CLINICAL STUDY

Percutaneous Cryoablation of Lung Tumors: Feasibility and Safety

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ABSTRACT

Purpose: To evaluate the safety and feasibility of cryoablation for lung tumors as well as the incidence of, and risk factors for, complications.

Materials and Methods: This study included 193 cryoablation sessions for 396 lung tumors in 117 consecutive patients. Univariate and multivariate analyses were performed to assess risk factors for common complications. Changes in laboratory values were analyzed the day after cryoablation.

Results: Pneumothorax, pleural effusion, and hemoptysis occurred after 119 (61.7%), 136 (70.5%), and 71 (36.8%) sessions, respectively. Phrenic nerve palsy, frostbite, and empyema occurred after one session each (0.52%). Proximal tumor implantation was observed in one of 471 punctures (0.20%). Of 119 sessions with pneumothorax, 21 (17.6%) required chest tube insertion and two (1.7%) required pleurodesis. Delayed and recurrent pneumothorax occurred in 15 of 193 sessions each (7.8%). A greater number of cryoprobes was a significant ($P = .001$) predictor of pneumothorax. Male sex ($P = .047$) and no history of ipsilateral surgery ($P = .012$) were predictors for the need for chest tube insertion, and no history of ipsilateral surgery ($P = .021$) was a predictor for delayed/recurrent pneumothorax. Greater number of cryoprobes ($P = .001$) and no history of ipsilateral surgery ($P = .004$) were predictors for pleural effusion. Greater number of cryoprobes ($P < .001$) and younger age ($P = .034$) were predictors for hemoptysis. Mean changes in white blood cell count, platelet count, hemoglobin level, and C-reactive protein level were 2,418/μL ± 2,260 ($P < .001$), $-2.0 \times 10^4/\mu$L ± 3.2 ($P < .001$), −0.77 mg/dL ± 0.89 ($P < .001$), and 3.0 mg/dL ± 2.9 ($P < .001$), respectively.

Conclusions: Percutaneous cryoablation could be performed minimally invasively with acceptable rates of complications.

ABBREVIATIONS

CTCAE = Common Terminology Criteria for Adverse Events, RF = radiofrequency

Primary and secondary lung tumors are the leading causes of cancer-related deaths worldwide (1). Lobectomy is the gold-standard treatment for early-stage non–small-cell lung cancer (2). For lung metastases, pulmonary metastasectomy is potentially curative, and good results have been reported after complete resection of pulmonary metastases from extrapulmonary malignancies (3). However, for various reasons such as the presence of multiple tumors, multiple previous surgeries, pulmonary dysfunction, or comorbid medical conditions, not all patients with non–small-cell lung cancer or lung metastasis are suitable candidates for tumor resection. This necessitates the development of alternative treatments.

Percutaneous image-guided ablation is a minimally invasive alternative treatment, and radiofrequency (RF) ablation has been used with increasing frequency for lung tumors (4–8). Percutaneous cryoablation possesses several properties that make it an attractive ablation option. Such advantages include good visualization under computed to-

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mography (CT) or magnetic resonance imaging guidance, preservation of collagenous architecture, and low intraprocedural pain (9). Therefore, despite the drawback posed by the thickness of a cryoprobe, percutaneous cryoablation has been also used to treat localized malignant tumors of the lung. However, its use is less widespread in that setting (10,11).

Percutaneous cryoablation for lung tumors under CT fluoroscopic guidance has been conducted at our institution since October 2002 (11,12). The purpose of this study is to evaluate the safety and feasibility of percutaneous cryoablation of lung tumors, as well as the incidence of complications and risk factors for various complications.

MATERIALS AND METHODS

Patients

Ethical approval for conducting percutaneous cryoablation of lung tumors was obtained from the Keio University Institutional Review Board (approval no. 14-23). Written informed consent was obtained from all patients. The institutional review board also provided approval and waiver of informed consent for retrospective review of radiologic and clinical data. From October 2002 to December 2008, a total of 193 sessions for 396 tumors in 117 consecutive patients were performed. Characteristics of patients and lung tumors are shown in **Table 1**. Inclusion criteria were as follows: (i) surgical unsuitability because of multiple previous thoracotomies, tumor multifocality, refusal of surgery, respiratory dysfunction, or advanced age; (ii) projected life expectancy greater than 1 year; (iii) absence of active extrapulmonary metastasis; (iv) performance status of 0 or 1 on the Eastern Cooperative Oncology Group scale; (v) written informed consent; (vi) platelet count more than 50,000/μL; and (vii) prothrombin time/International Normalized Ratio lower than 1.5.

Table 1. Characteristics of 117 Patients and 396 Lung Tumors Treated with Cryoablation

Characteristic	Value
Age (y)	
Mean ± SD	59 ± 15.7
Range	17–90
Male sex	78 (66.7)
Tract emphysema	8 (6.8)
History of ipsilateral pulmonary surgery	41 (35.0)
Primary lung tumors	13
Metastatic tumors	104
Colorectal cancer	34
Sarcoma	22
Lung cancer	17
Renal cell carcinoma	5
Hepatocellular carcinoma	4
Uterine cervix carcinoma	3
Adenoid cystic carcinoma	3
Salivary gland carcinoma	3
Esophageal cancer	2
Uterine corpus carcinoma	2
Other origin	9
Tumor size (mm)	
Mean ± SD	14.0 ± 8.0
Range	3–65
Tumors treated in one session	
Mean ± SD	2.1 ± 1.5
Range	1–10
Tumors treated per session	
1	34
≥ 2	159

Note.—Values in parentheses are percentages.

Cryoablation Technique

A CRYOcare cryosurgical unit (Endo-Care, Irvine, California) with 2.4- and 3.0-mm-diameter cryoprobes was used. Antibiotics (cefotiam hydrochloride) were given prophylactically before and for 1–2 days after the procedure. Before leaving the ward, each patient received an intramuscular injection of atropine sulfate (0.5 mg) and pentazocine (15 mg). An appropriate patient position on the CT table was determined depending on the distribution of the tumors. Electrocardiography and pulse oximetry with blood pressure monitoring were performed every 5 minutes throughout the procedure. Each procedure was performed by two of the authors who have percutaneous lung biopsy experience.

After a local anesthetic agent was administered, a 21-gauge guiding needle was inserted into the targeted tumor under intermittent 3-slice CT fluoroscopic guidance (Aquilion 64; Toshiba, Tokyo, Japan). Then, a modified coaxial system (Daimon coaxial system; Silux, Kawaguchi, Japan), which consisted of an 8- or 11-gauge stainless-steel coaxial system consisting of an inner guiding sheath and an outer sheath (**Fig 1**), was advanced over the guiding needle (11). After the inner sheath was removed, a cryoprobe was introduced into the outer sheath and the cryoprobe tip was located at the end of the sheath.

Figure 1. A 21-gauge guiding needle and the modified coaxial system.

The size and number of cryoprobes were determined on the basis of tumor size so that the expected ablation volume would cover the entire tumor volume with an ablative margin at least 5 mm (**Fig 2**). When a large pneumothorax (> 35%–40% of a hemithorax) occurred during the procedure, the pneumothorax was manually aspirated with an 18-gauge intravenous cannula.

Every procedure was performed with triple freeze/thaw

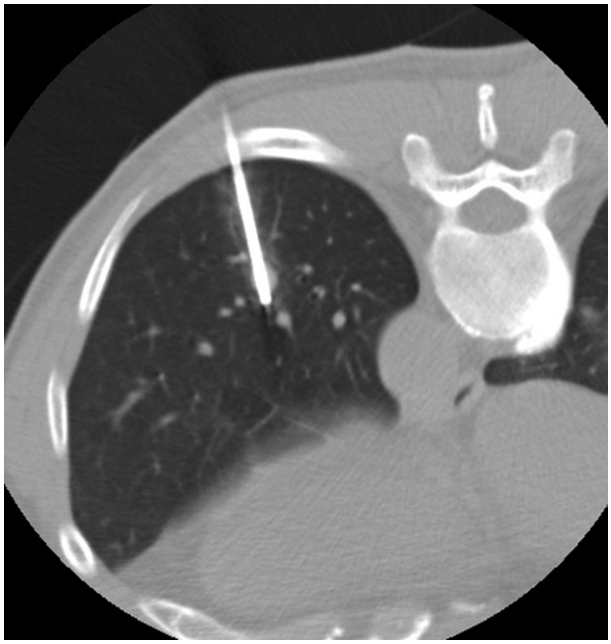

Figure 2. The modified coaxial system penetrates the center of a targeted tumor.

cycles. High-pressure argon gas was used for freezing. Before July 2006, freezing took 5 minutes for the first and second freezes and 10 minutes for the third freeze. After July 2006, freezing took 5 minutes for the first freeze and 10 minutes for the second and third freezes (13,14). Thawing with high-pressure helium gas was then performed until the temperature of the thermocouple in the cryoprobe reached 20°C.

Fibrin glue (Bolheal; Teijin, Tokyo, Japan) was then plugged along the tract through the outer sheath to prevent pneumothorax. A plain CT scan of the lung was performed immediately after the procedure.

Follow-up

Follow-up chest radiographs were obtained after 3 hours and the following day. A plain CT scan was performed the following day and then contrast-enhanced CT scans were performed at 1 week and 1 month and then at 3- to 4-month intervals.

Data Collection and Definition of Variables

Complications were recorded on a per-treatment basis and classified in accordance with the Common Terminology Criteria for Adverse Events (CTCAE) of the National Cancer Institute (15). Delayed pneumothorax was defined as pneumothorax that developed on follow-up chest radiographs or CT scan, and recurrent pneumothorax was defined as pneumothorax that existed during the procedure but worsened on follow-up chest radiographs or CT scan. Peripheral white blood cell count, platelet count, hemoglobin level, and C-reactive protein level were evaluated the day before the procedure and the following day, and changes between preprocedural and postprocedural values were evaluated. Body temperature after cryoablation during the hospital stay was also recorded every morning and as needed.

Variables were collected by three authors (M.I., S.N., H.Y.) by reviewing CT images, procedure records, patient charts, and the prospectively maintained database, which included (i) patient factors (eg, presence of pulmonary emphysema around lesions, history of pulmonary surgery, age, and sex); (ii) ablation factors (eg, size and number of cryoprobes); and (iii) tumor factors (eg, size, distance to pleura, and location). Pulmonary emphysema was determined to be present if pulmonary emphysema was observed in the vicinity of the tumors.

Statistical Analysis

Repeat ablation sessions were considered to be independent, and each session was regarded as a sample unit, except for tumor implantation. For tumor implantation, each cryoprobe was regarded as a sample unit. Data are expressed as means ± SD or as a percentage of sessions. A P value lower than .05 was considered to represent a statistically significant difference.

Each session was divided into groups according to the occurrence of complications. All sessions associated with pneumothorax were divided into groups according to the need for chest tube insertion and occurrence of delayed/recurrent pneumothorax.

Univariate analysis was performed to assess risk factors between groups by using the Student t test or Mann–Whitney U test for numeric values and χ^2 analysis or Fisher exact probability test for categoric values as appropriate. Multiple logistic regression analysis was performed to assess risk factors between groups, and variables with a P value lower than .20 on univariate analysis were included. A paired t test was used to analyze changes in laboratory data before and after the procedure. Data were analyzed by using SPSS statistical software (version 19.0; SPSS, Chicago, Illinois).

RESULTS

All patients tolerated the procedure well. The mean follow-up period was 899 days ± 778 (range, 13–2,927 d). The mean number of cryoprobes per a session was 2.4 ± 1.1 (range, 1–5). Complications are shown in **Table 2**. As multiple tumors were treated in most of sessions (159 of 193; 82.4%), we could not determine which tumor was responsible for complications in such sessions. Thus, tumor factors could not be evaluated in this study.

Pneumothorax occurred after 61.7% of ablation sessions (119 of 193). Of the 119 cases of pneumothorax, 21 (17.6%) required chest tube insertion and two (1.7%) required pleurodesis. Delayed and recurrent pneumothorax occurred in 15 of 193 sessions each (7.8%). Delayed/

Table 2. Complications of Cryoablation for Lung Tumor According to CTCAE Grade

Complications	No. of Sessions	CTCAE Grade	Comments
Pneumothorax	119 (61.7)	-	-
Requiring no additional treatment	63 (53.0)*	1	Delayed/recurrent pneumothorax observed in two sessions
Requiring manual aspiration	33 (27.7)*	2	Delayed/recurrent pneumothorax observed in 11 sessions
Requiring chest tube insertion	21 (17.6)*	2	Delayed/recurrent pneumothorax observed in 17 sessions
Refractory, requiring chest tube insertion/pleurodesis	2 (1.7)*	3	–
Empyema	1 (0.52)	3	Fenestration performed
Phrenic nerve palsy	1 (0.52)	2	–
Pleural effusion	136 (70.5)	1	–
Frostbite	1 (0.52)	2	Debridement performed
Tumor proximal implantation	1 (0.4)†	2	After adopting tract ablation, no proximal implantations observed
Self-limiting hemoptysis	71 (36.8)	1	No life-threatening hemoptysis observed
Pain treated with nonopioid analgesics	3 (1.6)	1	–
Fever (38.0°C–39.0°C)	6 (3.1)	1	–

Note.—Values in parentheses are percentages. CTCAE = Common Terminology Criteria for Adverse Events.
* Percentages calculated among cases with pneumothorax.
† Each needle regarded as a sample unit.

Table 3. Univariate Analyses of Potential Risk Factors for Pneumothorax, Chest Tube Insertion, and Delayed or Recurrent Pneumothorax (N = 193)

	Pneumothorax				Chest Tube Insertion				Delayed/Recurrent Pneumothorax			
Variable	Yes	No	*P* Value	OR	Yes	No	*P* Value	OR	Yes	No	*P* Value	OR
No. of pts.	119	74	–	–	–	–	–	–	–	–	–	–
Age at cryoablation (y)	58.8 ± 13.9	59.2 ± 16.07	.602	–	62.6 ± 10.1	58.5 ± 15.2	.387	–	61.0 ± 11.0	58.6 ± 15.3	.70	–
Sex	–	–	.007*	–	–	–	.015*	–	–	–	.42	–
Male (n = 134)	91	43	–	2.34	113	21		5.3	22	112	–	–
Female (n = 59)	28	31	Ref	1.00	2	57	Ref	1.00	7	52	–	–
Tract emphysema	–	–	.135	–	–	–	.129	–	–	–	.486	–
Yes (n = 11)	9	2	–	–	3	8	–	–	1	10	–	–
No (n = 182)	110	72	–	–	20	162	–	–	28	154	–	–
No. of cryoprobes	2.7 ± 1.2	2.0 ± 0.93	< .001*	NA	2.4 ± 0.90	2.4 ± 1.2	.889	–	2.4 ± 1.0	2.5 ± 1.0	.92	–
History of ipsilateral surgery	–	–	.1	–	–	–	.003*	–	–	–	.015*	–
Yes (n = 72)	39	33	–	–	2	70	Ref	1.00	5	67	Ref	1.00
No (n = 121)	80	41	–	–	21	100	–	7.35	24	97	–	3.31
Cryoprobe (3 mm)	–	–	.44	–	–	–	.613	–	–	–	.126	–
Yes	55	30	–	–	9	76	–	–	9	76	–	–
No	64	44	–	–	14	94	–	–	20	88	–	–

Note.—Values presented as means ± SD where applicable. NA = not available, OR = odds ratio, Ref = reference value.
* Significant at $P < .05$.

recurrent pneumothorax occurred at a mean of 3.2 days ± 4.6 after the procedure (range, 0–20 d). Of 30 cases of delayed/recurrent pneumothorax, 17 (56.7%) required chest tube insertion, and eight patients (26.7%) had to be readmitted to the hospital for chest pain or dyspnea.

Results of univariate analyses are shown in **Table 3**. Male sex and a greater number of cryoprobes were significant predictors for pneumothorax; male sex and no history of ipsilateral surgery were significant predictors for the requirement for chest tube insertion; and no history of ipsilateral surgery was a significant predictor for delayed or recurrent pneumothorax. The results of multivariate analysis were same as those of univariate analysis except for the risk factors for pneumothorax: only a greater number of

cryoprobes was a significant predictor for pneumothorax (**Table 4**).

Pleural effusion occurred after 136 sessions (70.5%) and required no additional treatment. Univariate and multivariate analyses suggested that a greater number of cryoprobes and no history of surgery were significant predictors for pleural effusion (**Tables 5, 6**). Hemoptysis occurred after 71 sessions(36.8%) and was self-limited. Univariate and multivariate analyses suggested that a greater number of cryoprobes and younger age were significant predictor for hemoptysis (**Tables 5, 7**). Phrenic nerve palsy, frostbite, and empyema occurred after one of 193 sessions each (0.52%). Frostbite and empyema required debridement and fenestration, respectively. All cases of pain after cryoablation were self-limited; however, three patients (1.6%) hoped to use nonsteroidal antiinflammatory drugs. Fever (38°C–39 °C) occurred in six sessions (3.1%). Proximal tumor implantation in the chest wall was observed in one of 471 punctures (0.20%) and was removed surgically.

Mean changes in white blood cell count, platelet count, hemoglobin level, and C-reactive protein level the day after cryoablation were 2,418/μL ± 2,260 ($P < .001$), $-2.0 \times 10^4/\mu$L ± 3.2 ($P < .001$), −0.77 mg/dL ± 0.89 ($P < .001$), and 3.0 mg/dL ± 2.9 ($P < .001$), respectively.

DISCUSSION

The present study indicates that percutaneous cryoablation for lung tumors is a safe and feasible procedure. CTCAE grade 4 and 5 complications were not observed. As for CTCAE grade 3 complication, one case of empyema requiring fenestration and two cases of pneumothorax requiring pleurodesis were observed.

To our knowledge, there are no published reports regarding the safety and feasibility of percutaneous cryoablation for lung tumors as well as the incidence of, and risk factors for, complications.

Pneumothorax was a common complication after percutaneous cryoablation, having been observed in 61.7% of sessions. Wang et al (10) reported that the rate of pneumothorax after percutaneous cryoablation of lung tumors was 11.8%, and stated that the reason for the lower rate of pneumothorax was preservation of collagenous architecture in virtual frozen tissue, which may facilitate the rapid natural closing of cryoprobe tracts. Reported rates of pneumothorax after RF ablation of lung tumors have ranged from 4.5% to 61.1% (7,8,16–21).

There are three possible reasons for the higher rate of pneumothorax in the present study versus other studies: the number of cryoprobes, the thicker modified coaxial system, and the modality used to detect pneumothorax. First, the mean number of cryoprobes used in the present study, which is equal to the number of pleural punctures, was 2.4 ± 1.1. According to large studies of RF ablation and cryoablation, the mean number of pleural punctures per session ranged from 1.2 to 1.8 (5,7,8,10,17,18,20). Our results showed that a greater number of pleural punctures is a risk factor for pneumothorax. Although risk factors for pneumothorax after RF ablation remain controversial (16–18), Hiraki et al (17) also suggested that a greater number of tumors ablated is a risk factor for pneumothorax.

Second, the ablation system we used (8–11-gauge) is thicker than an RF ablation needle (17-gauge) and can therefore create a larger pleural hole, resulting in higher rates of pneumothorax; however, there are two advantages of the use of this modified coaxial system. One advantage is that this system enables us to penetrate the targeted tumor precisely. In particular, the cutting quality of a cryoprobe is insufficient to penetrate small or hard lung tumors because lung parenchyma is soft and the tumors are easy to move. The other advantage is that we can plug the pathway with fibrin glue through the outer sheath, which may reduce the rate of pneumothorax.

Finally, we detected minimal pneumothorax by CT scan. Minimal pneumothorax could not be detected by chest radiography. Although the rate of pneumothorax is high, the rate of pneumothorax requiring chest tube insertion in the present study was 10.9%, which is comparable to that associated with RF ablation (3.3%–38.9%; mean, 11.2%) (8). Taking these things into consideration, the high rate of pneumothorax in the present study could be tolerable.

Our results also clarified that delayed/recurrent pneumothorax is relatively frequently encountered after cryoablation, and more than half of these cases required chest tube insertion. Yoshimatsu et al (19) reported delayed/recurrent pneumothorax after RF ablation in 33 of 194 sessions (17.0%), among which additional treatment was needed in four cases. de Baere et al (22) reported two cases of recurrent pneumothorax at days 5 and 20 among 74 RF ablation sessions. Chest tube insertion and pleurodesis were required in each case. Therefore, we must bear in mind that delayed/recurrent pneumothorax has a tendency to require additional treatments more frequently than nonprogressive pneumothorax.

It is reasonable that no history of ipsilateral pulmonary surgery is one of the risk factors for pneumothorax, chest tube insertion for pneumothorax, and pleural effusion because past pulmonary surgery induces pleural adhesion and therefore prevents these complications. Male sex is one of the risk factors for pneumothorax, which could be explained by the fact that the greater vital capacity of men might induce greater respiratory movement, resulting in pleural tear (17). Pulmonary emphysema was not a risk factor for pneumothorax; however, this result is not conclusive because the number of patients with emphysema was too small to be analyzed and there were no patients with severe emphysema in the study.

The rate of hemoptysis was 36.8% in the present study. Reported rates of hemoptysis after RF ablation range from 3.3% to 18.2% (8). Higher rates of hemoptysis may be caused by a greater number of cryoprobes, which is a significant predictor for hemoptysis; however, all cases of hemoptysis in the present study were self-limited. Herrera

Table 4. Multivariate Analyses of Potential Risk Factors for Pneumothorax, Chest Tube Insertion, and Delayed or Recurrent Pneumothorax (N = 193)

	Pneumothorax				
Variable	**Yes**	**No**	***P* Value**	**OR**	**95% CI**
No. of pts.	119	74	–	–	–
Sex	–	–	.071	–	–
Male (n = 134)	91	43	–	–	–
Female (n = 59)	28	31	–	–	–
Tract emphysema	–	–	.22	–	–
Yes (n = 11)	9	2	–	–	–
No (n = 182)	110	72	–	–	–
No. of cryoprobes	2.7 ± 1.2	2.04 ± 0.93	.001*	12.07	0.413–0.781
History of ipsilateral surgery	–	–	.28	–	–
Yes (n = 72)	39	33	–	–	–
No (n = 121)	80	41	–	–	–
Cryoprobe (3 mm)	–	–	.59	–	–
Yes	55	30	–	–	–
No	64	44	–	–	–

Note.—Values presented as means ± SD where applicable. OR = odds ratio, Ref = reference value.
* Significant at $P < .05$.

Table 5. Univariate Analyses of Potential Risk Factors for Hemoptysis and Pleural Effusion (N = 193)

	Hemoptysis				Pleural Effusion			
Variable	**Yes**	**No**	***P* Value**	**OR**	**Yes**	**No**	***P* Value**	**OR**
No. of pts.	71	122	–	–	136	7	–	–
Age at cryoablation (y)	55.0 ± 14.0	61.9 ± 14.8	–	–	58.4 ± 14.7	60.2 ± 15.0	.465	–
0–65 (n = 121)	51	70	.045*	1.89	–	–	–	–
> 66 (n = 72)	20	52	Ref	1.00	–	–	–	–
Sex	–	–	.872	–	–	–	.234	–
Male (n = 134)	50	84	–	–	98	36	–	–
Female (n = 59)	38	21	–	–	38	21	–	–
Tract emphysema	–	–	.058	–	–	–	.512	–
Yes (n = 11)	1	10	–	–	2	9	–	–
No (n = 182)	70	112	–	–	55	127	–	–
No. of cryoprobes	2.9 ± 1.1	2.2 ± 1.1	–	–	2.6 ± 1.2	2.1 ± 0.9	–	–
1	5	34	Ref	1.00	19	20	Ref	1.00
2–3	45	75	.004*	4.08	85	35	.012*	2.56
4–5	21	13	< .001*	11.00	32	2	< .001*	16.84
History of ipsilateral surgery	–	–	.647	–	–	–	.001*	–
Yes (n = 72)	28	44	–	–	41	31	Ref	1.00
No (n = 121)	43	78	–	–	95	26	–	1.8
Cryoprobe (3 mm)	–	–	1.00	–	–	–	.345	–
Yes (n = 85)	31	54	–	–	63	22	–	–
No (n = 108)	40	68	–	–	73	35	–	–

Note.—Values presented as means ± SD where applicable. OR = odds ratio, Ref = reference value.
* Significant at $P < .05$.

et al (23) reported one case of death from massive hemoptysis after RF ablation of centrally located lung tumor. A few studies have reported massive hemoptysis from pulmonary pseudoaneurysm after lung RF ablation (24,25). The cause of pseudoaneurysm may be thermal injury or direct puncture of the pulmonary artery. Cryoablation is safer than RF ablation because cryoablation preserves collagenous architecture. Multivariate analysis also suggested that younger age was a significant predictor for hemoptysis, which could be explained by the fact that the greater vital

Table 4. Continued

Chest Tube Insertion					Delayed/Recurrent Pneumothorax				
Yes	**No**	***P* Value**	**OR**	**95% CI**	**Yes**	**No**	***P* Value**	**OR**	**95% CI**
–	–	–	–	–	–	–	–	–	–
–	–	.047*	–	1.023–21.876	–	–	.386	–	–
113	21	–	3.958	–	22	112	–	–	–
2	57	Ref	1.00	–	7	52	–	–	–
–	–	.36	–	–	–	–	.421	–	–
3	8	–	–	–	1	10	–	–	–
20	162	–	–	–	28	154	–	–	–
2.4 ± 0.9	2.4 ± 1.2	.54	–	–	2.4 ± 1.0	2.5 ± 1.0	.801	–	–
–	–	.012*	–	0.033–0.661	–	–	.021*	–	0.107–0.833
2	70	Ref	1.00	–	5	67	Ref	1.00	–
21	100	–	6.25	–	24	97	–	5.33	–
–	–	.55	–	–	–	–	.115	–	–
9	76	–	–	–	9	76	–	–	–
14	94	–	–	–	20	88	–	–	–

Table 6. Multivariate Analyses of Potential Risk Factors for Pleural Effusion (N = 193)

Variable	Yes	No	*P* Value	OR	95% CI
No. of pts.	119	74	–	–	–
No. of cryoprobes	2.7 ± 1.2	2.04 ± 0.93	.001*	1.74	1.242–2.421
History of ipsilateral surgery	—	—	.004*	2.7	1.377–5.128
Yes (n = 72)	39	33	—	—	—
No (n = 121)	80	41	—	—	—

Note.—Values presented as means ± SD where applicable. OR = odds ratio.
* Significant at $P < .05$.

Table 7. Multivariate Analyses of Potential Risk Factors for Hemoptysis (N = 193)

Variable	Yes	No	*P* Value	OR	95% CI
No. of pts.	71	122	—	—	—
Age (y)	55.0 ± 14.0	61.9 ± 14.8	.034*	0.024	1.002–1.046
No. of cryoprobes	2.7 ± 1.2	2.04 ± 0.93	< .001*	1.9	1.408–2.506

Note.—Values presented as means ± SD where applicable. OR = odds ratio.
* Significant at $P < .05$.

capacity of younger patients might induce greater respiratory movement, resulting in alveolar hemorrhage. Finally, changes in blood count and inflammatory marker levels were slight. Most patients had almost no symptoms, and only six patients had fever (38°C–39 °C), suggesting that the overall inflammatory response of percutaneous cryoablation for lung tumor is minimal and ignorable clinically.

Some limitations of the present retrospective study should be mentioned. First, our review involved collection of data from all imaging and medical reports. However, the radiologists reviewed all follow-up imaging studies and applied the same protocol to identify complications. Second, analysis of tumor factors was not performed because of the small number of sessions during which a single tumor was ablated. Third, the presence of pulmonary emphysema was not indicated as a risk factor for pneumothorax, but this result was obtained from an analysis in which the number of patients with emphysema was small and no patients had severe emphysema. Severe pulmonary emphysema might be a risk factor for pneumothorax.

Despite these issues, the variables with high odds ratios likely represent risk factors, and attention should be given to the patients with these risk factors. We believe it is helpful in reducing complications to know the risk factors of complications and the characteristic complications associated with cryoablation.

In conclusion, percutaneous cryoablation for lung tumor could be performed minimally invasively with acceptable rates of complications. CTCAE grade 4 and 5 complications were not observed. Although the rate of pneumothorax is high, the rate of pneumothorax requiring chest tube insertion is comparable to that associated with RF ablation. It is important to know the risk factors of complications and the characteristic complications associated with cryoablation. We believe the present study results reveal percutaneous cryoablation for lung tumor to be minimally invasive and associated with improved safety.

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