fatal complications, as occurred in one case in that series. More recently, Fernando and colleagues from the same Institute presented an update of their experience in patients with primary NSCLC.\(^6\) At a mean follow-up period of 14 months, they reported 63% of the patients having a complete response, which is comparable to our results. In a series of 54 primary and secondary lung tumors, Akeboshi et al.\(^7\) reported a complete necrosis rate of 59%, with a better response for smaller lesions.\(^7\) They distinguished lesions smaller than or equal to 3 cm from lesions greater than 3 cm and found a statistically significant difference in the complete response rate between the two groups (69% vs 39%; \(p < 0.05\)). These findings were confirmed by Lee and colleagues,\(^8\) who reported a complete necrosis rate of 38% at a mean follow-up of 12.5 months with a statistically significant difference for lesions smaller than 3 cm (100% complete necrosis rate) compared with those measuring 3 to 5 cm (38%; \(p < 0.05\)) and those larger than 5 cm (only 8% complete necrosis rate). We have recently reported our experience with medium-term results.\(^9\) Our data confirm all the previous reports, with an overall radiological complete response rate (CRR) of 61.9% (39 of 63 lesions) at a mean follow-up period of 23.7 months (median 24; range, 6–50). The results seemed to be better for lesions smaller than 3 cm (CRR 69.7% vs 50%). Moreover, in our study, pulmonary function tests performed before and after RFA at several time points showed a slight reduction of FVC and FEV\(_1\) at the end of the first month (not statistically significant), but they returned to pretreatment values after 3 months.

RFA of lung tumors may also be combined with other treatment options (e.g., radiotherapy and chemotherapy) to have more control of the disease. In fact, Grieco et al. obtained better results with RFA combined with RT compared with either modality alone. At a median follow-up period of 19.5 months, they reported a CRR of 75.6%.\(^10\) Instead, in an experimental study on an animal model, Ahmed and colleagues achieved an increase in tumor destruction combining RFA with intravenous administration of liposomal doxorubicin.\(^11\)

In conclusion, RFA of lung tumors may play a role in the treatment of NSCLC. Expected further improvements of the technology and combinations with other therapies may increase its efficacy. However, it is important to stress that RFA is devoted to local treatment of lesions, and this is certainly a limitation of this procedure. Compared with surgical resection, it has a higher incidence of local and distant recurrence. For this reason, this procedure should only be intended as a compromise in treating patients who are at high risk for surgical resection because of their clinical status.

**REFERENCES**