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Percutaneous cryoablation for inoperable malignant lung tumors: Midterm results ☆

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ABSTRACT

Objective: To retrospectively analyze the efficacy and short- to mid-term survival rate of cryoablation for malignant lung tumors.
Methods: Percutaneous CT-guided cryoablation for 45 malignant lung tumors in 26 patients during 41 sessions from 2009 to 2013 were performed. Follow up CT-scan were used to determine local tumor progression. Survival rate, local tumor control rate and associated risk factors were analyzed.
Results: The immediate during and short-term complications with CTCAE grade 2 or upper include pneumothorax (15%), pleural effusion (20%), pulmonary hemorrhage (24%), pneumonitis (15%), hemothorax (15%), hemoptysis (10%), pain (20%), bronchopleural fistula ($n = 1$), and empyema ($n = 2$). Life-threatening bleeding or hemodynamic instability was not observed. There was no procedural-related mortality. Overall survival rate of 1, 2, 3 years are 96%, 88%, 88%. For curative intent, local tumor control (LTC) rate of 1, 2, 3 years are 75%, 72%, 72%.
Conclusion: Cryoablation for malignant lung tumors is effective and feasible in local control of tumor growth, with good short- to mid-term survival rate, as an alternative option for inoperable patients.

Introduction

For stage I non-small cell lung cancer and pulmonary oligometastases, surgical resection is the gold standard and poses low recurrent rate [12]. However, for patients who are comorbid or refuse to have surgery, minimally invasive procedures or local treatment offer an alternative choice with comparable tumor control rate in recent studies [7,10,23]. For palliative intent in tumor volume reduction and synergistically in patients receiving chemotherapy, local treatment also provides some benefits [21]. Radiofrequency ablation (RFA) has been used for local lung tumor treatment for a longer history [8,11,18], while some advantages derived from the application with percutaneous cryoablation had been demonstrated [15,21,36]. Unlike heat-based ablation, percutaneous cryoablation is better for pain-relief and not limited to pleura-based lesions, as well as in preservation of collagenous architecture of cell, which can be widely applied in soft tissue tumors in the body [15]. The factors associated with complication, local control and mid- to long-term survival are not well studied [24]. This study analyzed the mid-term survival, local control rate, and the factors associated with complications.

Materials and methods

Ethics

Informed consent was signed by each patient before the procedure. The institutional review board of Taipei Veterans General

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Hospital provided approval and waiver of informed consent for retrospective review of radiologic and clinical data.

Patient selection

From 2009 to 2013, a total 41 sessions of cryoablation for 45 tumors in 26 patients were performed. Patients who had received one or more sessions of cryoablation with at least 12 months follow up were reviewed. Indication of the cryoablation for the patients are: (1) multiple prior surgical resections with recurrence; (2) advanced age; (3) poor lung function; (4) refuse to surgery; (5) comorbidities not suitable for surgery; (6) synergic with chemotherapy for advanced disease; and (7) palliative for tumor volume reduction. The exclusion criteria are: (1) platelet count less than 80,000/μl; (2) Prothrombin time international normalized ration more than 1.3; (3) lung function test with forced expiratory volume in one second less than 0.6 L; (4) tumor location where cryoprobe could not be safely positioned; and (5) patient could not obey the orders during the procedure. Primary tumors were all confirmed pathologically via CT-guided fine needle biopsy. Metastatic tumors were diagnosed as new and growing pulmonary nodules in serial CT scan follow up with or without pathological tissue proof.

Cryoablation techniques

Procedures were performed under CT-fluoroscopic guidance (Somatom Sensation 16 or Miyabi, Siemens, Erlangen, Germany), Patients were positioned as supine or prone for the planned routes for cryoprobes, and nasal cannula with 3 L/min O2 flow was routinely supplied. Anesthesiologist explained the risk of using sedative and analgesic drugs. If necessary, hypnotic agent, such as propofol, was administered and patients' vital signs were monitored. Local anesthesia was applied in the skin and pleural surface. Under CT-guidance fluoroscopy, one or more cryoprobes (Endocare, Irvine, CA, 2.4 mm or 1.7 mm in diameter; Galil, Israel, 1.47 mm in diameter) were introduced targeting the lesion with the tip placed on the distal end of the tumor, where the calculated effective ice-ball coverage at least 5 mm beyond the tumor margin. Two consecutive cycles each consist 10 min of freeze and 5 min of thaw or three cycles with the first cycles consist of 3 min of freezing and 3 min of thawing, the second cycle consists of 7 min of freezing and 7 min of thawing and the third cycle consisted of 5 min of freezing and 5 min of thawing was performed. Adjustment in adding or reducing the freezing time was according to the ice-ball size, and patients' condition (e.g. massive hemoptysis, hemothorax, unstable vital sign). Whole lung CT-scan survey after withdrawing the cryoprobe(s) was performed to ensure the safety and re-check the possible progression of complications (e.g. pneumothorax, pulmonary hemorrhage, pleural effusion or hemothorax). Pulmonary hemorrhage was defined as ground glass appearance in CT images, representing hyperemia, ice-ball thawing or hemorrhage. Pneumonitis was defined as lung parenchyma inflammation and appeared to be consolidation around the ablation site.

Follow-up

Dynamic CT scan of thorax with contrast medium injection was performed in each case at 1, 3, 6, 9, 12, 18, and 24 months after the procedure, and then annually after two years for evaluating the image change and local control of tumor. The complications were classified with Common Terminology Criteria for Adverse Events (CTCAE) v.4.0. Local tumor progression was recorded either when the size meet progression criteria of Response Evaluation Criteria in Solid Tumors (RECIST) v.1.1 or tumor enhancement with at least increase 15 Hounsfield Units (HU) between pre- and post-contrast phases of CT scan for curative intent cases [13,24,25]. Radiographic evaluation was reviewed by two radiologists who had more than 6 years' experiences in thoracic imaging.

Statistics

Categorical variables were analyzed by Chi-square test. The overall survival and local tumor control rate were analyzed with Kaplan–Meier method. We tried to identify factors that were associated with local tumor progression by Cox regression. Statistical significance was defined at $p < 0.05$. Statistical analysis was performed using SPSS (Version 20.0, IBM, Armonk, NY) software.

Results

Characteristics of patients are shown in Table 1. Total 21 males (81%) and 5 females (19%) with 65 ± 18 years of age, 2.03 ± 0.87 L of FEV1 (forced expiratory volume in 1 s), and 73.8 ± 15.8% of FEV1/FVC (forced vital capacity) were reviewed.

The follow-up period was 867 ± 445 days (mean ± SD). The overall survival and local tumor control rate (LTC) of 1, 2, 3 years are shown in Figs. 1 and 2. The observed common complications are listed in Table 2, including pneumothorax (37%), pneumonitis (56%), pleural effusion (56%), hemothorax (22%), cough (20%), hemoptysis (29%), pain (34%), and fever (17%). Grading by CTCAE with grade 2 or greater (symptomatic and intervention indicated) include pneumothorax (15%), pleural effusion (20%), pulmonary hemorrhage (24%), pneumonitis (15%), hemothorax (15%), hemoptysis (10%), pain (20%), bronchopleural fistula ($n = 1$), and empyema ($n = 2$). Among them, there were only two complications with

Table 1
Patient characteristics.

	$N = 26$
Age, year, mean ± SD[a]	65 ± 18
Gender (%)	
Male	21 (81)
Female	5 (19)
Lung function test, mean ± SD	
FEV1[b], L	2.03 ± 0.87
FEV1/FVC[c], %	73.8 ± 15.8
Comorbidities (%)	
Hypertension	12 (46)
COPD[d]	10 (38)
Diabetes mellitus	7 (27)
Renal insufficiency	2 (8)
Liver cirrhosis	1 (4)
Operative history (%)	
Either lung	14 (54)
Ipsilateral lung	8 (31)
Treatment before ablation (%)	
Chemotherapy	15 (58)
Radiotherapy	1 (4)
Tumor histology (%)	
Lung cancer	12 (46)
Colon cancer	4 (15)
Esophageal cancer	2 (8)
Osteosarcoma	1 (4)
Chondroma	1 (4)
Chondrosarcoma	1 (4)
Leiomyosarcoma	1 (4)
Synovial sarcoma	1 (4)
Endometrial stroma sarcoma	1 (4)
Invasive thymoma	1 (4)
Renal cell carcinoma	1 (4)

[a] Standard deviation.
[b] Forced expiratory volume in 1 s.
[c] Forced vital capacity.
[d] Chronic obstructive pulmonary disease.