

# Epithelioid hemangioendothelioma in the thorax: Clinicopathologic, CT, PET, and prognostic features

Jung Han Han, MD<sup>a</sup>, Tae Jung Kim, MD, PhD<sup>a</sup>, Kyung Soo Lee, MD, PhD<sup>a,\*</sup>,  
Tae Sung Kim, MD, PhD<sup>a</sup>, Byung-Tae Kim, MD, PhD<sup>b</sup>

## Abstract

Little is known about prognostic factors in epithelioid hemangioendothelioma (EHE). We aimed to identify prognostic factors among various clinicopathologic and imaging features of thoracic EHEs.

Forty-two patients (male:female=20:22; median age, 49 years) of EHEs with (n=19) and without (n=23) thoracic involvement were included. We reviewed electronic medical records for clinical information and computed tomography (CT) features for thoracic involvement. Differences in demographics and survival outcomes of patients with and without thoracic involvement were assessed. We also estimated overall survival.

The most common pattern of thoracic involvement was multiple pulmonary nodules (n=10), followed by parenchymal tumor with pleural invasion (n=4), reticulonodular opacities (n=3), and diffuse pleural thickening (n=2). No significant difference in survival was found between the thoracic EHE group and nonthoracic EHE group ( $P=0.68$ ). Among 4 different thoracic involvement types, the lung multinodular pattern tended to demonstrate longer median survival (8.5 months) than other patterns, whereas the shortest median survival (1 month) was observed for the nodule/mass with pleural involvement pattern ( $P=0.038$ ).

CT manifestations of thoracic EHEs are classified into 4 patterns, of which lung multinodular pattern is associated with longer survival. Survival is not different between patients with and without thoracic involvement.

**Abbreviations:** 18-FDG PET/CT = fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography, EHE = epithelioid hemangioendothelioma, OS = overall survival, SUVmax = maximum standardized uptake values.

**Keywords:** epithelioid hemangioendothelioma, multidetector computed tomography, pathology, positron-emission tomography, thorax

## 1. Introduction

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor characterized histopathologically by the features of epithelioid and histiocytoid cells, but originates from vascular endothelial or pre-endothelial cells. This tumor, which was first described by Dail and Liebow<sup>[1]</sup> in 1975, represents fewer than 1% of vascular tumors. The original name of intravascular bronchioloalveolar tumor was

replaced with the term pulmonary EHE in 1982 by Weiss and Enzinger,<sup>[2]</sup> who described a vascular tumor of bone and soft tissue exhibiting features of both hemangioma and sarcoma. Thereafter, the vascular endothelial origin was confirmed by demonstrating tumor cells of endothelial lineage by immunohistochemistry<sup>[2]</sup> and by cytoplasmic staining of tumor cells with a factor VIII-related antigen by electron microscopy.<sup>[3]</sup>

EHE in the thorax involves not only the lungs but also the pleurae and the mediastinum. In the lungs, EHE usually presents as multiple lung nodules.<sup>[4–7]</sup> When the disease presents as an isolated pleural lesion, it typically exhibits pleural effusion and pleural nodules or thickening and simulates malignant pleural mesothelioma.<sup>[8–10]</sup> Extrathoracic organ involvement includes the liver, long bones, spine, and the soft tissues in the body.<sup>[7]</sup>

Because EHE manifests either as an isolated organ lesion or combined multiorgan lesions, the optimal treatment option and prediction of patient prognosis have not been fully addressed. In an analysis of patient survival in 206 patients with EHE registered via an internet survey, Lau et al<sup>[7]</sup> found that the presence of lesions without distinct borders (e.g., pulmonary infiltrates rather than discrete nodules, pleural effusions, or ascites), hemoptysis, or involvement of more than 2 bones was associated with reduced survival. However, prognostic factors in EHE have not been fully validated. Therefore, the purpose of our study was to describe clinical, pathologic, and imaging features of thoracic EHEs seen in a single tertiary referral center and to identify prognostic factors for EHE.

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JHW and TJK have contributed equally to writing this manuscript.

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<sup>a</sup> Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, <sup>b</sup> Department of Nuclear Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

\* Correspondence: Kyung Soo Lee, Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine (SKKU-SOM), 50, Ilwon-Dong, Kangnam-Gu, Seoul 135-710, Korea (e-mail: kyungs.lee@samsung.com).

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## 2. Materials and methods

Institutional review board of our institution approved this retrospective study, and patient consent for the use of clinical data was waived.

### 2.1. Study patients

Forty-two patients with EHE with ( $n=19$ ) and without ( $n=23$ ) thoracic involvement were included in our analysis. We identified patients by a review of the pathology database at our institution from November 1994 through September 2015.

Nineteen (45%) patients with thoracic involvement were identified, for which histopathologic diagnoses of EHE were established. Biopsy specimens were obtained from the thorax (lung, pleura, and mediastinum;  $n=13$ ) or the liver ( $n=6$ ). In 6 patients for whom we obtained liver biopsy specimens only, thoracic involvement of the disease was presumed based on findings of the multidisciplinary approach of clinicians, radiologists, and pathologists. Among these 6 patients, different patterns of disease progression in terms of organ involvement were observed with management: stable lung and liver disease ( $n=3$ ) versus progressive lung and liver disease ( $n=3$ ).

### 2.2. Clinical assessment

One of the authors reviewed electronic medical records for clinical information. Clinicodemographic features such as gender, symptoms, age at diagnosis, premorbid medical conditions, involved organs, histopathologic results, and response to treatments were included in the analysis. We assessed overall survival (OS) by reviewing medical records and data from the Korea National Statistical Office. OS was defined as the interval from the time of diagnosis to the date of death or final follow-up visit.

### 2.3. Image acquisition and interpretation

Serial chest computed tomography (CT) studies were available in 16 patients with thoracic EHE, with follow-up loss in 3 patients. CT scans were performed using various helical CT scanners at 120 kVp, 114 to 210 mA, and at a pitch of 1.375 to 1.5. Intravenous contrast medium was administered in 12 patients.

Two radiologists (with 26 and 16 years of experience in chest imaging interpretation, respectively) evaluated the CT features of tumors. They assessed the following features: major patterns of parenchymal involvement (multiple pulmonary nodules [multinodular], multifocal areas of reticulonodular lesions [reticulonodular], diffuse pleural thickening with pleural effusion [diffuse pleural], and parenchymal nodule/mass with pleural invasion [nodule/mass with pleural]); tumor number; tumor location (involved lobes and uni/bilaterality); tumor size (maximum diameter); tumor margin; presence of calcification; and tumor homogeneity on contrast-enhanced CT and enhancement relative to the adjacent muscle (hypo-, iso-, or hyper-attenuating).

Coexistent imaging features such as presence of pleural lesions (pleural thickening and pleural effusion), interlobular or bronchovascular septal thickening, lymphadenopathy, extrapulmonary lesions, and tendency for zonal predominance were evaluated; all findings were recorded by consensus.

Fifteen patients underwent fluorine-18-fluorodeoxyglucose positron emission tomography/CT (18F-FDG PET/CT). PET/CT images were reviewed by a nuclear medicine physician with 21 years of experience in PET/CT interpretation. When possible,

maximum standardized uptake values (SUVmax) of thoracic lesions were measured.

### 2.4. Pathologic features

One pathologist (with 23 years of experience in lung pathologic interpretation) interpreted all tissue sections, and diagnoses were made according to the criteria established in the soft tissue literature. In 13 patients with pathologic confirmation of thoracic EHEs, specimens were obtained by video-assisted thoracoscopic surgery ( $n=9$ ), transthoracic needle biopsy ( $n=3$ ), or open surgical lung biopsy ( $n=1$ ). Parenchymal abnormalities seen on CT images were correlated with microscopic findings, and agreement on the correlation was reached among 2 radiologists and a pathologist.

### 2.5. Patient treatment

Of 19 patients with thoracic EHE, 5 patients were treated with chemotherapy using diverse regimens (carboplatin, paclitaxel, and bevacizumab; carboplatin and etoposide; adriamycin, dacarbazine, and ifosfamide). Surgery (wedge resection) was performed in 2 patients. During the follow-up period, 3 patients with chemotherapy showed progressive disease whereas 2 patients demonstrated stable disease. No recurrence was reported in 2 patients who underwent surgical resection. In 7 patients who received treatment (either chemotherapy or surgery) did not reveal significant difference in the OS compared to patients with conservative treatment (23.4 vs 25.2 months, respectively;  $P=0.066$ ).

In 23 patients without thoracic involvement, mass excision was performed in 6 patients (soft tissue,  $n=4$ ; bone,  $n=2$ ), liver transplantation in 3 patients, and conservative treatment in the remaining 14 patients. Patients who underwent mass excision received adjuvant radiotherapy ( $n=4$ ) or chemotherapy ( $n=2$ ). In 9 patients who received surgical treatment, no significant difference in the OS was observed when compared to patients with conservative treatment (19.1 vs 21.4 months, respectively;  $P=0.091$ ).

### 2.6. Statistical analysis

Differences in demographics and survival outcomes of thoracic EHE and nonthoracic EHE groups were assessed by Fisher exact test or Student *t* test. We estimated OS using the Kaplan–Meier method and log-rank test to evaluate differences among the subgroups. Multivariate analysis of various prognostic factors was performed using the Cox proportional hazards model. Outcome time for each case was calculated from the date of the initial diagnosis ( $t=0$ ) to date of an event (e.g., death) or the date of the last follow-up. Statistical analyses were performed with SPSS software (version 19.0, SPSS, Chicago, IL). A  $P$  value  $<0.05$  was considered to indicate a significant difference. A Bonferroni correction was applied to adjust for multiple comparisons.

## 3. Results

### 3.1. Demographic data

Among 42 EHE patients with or without thoracic involvement, 22 were women (52%) and 20 were men (48%). Median age at diagnosis was 49 years (range, 7–79 years). The median duration of follow-up was 9.2 months (range, 0.4–147 months). Sixteen (21%) deaths of various causes were reported by October 2015.

**Table 1****Clinicodemographic findings of 19 patients with thoracic epithelioid hemangioendothelioma.**

Variables	Number of patients (%)
Age, y	48, median (range, 7–79)
Sex	9 male (47%), 10 female (53%)
Follow-up, mo	9.2, median (range, 0.4–147)
Death	7 deaths (37%; mean age 55 y)
Premorbid condition	
Asthma	1 (5%)
Hepatitis B or C	2 (10%)
Myocardial infarction	1 (5%)
Diabetes	1 (5%)
Hypertension	1 (5%)
Tuberculosis	2 (10%)
Deep venous thrombosis	1 (5%)
Extrathoracic involvement	
Thorax only	8 (42%)
Bone	4 (21%)
Liver	5 (26%)
Adrenal gland	1 (5%)
Peritoneum	1 (5%)
Symptoms	
Chest pain	6 (32%)
Respiratory symptoms (cough, sputum, and dyspnea)	4 (21%)
Systemic symptoms (weight loss and anorexia)	2 (10%)
Hemoptysis	1 (5%)

Mean age at death was 55 years (standard deviation, 19 years; range, 18–84 years).

**3.2. Clinical features of thoracic EHE**

Of 19 patients (male:female=9:10; median age, 48) with confirmed thoracic EHE, 7 had premorbid medical conditions: asthma (n=1), hepatitis B or C virus carrier (n=2), myocardial infarction (n=1), diabetes and hypertension (n=1), tuberculosis (n=2), and deep venous thrombosis (n=1). Symptoms and signs

were observed in 10 of 19 patients (53%): respiratory symptoms such as cough, sputum, and dyspnea in 4 patients (21%), chest pain in 6 (32%), weight loss and anorexia in 2, and hemoptysis in 1 (5%) (Table 1).

During a median follow-up of 9.1 months, 7 of 19 patients (37%) with thoracic EHE died as a result of disease progression (n=3), respiratory failure (n=3), or unspecified cause (n=1).

**3.3. Imaging findings and CT-pathologic correlation**

The patterns and distribution of CT findings are summarized in Table 2. The most common pattern of thoracic involvement was multiple pulmonary nodules (n=10), followed by parenchymal nodule/mass with pleural invasion (n=4), reticulonodular opacities (n=3), and diffuse pleural thickening (n=2).

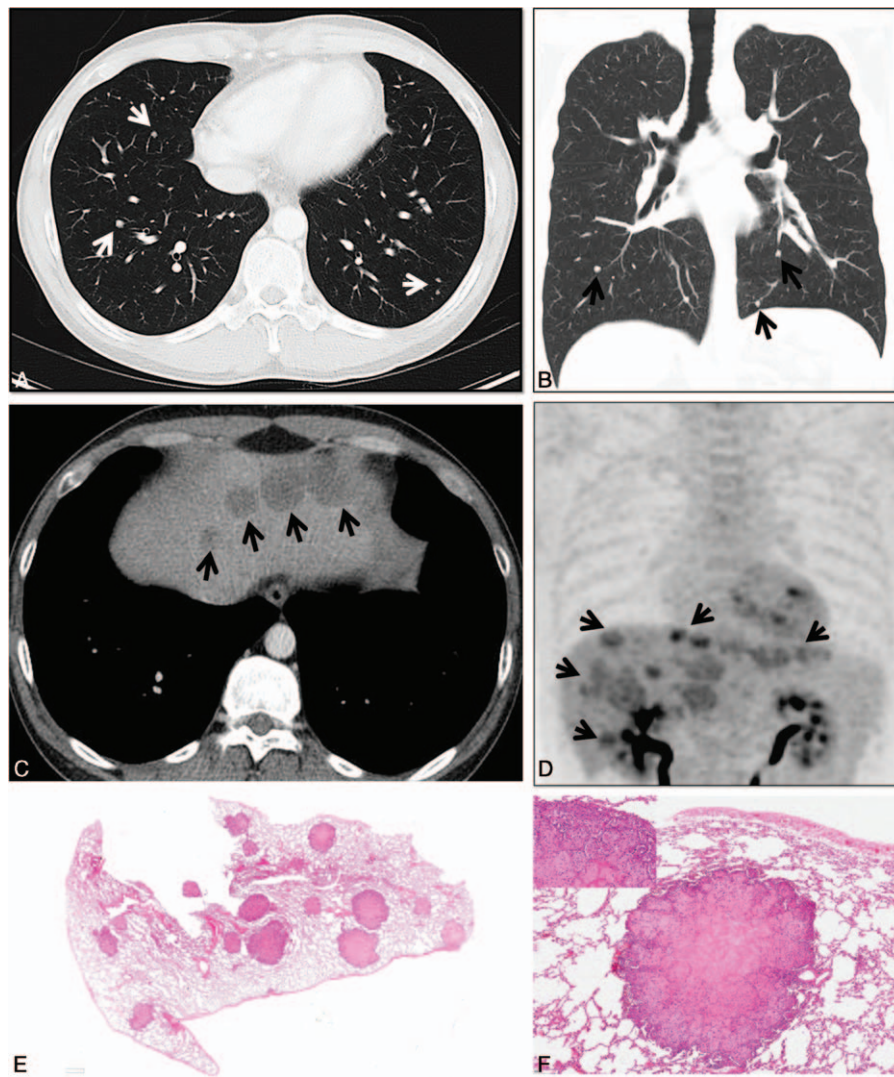
**3.3.1. Multiple pulmonary nodular pattern (multinodular) (n=10).** This pattern (Fig. 1A and B) was observed in 10 patients. Multiple bilateral nodules of iso-attenuation to the chest wall were seen (n=8). The margin and border of nodules were characterized as poorly defined (n=5) or well-defined (n=5) and as lobulated (n=5), smooth (n=4), or spiculated (n=1). Nodules were <1 cm in diameter in 8 patients, and calcifications were present in 4 patients. Features of bronchovascular bundle or interlobular septal thickening were seen in 2 patients and pleural effusion was observed in another 2 patients. Extrathoracic involvement was present in 5 patients: liver (Fig. 1C and D) in 4 patients and bone in 1 patient.

Multiple small nodules were composed predominantly of intra-alveolar, homogeneously eosinophilic matrix with a few small cells embedded (Fig. 1E and F). These nodules were accompanied by partial or complete calcification and ossification of small nodules. Most of the small nodules were located close to bronchioles, bronchi, and blood vessels.

**3.3.2. Multifocal areas of reticulonodular lesions (reticulonodular) (n=3).** Lesion margin was poorly defined in all 3 patients (Fig. 2A). Pleural thickening was present in 2 patients,

**Table 2****Imaging features of 4 different patterns of thoracic involvement in epithelioid hemangioendothelioma.**

Imaging features	Multinodular (n=10)	Reticulonodular (n=3)	Diffuse pleural (n=2)	Nodule/mass with pleural (n=4)
Enhancement to adjacent muscles				
Iso-enhancement	9	1	1	4
Noncontrast	1	2	1	0
Tumor number				
Single	0	2	1	2
Multiple	10	1	1	2
Tumor margin				
Well defined	5	0	0	1
Poorly defined	5	3	2	3
Size, cm				
<1	8	2	0	0
>1	2	1	2	4
Border				
Smooth	4	0	0	1
Lobulated	5	2	0	2
Spiculated	1	1	2	1
Ground-glass opacity	3	1	1	0
Pleural effusion	2	1	2	3
Calcification	4	1	0	1
Bronchovascular thickening	2	3	2	3
Interlobular thickening	2	3	2	3



**Figure 1.** Epithelioid hemangioendothelioma of multiple nodular pattern in a 33-y-old man. (A and B) Lung window and coronal reformatted (2.0-mm section thickness) image shows multiple small well-defined nodules (arrows) in both lungs. (C) Mediastinal window image of enhanced CT scan (5.0-mm section thickness) demonstrates multiple variable-sized liver tumors (arrows) at the dome portion. (D) PET/CT image depicts high FDG uptake within multiple variable-sized liver tumors (arrows). Note scanty FDG uptake in bilateral lung nodules. (E) Low-magnification photomicrograph obtained from a different patient (22-y-old man) reveals multiple well-defined nodules. (F) Another low-magnification photomicrograph reveals nodule showing myxoid or hyalinized central core and cellular periphery. (Inset: High-magnification photomicrograph demonstrating tumor cells containing prominent cytoplasmic vacuoles and extending to alveolar spaces.) CT = computed tomography, FDG = fluorodeoxyglucose, PET = positron emission tomography.

and pleural effusion in 1 patient. Extrathoracic involvement was identified in all 3 patients; the involved organs were bone ( $n=1$ ), peritoneum ( $n=1$ ), and liver ( $n=1$ ) (Fig. 2B). Histopathologically, the lesions represented areas of multiple, small, infiltrating nodular proliferation of neoplastic cells within the lumina of small blood vessels and lymphatic vessels.

### 3.3.3. Diffuse thickening of the pleura (diffuse pleural) ( $n=2$ ).

Of 2 patients of diffuse pleural pattern, only 1 underwent a contrast-enhanced study. Pleural lesions showed iso-attenuation to chest wall muscle on enhanced scan (Fig. 3A and B). Both cases showed a poorly defined margin with unilateral involvement, accompanied by decreased volume in the hemithorax suggesting a chronic indolent nature of the lesions. Pleural effusion was present in 1 of 2 patients.

Histopathologically, the pleural lesions were composed of diffuse irregular thickening of pleura and multifocal and

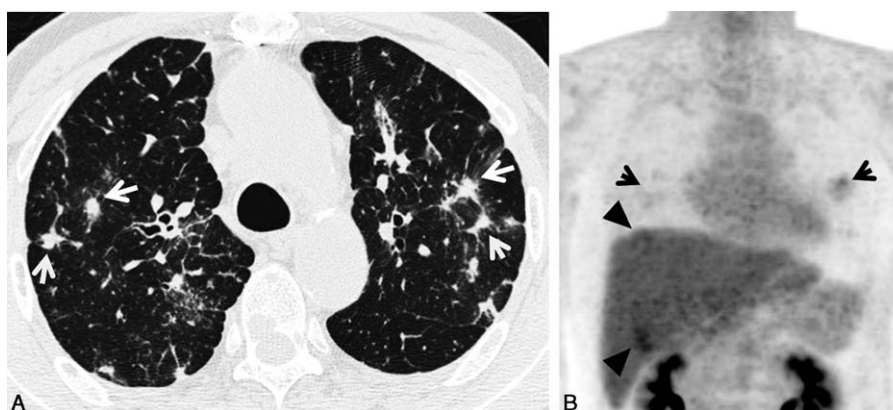
variable-sized subpleural and intra-parenchymal nodules of infiltrative growth.

### 3.3.4. Parenchymal tumor with pleural thickening (nodule/mass with pleural) ( $n=4$ ).

In all 4 patients, parenchymal lesions appeared as hypo-attenuated (range, 25–70 HU) lesions compared with chest wall muscle (Fig. 4A–C); the tumors were solitary in 2 patients and multiple in the other 2 patients. All tumors were  $>1$  cm in diameter (range, 1.3–4.0 cm). Histopathologically, the lesions represented dominant large masses mainly consisting of small nests, cords, and strands of epithelioid cells embedded in a highly eosinophilic stroma (Fig. 4D and E).

### 3.4. $^{18}\text{F}$ -FDG PET/CT findings ( $n=15$ )

At FDG PET/CT performed in 15 of 19 patients with thoracic involvement, the main lesions showed higher FDG uptake than



**Figure 2.** Epithelioid hemangioendothelioma of multifocal areas of reticulonodular pattern in a 63-y-old man. (A) Lung window image of CT scan (2.5-mm section thickness) obtained at the level of aortic arches shows multiple poorly defined nodular lesions (arrows) together with irregular thickening of bronchovascular bundles in both lungs. (B) PET/CT image depicts somewhat higher FDG uptake within bilateral lung nodules (arrows) and liver tumors (arrowheads) than mediastinal blood pool and liver uptake, respectively. CT = computed tomography, FDG = fluorodeoxyglucose, PET = positron emission tomography.

the mediastinal blood pool uptake in 11 (73%) patients and similar uptake in 4 (27%) patients. The SUVmax values (range, 1.7–14.3; median, 5) measured in 8 patients were as follows: 1.7 to 14.3 (median, 5) in 3 patients with multinodular pattern; 2.4 in a patient with reticulonodular pattern; 6.0 to 7.3 (median, 5) in 3 patients with diffuse pleural pattern; and 14.3 in a patient with nodule/mass with pleural pattern. In 7 patients in whom the SUVmax could not be measured, the lesions showed increased FDG uptake compared with mediastinal blood pool in 3 patients (nodule/mass with pleural lesion,  $n=2$ ; reticulonodular pattern,  $n=1$ ) and similar uptake to the mediastinal blood pool in 4 patients (multinodular,  $n=4$ ).

### 3.5. Survival demographics and correlation with organ involvement

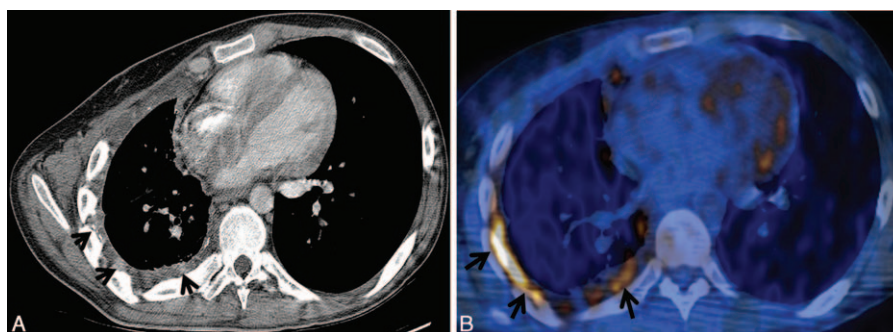
The OS of all EHE patients with and without thoracic involvement was 35% at 1 year and 15% at 5 years. Through multivariable Cox proportional-hazards regression analysis, age  $>55$  years at diagnosis was the only variable associated with decreased survival ( $P=0.036$ ). None of the clinical symptoms investigated were significantly related to reduced OS. Symptomatic patients ( $n=10$ ) showed a trend toward a worse prognosis compared to asymptomatic patients ( $n=9$ ), although the

difference was insignificant ( $P=0.57$ ). Also, survival was unaffected by single (thoracic involvement was considered as single) versus multiple organ involvement ( $P=0.67$ ).

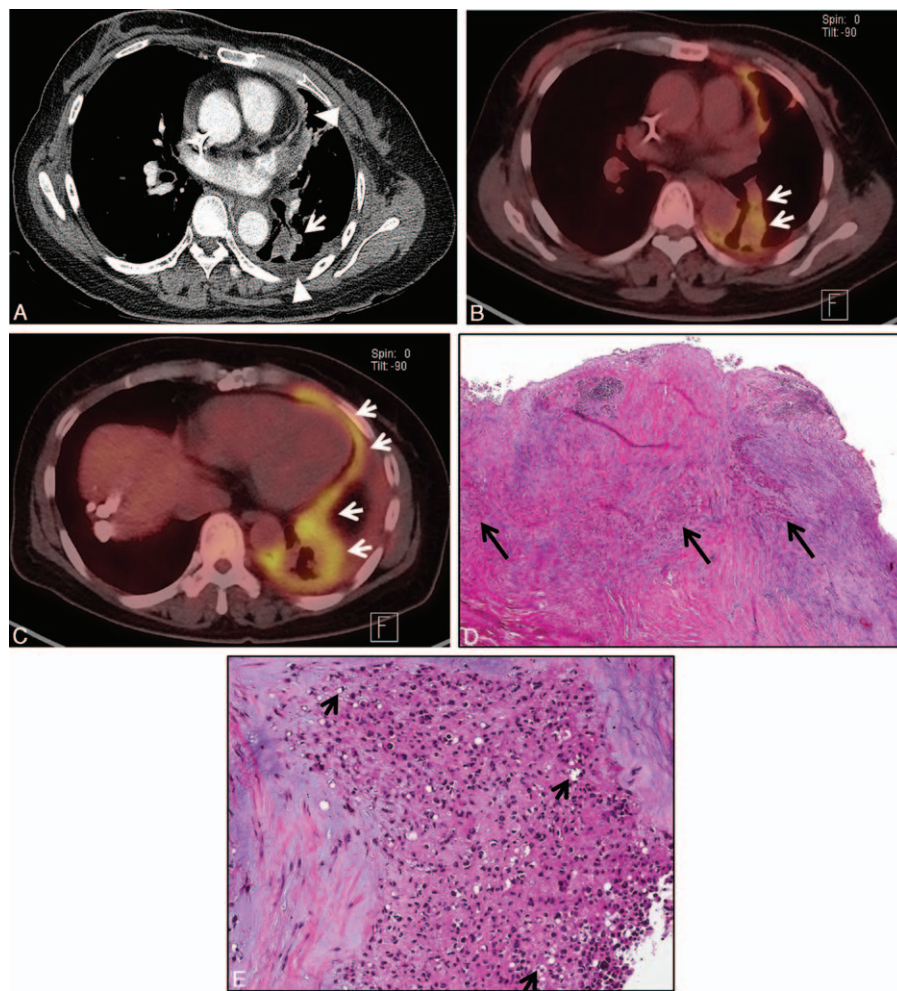
### 3.6. Survival comparisons: thoracic versus nonthoracic groups

Seven of 19 patients with thoracic EHE died during the follow-up period, and the median OS for all patients was 8.5 months (range, 0.8–144.6 months). Median survival was 5.1 months (range, 1.0–72.2 months) in 7 patients with fatal course, whereas the median follow-up duration was 9.1 months (range, 0.4–146.6 months) in the remaining survivors. Eight of 23 patients in the nonthoracic EHE group died, and the median survival for the total group was 11.5 months (range, 1.1–113.6 months).

No significant difference in survival was found between the thoracic EHE group and the nonthoracic EHE group ( $P=0.68$ ). Among 4 different pulmonary parenchymal involvement types, the multinodular pattern was associated with the longest median survival of 8.5 months, whereas the nodule/mass with pleural pattern showed the shortest median survival of 1 month ( $P=0.038$ ) (Fig. 5). After Bonferroni correction, the significance level became  $P=0.013$  instead of  $P=0.05$ .



**Figure 3.** Epithelioid hemangioendothelioma of diffuse pleural pattern in an 18-y-old man. (A) Lung window image of enhanced CT scan (5.0-mm section thickness) obtained at level of left inferior pulmonary vein shows mixed pleural tumor and effusion (arrows) in right pleural space. Also, note marked volume decrease in right hemithorax together with thickened ribs and narrowed intercostal spaces, suggesting the indolent nature of the disease process. (B) PET/CT image obtained at the level of right inferior pulmonary vein demonstrates increased FDG uptake (arrows) in pleural lesions. CT = computed tomography, FDG = fluorodeoxyglucose, PET = positron emission tomography.



**Figure 4.** Epithelioid hemangioendothelioma of parenchymal tumor(s) with pleural extension pattern in a 53-y-old woman. (A) Mediastinal window images of enhanced CT scan demonstrate subpleural lung tumor (arrow) and tumor pleural seeding (arrowheads). (B and C) PET/CT images obtained at the levels of right inferior pulmonary vein (B) and liver dome (C) depict increased FDG uptake in lung (arrows in B) and pleural (arrows in C) lesions. (D) Low-magnification photomicrograph of parietal (diaphragmatic) pleural biopsy specimen depicts thickened pleura containing areas of tumor cells (arrows). (E) High-magnification photomicrograph reveals epithelioid tumor cells containing prominent cytoplasmic vacuoles or intracytoplasmic lumina (arrows). CT = computed tomography, FDG = fluorodeoxyglucose, PET = positron emission tomography.

#### 4. Discussion

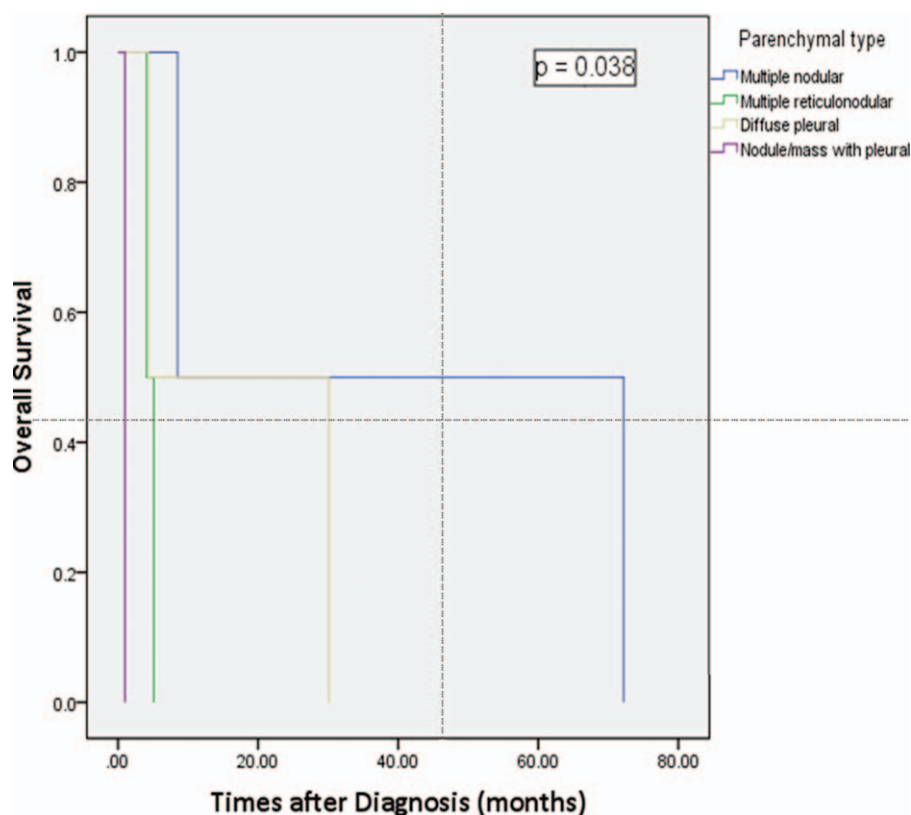
In our study, the pulmonary reticulonodular pattern of EHE had clinical significance in its similarity to hematomatous pulmonary metastases in terms of patient prognosis.<sup>[8]</sup> All 3 patients with this pattern manifested bronchovascular bundle (axial) and interlobular septal (peripheral interstitial) thickening. These CT features are consistent with previous reports on this unusual CT pattern of thoracic EHEs.<sup>[11–13]</sup> These imaging features may represent pathologic findings of infiltrative nodular proliferation of tumor cells within the vessel lumina, differently from more typical formation of well-demarcated interstitial nodules.<sup>[12,14]</sup> This pattern may also suggest more aggressive infiltrative tumor growth into the lung interstitium, which differs from a more typical indolent micropolypoid tumor growth.<sup>[12,14]</sup>

Recently, few studies have reported distinguishing and unique features of diffuse pleural thickening, in particular male predominance, the presence of symptoms (e.g., chest pain), and an aggressive clinical course with early metastasis, resulting in poor prognosis.<sup>[15,16]</sup> In fact, 2 patients with pleural thickening pattern in our series died within 6 months after the initial diagnosis. Pleural-based EHEs manifested as diffuse nodular pleural

thickening with pleural effusions, thus mimicking malignant pleural mesothelioma or diffuse pleural carcinomatosis.<sup>[15,16]</sup>

Parenchymal nodule/mass with pleural invasion type is a rare pattern with only few antecedent reports.<sup>[6,17–20]</sup> This pattern draws particular clinical attention because of its strikingly similar imaging features to those of primary nonsmall cell lung cancer. In fact, in all 4 of our patients, primary lung cancer with pleural seeding was the initial differential diagnosis. These lesions were composed of relatively large lung tumors (all >1 cm; maximum diameter, 4 cm) and malignant pleural effusions.

On PET/CT, thoracic EHEs have been reported to show variably increased FDG uptake.<sup>[20–22]</sup> Indeed, most patients who underwent PET/CT in our study showed increased FDG uptake at the corresponding lung lesions on CT. There was a trend of a wider range of SUVmax in the multinodular pattern, compared with relatively higher SUVmax in diffuse pleural and nodule/mass with pleural pattern. However, in most patients with the multinodular pattern, the lung nodules were 20 mm or less in diameter, which limits SUVmax measurement in these nodules as a result of partial volume averaging and might be responsible for inhomogeneity and underestimation of real metabolic activity of



**Figure 5.** Kaplan–Meier survival curve for comparison of survival between patients with different types of pulmonary parenchymal involvement pattern. Although the multinodular pattern tended to show better survival than other patterns, according to Bonferroni correction the *P* value of 0.038 is considered insignificant for survival difference ( $<0.013$  [ $0.05/4$ ] required for significance).

EHE nodules.<sup>[22,23]</sup> Although a significant difference in SUVmax was not observed among the 4 different patterns of thoracic involvement, we think that this might be due to the low statistical power of our study related to small sample size.

There have been several reports on possible prognostic factors in EHEs; for example, lesions without distinct borders, signs of uncontained spread (e.g., pleural effusion or ascites), hemoptysis, and tumor in 3 or more bones are associated with worse prognosis.<sup>[6,7,24–26]</sup> These findings were not validated in our analysis, probably because of the relatively small number of patients. In the multivariable regression analysis, only age  $>55$  years was significantly correlated with poor OS of our patients.

There was a trend toward longer survival for the multinodular pattern compared with other unusual patterns of reticulonodular, diffuse pleural, and nodule/mass with pleural patterns ( $P=0.038$ ), although this was insignificant after Bonferroni correction. Categorization of parenchymal pattern at the initial diagnosis might be helpful in predicting prognosis and disease progression of patients with EHE.

There are several limitations in our study. First, the study was retrospective in nature and performed in a single institution and was inevitably vulnerable to selection bias. To overcome the rarity of pulmonary EHE, we examined the pathologic database at our institution covering a period of 20 years and identified 19 patients with thoracic involvement. Due to the relatively small sample size, our power of comparison was limited. Second, no targeted lung biopsy was performed, limiting the evaluation of precise CT-pathologic correlation. However, we tried to match histopathology of lung lesions with CT findings at biopsy sites

selected on CT by reviewing surgical and pathologic reports. Third, the patients were followed up for a relatively short term with inevitable follow-up loss in 3 patients. Last, inhomogeneity of treatment modality (chemotherapy, surgery, and conservative treatment) may have decreased the accuracy of our data.

In conclusion, thoracic EHE can be categorized into 4 major parenchymal patterns: multiple pulmonary nodules, reticulonodular opacities, diffuse pleural thickening, and parenchymal nodule/mass with pleural invasion. Several prognostic factors that have reported in previous studies were validated in our analysis, but only age  $>55$  years was proven to be statistically significant. Due to the limited statistical power resulting from the rarity of EHE, a multicenter study remains to be performed to further validate our categorization.

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