Percutaneous radiofrequency ablation of clinical stage I non–small cell lung cancer

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Objective: This study aimed at retrospectively evaluating the outcomes of radiofrequency ablation of clinical stage I non–small cell lung cancer.

Methods: This study was carried out on 50 nonsurgical candidates (29 men and 21 women; mean age, 74.7 years) with clinical stage I (IA, n = 38; IB, n = 12) histologically proven non–small cell lung cancer. A total of 52 tumors were treated with 52 ablation sessions. Radiofrequency ablation was performed percutaneously under computed tomography fluoroscopic guidance. The outcomes of radiofrequency ablation were evaluated, including toxicity, local efficacy, and patient survival. Toxicity was evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0. Local efficacy was evaluated by using computed tomography scan with a contrast medium. The overall, cancer-specific, and disease-free survivals were estimated with Kaplan–Meier analysis.

Results: Grade 2 and 3 adverse events occurred after 6 (12%) and 3 (6%) of the 52 sessions, respectively. The median follow-up period was 37 months. Local progression was observed in 16 (31%) of the 52 tumors. The median survival time was 67 months. The overall, cancer-specific, and disease-free survivals were 94%, 100%, and 82% at 1 year, 86%, 93%, and 64% at 2 years, and 74%, 80%, and 53% at 3 years, respectively.

Conclusions: Radiofrequency ablation of clinical stage I non–small cell lung cancer was minimally invasive and provided promising patient survival, although the local efficacy needs to be improved. (J Thorac Cardiovasc Surg 2011;142:24-30)

Primary lung cancer is the most common malignancy and the leading cause of death from cancer worldwide. Surgical resection with a lobectomy is suggested as the first-line treatment for treating early-stage non–small cell lung cancer (NSCLC). Unfortunately, certain patients are considered medically inoperable, and conventional external beam radiation therapy (XRT) has been traditionally administered to such patients. A meta-analysis of patients with stage I NSCLC treated by conventional XRT revealed mean overall and cause-specific survivals at 3 years of 34% and 39%, respectively.[1] Because such survival outcomes after XRT are unsatisfactory, various alternative modalities have been the focus of many studies. For example, stereotactic radiation therapy shows favorable survivals for patients with stage I NSCLC: 56% to 60% at 3 years.[2-4] Radiofrequency ablation (RFA) has received considerable attention as a local therapy mainly for hepatic cancer. The favorable outcomes of RF ablation of hepatic cancer have facilitated the application of this technique to lung cancer. Currently, RFA is gaining popularity as a treatment of lung cancer. The purpose of this study was to retrospectively evaluate the outcomes of RFA on nonsurgical candidates with clinical stage I NSCLC.

MATERIALS AND METHODS

Study Population

Approval from the institutional review board and informed consent from the patients were obtained to perform RFA of lung cancer. Our institutional review board also provided approval for our retrospective study. From July 2002 to September 2009, we treated 56 patients with clinical stage I primary lung cancer at Okayama University Medical School. We excluded 6 of these patients, because the tumor was also treated with adjuvant radiation therapy (n = 4), the patient was lost to follow-up (n = 1), or the tumor was not histologically proven (n = 1). Thus, this study consisted of 50 patients with histologically proven clinical stage I NSCLC. Twenty patients who were previously reported in the literature[5] were included in this study, although their follow-up information was updated. Two patients had synchronous double primary lung cancers; thus, a total of 52 tumors were treated with 52 ablation sessions.

For clinical staging, chest and abdomen computed tomography (CT) scans were performed in all patients; positron emission tomography (PET) scanning was performed in 29 patients, and brain magnetic resonance imaging was performed in 26 patients. Lymph node metastasis was considered absent, because none of the lymph nodes were larger than 1.0 cm in short-axis diameter and there was no more accumulation of ^{18}F-fluorodeoxy glucose in the lymph nodes than mediastinal structures when PET was performed. This led to the diagnosis of clinical stage IA and IB cancers in 38 and 12 patients, respectively.

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Abbreviations and Acronyms

CT = computed tomography
NSCLC = non–small cell lung cancer
PET = positron emission tomography
RFA = radiofrequency ablation
XRT = external beam radiation therapy

The characteristics of the 50 patients and the 52 tumors are summarized in Table 1. There were 29 men and 21 women (mean age, 74.7 years; range, 52–88 years). Sixteen patients had a history of surgery for the following types of cancer: lung cancer (n = 9), esophageal cancer (n = 2), cholangiocarcinoma (n = 2), hepatocellular carcinoma and pulmonary metastasis (n = 1), breast cancer (n = 1), and colon, uterus, and ureter cancer (n = 1). The mean long-axis tumor diameter was 2.1 cm (median, 1.8 cm; range, 0.7–6.0 cm). There were 41 adenocarcinomas and 11 squamous cell carcinomas. Eleven tumors in 10 patients were adenocarcinomas showing pure ground-glass opacity on CT images.

Patients were first referred to the department of thoracic surgery. All patients were determined to be nonsurgical candidates by a surgeon because of one or more of the following reasons: poor pulmonary function (predicted forced respiratory volume in 1 second $\leq$ 1000 mL), poor cardiac function (New York Heart Association class $\geq$ III), advanced age ($\geq$80 years), poor performance status ($\geq$2), substantial comorbidity, or refusal to undergo surgery. Fourteen patients had poor pulmonary function, 1 patient had poor cardiac function, 7 patients had advanced age, 1 patient had poor performance status, 7 patients had substantial comorbidity, and 9 patients had combinations of 2 of those reasons. The remaining 11 patients were deemed operable but refused to undergo surgery. For the 27 patients whose vital capacity was examined before RFA, the mean value was 2.53 L (range, 1.06–3.97 L); for the 30 patients whose forced expiratory volume and volume percentage in 1 second were examined before RFA, the mean values were 1.68 L (range, 0.41–3.19 L) and 68.6% (range, 42.3%–96.3%), respectively. No patient received concurrent or adjuvant therapy.

Radiofrequency Ablation Technique

RFA was always performed percutaneously using CT fluoroscopy (Asteion; Toshiba, Tokyo, Japan). Intraprocedural pain was treated by using local anesthesia or epidural anesthesia along with conscious sedation with an intravenous drip infusion of 0.3 mg fentanyl and an intramuscular injection of 25 mg hydroxyzine. In the case of expected severe procedural pain, for example, when the tumor was close to the pleura, or if the patient asked for it, epidural anesthesia was administered. Thus, epidural anesthesia was used in 15 sessions (15 patients). General anesthesia was not used for any of the patients.

Patients were placed in a supine or prone position according to the location of the tumor, and grounding pads were placed on their thighs. An initial CT examination was scanned to identify the precise location of the tumor and decide the pathway of electrode insertion. The skin at the entry site of the electrode was sterilized. After the administration of anesthesia, the electrode was introduced into the tumor and connected to a generator. The electrodes that were used for the ablation included a multitined expandable electrode (LeVeen; Boston Scientific, Natick, Mass) with an array diameter of 2 cm (n = 15), 3 cm (n = 15), 3.5 cm (n = 4), or 4 cm (n = 2); a single internally cooled electrode (Cool-tip; Valleylab, Boulder, Colo) with a 1-cm (n = 3), 2-cm (n = 7), or 3-cm (n = 4) noninsulated tip; or a cluster internally cooled electrode (n = 2) (Cool-tip; Valleylab). In the case of the Valleylab device, radiofrequency energy was applied with an impedance control algorithm for 12 minutes during the internal cooling of the electrode. The temperature of the tumor at the electrode tip was measured immediately after the generator was turned off. When the temperature failed to reach 60°C, additional application at the same site was then required. When using the Boston Scientific device, the energy was applied until the impedance showed a rapid increase or an automatic shut-off occurred after 15 minutes; this was repeated once at each site. To obtain the ablative margin, multiple overlapping ablation zones were created whenever deemed necessary.

A chest CT scan was performed immediately after the procedure to evaluate ablation zone and procedural complications. A chest radiograph was obtained 3 hours later and the following morning to assess the occurrence of complications, such as pneumothorax, hemothorax, and pleural effusion. A complete blood count and blood biochemistry were examined at 1 and 3 days after RFA.

Follow-up

The patients were followed up, whenever possible, at 1, 3, 6, 9, and 12 months, and thereafter at 6-month intervals. At every follow-up session, a chest CT scan was performed with 5-mm collimation before and 30 and 90 seconds after the intravenous administration of a contrast medium (iopamidol, Iopamiron 300; Nihon Schering, Osaka, Japan) at a rate of 3 mL/s to assess local efficacy. The size of the ablated lesion usually exceeds the preprocedural tumor size on CT images for the first 3 months after RFA, because the ablated lesion is detected together with the ablated marginal parenchyma.[6] During this period, thus, the effectiveness of RF ablation cannot be determined by comparing the tumor size but can be determined by contrast enhancement. That is, the tumor is considered to be completely treated when the entire ablation zone is not contrast-enhanced or when the ablation zone exhibits contrast enhancement; however, the enhancement zone is peripheral, concentric, symmetric, and uniform with smooth inner margins. Such enhancement zone is considered to correspond to reactive hyperemia, inflammation, or granulation at the marginal parenchyma.[7] Thereafter, local efficacy was evaluated by comparing the size and geometry of the ablation zone in the previous CT images. Local progression was defined as tumor progression at the ablation zone and considered to have occurred when the ablation zone was circumferentially enlarged or an irregular, scattered, nodular, or eccentric focus in the ablation zone appeared. The focus generally exhibited some degree of contrast enhancement, and thus contrasted against the unenhanced necrotic tumor tissue.

For the assessment of hematogenous metastasis, an abdominal CT scan was generally performed with a contrast medium at 6-month intervals. Although PET was not included in our routine follow-up modalities, for 29 patients, PET examinations were also performed to evaluate the outcomes of RFA and hematogenous metastasis. When symptoms suggesting brain or bone metastasis were observed, a radiologic examination such as magnetic resonance imaging or a bone scintigram was performed.

Study End Points and Statistical Analysis

The study end points included toxicity, local efficacy, and patient survival. Toxicity was evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0, and adverse events of grade greater than 1 were noted. The forced expiratory volume in 1 second 1 to 3 months after RFA was compared with that before RFA by using the paired *t* test. Local efficacy was evaluated by the presence of local tumor progression, which was diagnosed with the aforementioned criteria. The overall local progression rates and the local progression rates according to tumor size were calculated. Further, the local progression rates according to type of electrode used (internally cooled electrode or multitined expandable electrode) were compared by using the log-rank test. In addition to local progression, parenchymal recurrence (defined as recurrence in the same lobe but away from ablation zone), regional recurrence (defined as hilar and ipsilateral mediastinal lymph nodes recurrence), and distant recurrence (all other recurrences) were also evaluated.

The overall, cancer-specific, and disease-free survivals were estimated with Kaplan–Meier analysis. For estimation of cancer-specific survival