


ORIGINAL ARTICLE

Solitary fibrous tumors of the pleura: A single center experience at National Cancer Center, China

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Abstract

Background: This study explored the clinicopathological features, predictive factors of malignancy, effectiveness of video assisted thoracic surgery (VATS), and prognosis of solitary fibrous tumor of the pleura (SFTP).

Methods: A single-center retrospective study of the data of 82 patients with SFTP who were surgically treated in our department between January 2003 and December 2015 was conducted.

Results: A total of 82 SFTPs (70 benign, 12 malignant) were included and all patients underwent complete en bloc resection. SFTPs originated from the visceral pleura in 47 (57%) and the parietal pleura in 35 (43%) patients. In our cohort, malignant tumors were often symptomatically large, and the patients with malignant SFTPs (mSFTPs) often had a family history of neoplasms. Patients in the VATS group ($n = 22$) had tumors with significantly smaller diameters, required a shorter surgical duration and shorter hospital stay, and experienced less intraoperative blood loss and less postoperative chest tube drainage compared to the thoracotomy group ($n = 60$). No tumor recurrence was found in benign SFTP (bSFTP) patients. The long term survival and disease-free survival rates of mSFTP patients were 76% and 53%, respectively.

Conclusion: Larger tumor diameter and a family history of neoplasm may be predictive factors for mSFTP; however, this conclusion needs to be verified in large cohort. VATS is safe and reliable for treating selected SFTP patients. Local recurrence is associated with mSFTP patient death, thus close follow-up of such patients is crucial.

Introduction

Solitary fibrous tumors (SFTs) are rare neoplasms of mesenchymal origin. It is now widely accepted that SFTs originate from dendritic interstitial cells expressing CD34.¹ Dendritic interstitial cells are widely distributed in the connective tissue of the whole body; therefore SFTs may occur in different parts of the body, including the head, neck, thorax, abdomen, and extremities. An SFTP is an SFT that originates from the pleura and

accounts for 90% of SFT cases and < 5% of all pleural neoplasms.² Wagner first reported the histological features of SFTP in 1870.³ Klemperer and Rabin described detailed pathologic characteristics of SFTP in 1931 and divided the primary pleural tumor into diffuse and localized pleural mesothelioma.⁴ Diffuse pleural mesothelioma originated from the pluripotent mesothelial cells and showed biological behavior of malignancy, while localized pleural mesothelioma originated from the subpleural tissue and appeared mostly benign.⁴ Since then, localized

pleural mesothelioma SFTP has been formally classified as an independent disease, and the description of its pathological features has proven comprehensive and accurate. In recent years, analysis of the histochemical characteristics of tissues has shown that an SFTP is a neoplasm of fibroblasts/primitive mesenchymal cells featuring multidirectional differentiation.⁵ Approximately 90% of SFTPs are benign while 10% are malignant.⁶ A benign or malignant diagnosis mainly depends on the pathological criteria proposed by England *et al.*⁷ Preoperative imaging to identify benign and malignant tumors lacks sensitivity and specificity. SFPTs in most patients can be cured after radical surgery; however, approximately 10% of SFPT cases have malignant pathological features. Although some patients with malignant SFPTs (mSFPTs) are cured after radical resection, others patients show recurrence. To date there are no uniform standards for a comprehensive treatment scheme and follow-up strategy for malignant SFTPs. Therefore, we report the clinicopathological features of benign and malignant SFTPs, the factors predicting SFTP malignancy, postoperative recovery after different surgical methods, and long-term follow-up results in a single center in China.

Methods

Patients

Based on pathological diagnoses, we selected SFTP patients who underwent surgery from January 2003 to December 2015. A total of 82 patients with SFTP were surgically treated in our department (Fig 1). Because our research used anonymized data the ethical review committee of the Cancer Hospital Chinese Academy of Medical Sciences waived the need for approval.

Preoperative and postoperative diagnosis

All patients underwent chest computed tomography (CT) examinations of chest lesions before surgery (Fig 2). Seven patients underwent bronchoscopy and bronchocytological brush before surgery but no definite tumor was observed. All pathological sections of the lesion were clearly diagnosed by two pathologists (at least one senior pathologist). The pathological criteria proposed by England *et al.* were used to diagnose mSFPT. A tumor was diagnosed as an mSFPT if any of the following criteria were met: (i) mitotic count >

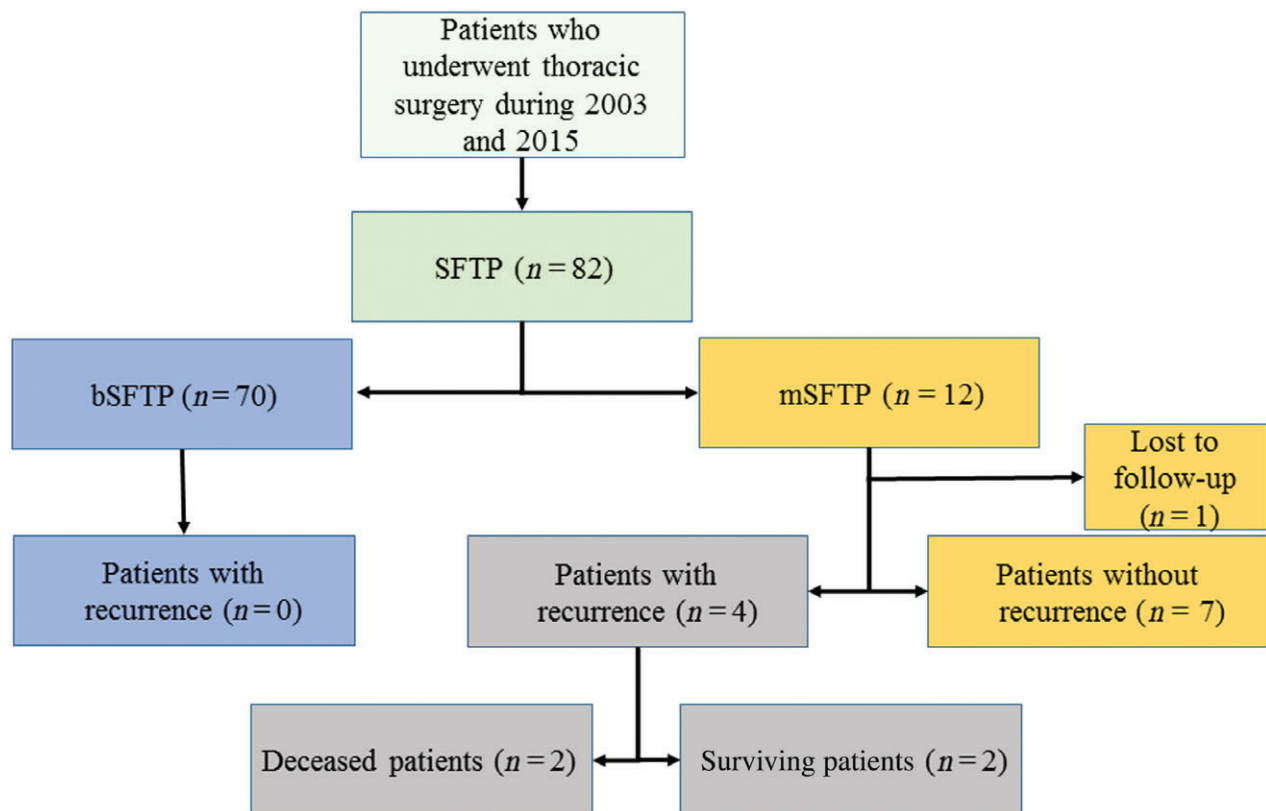


Figure 1 Flow chart of patient selection. bSFTP, benign solitary fibrous tumor of the pleura; mSFTP, malignant SFTP.

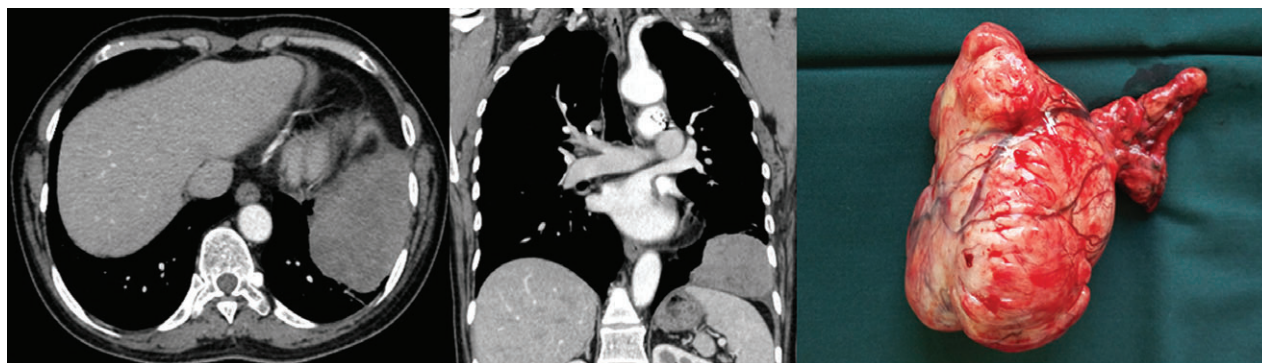


Figure 2 Images of solitary fibrous tumor of the pleura and resected tumor.

4 mitoses/10 high-power fields; (ii) presence of necrosis; (iii) hypercellularity, as judged by nuclear crowding and overlapping; and (iv) the presence of nuclear atypia.⁷ A total of 60 patients were diagnosed with benign SFTP (bSFTP) and 12 with mSFTP.

Surgical intervention and other treatment

All patients underwent surgical treatment: wedge resection ($n = 39$), associated chest wall resection ($n = 27$), associated mediastinum resection ($n = 8$), lobectomy ($n = 7$), and pneumonectomy ($n = 1$). None of the patients were administered preoperative adjuvant therapy. Two patients with mSFTP received one and three cycles of chemotherapy, respectively. Four patients with mSFTP developed local recurrence after surgery. Of these, three underwent reoperation and one showed recurrence and thus underwent a third operation. Seven patients in the whole group experienced postoperative complications but all recovered after conservative treatment, and no surgery-related death occurred. The overall rates of postoperative complications and mortality were 9% and 0%, respectively.

Clinical information and follow-up

The clinical data of the patients were obtained from the medical record database center, including: gender, age, symptoms, smoking history, personal history, family history of malignant tumor, location of the primary tumor, surgical procedures, operative duration, intraoperative blood loss, number of chest tubes (1 or 2), chest tube indwelling time, postoperative chest tube drainage, postoperative hospital stay, postoperative complications, and postoperative treatment. Survival information was obtained from the follow-up center. The median follow-up period was 56 months. Overall survival (OS) was

defined from the date of thoracic surgery to the date of death or the last follow-up.

Statistical analysis

T, χ^2 , and Fisher's exact tests were used for analysis where appropriate. The ability of preoperative factors to predict mSFTP was assessed using log-logistic regression. Patient survival and DFS rates were obtained by using the Kaplan–Meier method. Differences were considered significant when $P < 0.05$.

Results

Clinical features

The demographics and clinical and pathological features are summarized in Table 1. A total of 37 men and 45 women ranging in age from 29 to 79 years (median: 58 years) were included. At the time of diagnosis, 33 patients presented symptoms related to pleural fibroma, and no history of asbestos exposure was recorded. The predominant presenting symptoms included dyspnea, cough, chest pain, and fever. Nine patients exhibited more than one symptom. Among the 72 patients, 18 were smokers, 5 had a history of neoplasia (including lung, ovarian, breast, thyroid, and fallopian tube cancers), and 29 had morbidities (such as hypertension and diabetes). Tumors were benign in 60 patients and malignant in 12. Tumors were observed in the visceral pleura in 47 patients and the parietal pleura in 35. The tumor was right-sided in 39 patients and left-sided in 35, and in eight cases the neoplasms were located in the mediastinum. All patients underwent curative resection of the tumor, including wedge resection in 39 patients, associated chest wall resection in 27, associated mediastinum resection in 8, lobectomy in 7, and pneumonectomy in 1 patient.

Table 1 Clinical features of the study population

Patient characteristics	Results
Age (year), median (range)	58 (29–79)
Gender, N (%)	
Male	37 (45%)
Female	45 (55%)
Smoker, N (%)	23 (28%)
History of neoplasia, N (%)	
Lung	1 (1%)
Ovarian	1 (1%)
Breast	1 (1%)
Thyroid	1 (1%)
Fallopian tube	1 (1%)
Family history of malignant tumor, N (%)	
Yes	18 (22%)
No	64 (78%)
Presenting symptoms, N (%)	33 (40%)
Symptoms, N (%)	
Dyspnea	17 (21%)
Cough	15 (18%)
Chest pain	8 (10%)
Fever	2 (24%)
Comorbidities, N (%)	
Hypertension	16 (20%)
Diabetes	7 (9%)
Coronary heart disease	2 (2%)
Premature ventricular contraction	2 (2%)
Asthma	1 (1%)
Cerebral infarction	1 (1%)
Malignancy of tumor, N (%)	
Benign	70 (85%)
Malignant	12 (15%)
Pleural location, N (%)	
Parietal	35 (43%)
Visceral	47 (57%)
Location of tumor, N (%)	
Right thorax	39 (47%)
Left thorax	35 (43%)
Mediastinum	8 (10%)
Surgical procedure, N (%)	
Wedge resection	39 (48%)
Associated chest wall resection	27 (33%)
Associated diaphragm resection	8 (10%)
Lobectomy	7 (8%)
Pneumonectomy	1 (1%)

Comparison of video-assisted thoracoscopic surgery and thoracotomy groups

Of the 72 patients, 22 were treated with thoracoscopic surgery (3 were uniportal), and 60 were treated with thoracotomy. Compared to the thoracotomy group, the VATS group had tumors with significantly larger diameters ($P < 0.001$), required shorter surgical duration ($P = 0.048$) and shorter hospitalization time after surgery ($P < 0.001$), and experienced less blood loss during surgery ($P = 0.005$)

Table 2 Comparison of VATS and thoracotomy groups

Items	VATS group	Thoracotomy group	<i>P</i>
Number	22	60	—
Diameter of tumor (cm)	5.03 ± 0.57	11.28 ± 0.81	< 0.001
Operation duration (minutes)	86.64 ± 8.37	135.60 ± 22.87	0.048
Blood loss during operation (mL)	65.0 ± 16.45	272.70 ± 69.15	0.005
Postoperative chest tube drainage (mL)	430.90 ± 84.41	1189.00 ± 195.20	< 0.001
Hospitalization time after operation (day)	4.46 ± 0.72	7.67 ± 0.45	< 0.001
Postoperative complications	1 (5%)	6 (10%)	0.668
Number of chest tubes (1)	19 (86%)	50 (83%)	1.000
Postoperative chest tube indwelling time (day)	3.91 ± 0.69	5.20 ± 0.36	0.109

Bold values indicate $P < 0.050$ and thus a significant difference between the groups. VATS, video-assisted thoracic surgery.

and less postoperative chest tube drainage ($P < 0.001$). There was no significant difference in the incidence of postoperative complications, number of chest tubes, and the postoperative chest tube indwelling time between the two groups (Table 2). VATS was safe and effective for resecting relatively small SFTPs and was significantly advantageous to the postoperative recovery of patients.

Factors predicting the malignancy of solitary fibrous tumors of the pleura

Table 3 lists the factors that are associated with malignancy. Univariate analysis showed that malignant tumors were more often larger ($P = 0.016$), with lower forced expiratory volume in 1 second/predicted ($P = 0.042$), and patients had a family history of malignant tumors ($P = 0.024$). Multivariate analysis showed that the tumor diameter ($P = 0.011$) and a family history of malignant tumors ($P = 0.017$) were significant predictive factors of SFTP malignancy. None of the other factors, such as symptom presentation, age, body mass index, pleural location of the tumor, gender, smoking history, or tumor location were predictive of SFTP malignancy ($P > 0.050$).

Long-term survival

The median follow-up time was 56 months. During the follow-up period, no tumor recurrence was observed in the bSFTP group. Local recurrence occurred in four cases in the mSFTP group; one patient died after conservative treatment, while three patients underwent local reoperation. Of

Table 3 Factors predicting malignancy in solitary fibrous tumors of the pleura

Factors	Benign	Malignant	Univariate <i>P</i>	Multivariate <i>P</i>
Symptomatic, N (%)	25 (36%)	7 (58%)	0.146	—
Age (years), mean ± SD	55.83 ± 11.57	61 ± 11.62	0.148	—
Diameter (cm), mean ± SD	8.89 ± 5.92	13.79 ± 6.34	0.016	0.011
BMI, mean ± SD	1.36 ± 0.07	1.66 ± 0.02	0.527	—
FEV1/predicted (%), mean ± SD	79.60 ± 2.40	75.40 ± 5.30	0.042	0.555
Pleural location, N (%)			0.695	—
Parietal	31 (44%)	4 (33%)	—	—
Visceral	39 (56%)	8 (66%)	—	—
Gender, N (%)			0.575	—
Male	31 (44%)	6 (50%)	—	—
Female	39 (56%)	6 (50%)	—	—
Smoker, N (%)			0.583	—
Yes	20 (29%)	3 (25%)	—	—
No	50 (71%)	9 (75%)	—	—
Family history of malignant tumor, n (%)			0.024	0.017
Yes	12(17%)	6 (50%)	—	—
No	58(83%)	6 (50%)	—	—
Location of tumor, n (%)			0.325	—
Right thorax	37 (53%)	2 (17%)	—	—
Left thorax	27 (39%)	8 (66%)	—	—
Mediastinum	6 (8%)	2 (17%)	—	—

Bold values indicate $P < 0.050$ and thus a significant difference between the groups. BMI, body mass index; FEV1, forced expiratory volume in 1 second; SD, standard deviation.

the three patients who underwent local reoperation, one died, one was still alive, and one experienced recurrence again and underwent a third surgery. The patient who underwent a third surgery is still alive and has survived for 33 months. The total DFS and OS of mSFTP patients was 53% and 76%, respectively (Fig 3).

Discussion

Solitary fibrous tumors of the pleura are uncommon neoplasms arising from the mesenchymal cells beneath the mesothelial lining of the pleura. SFTPs commonly occur in

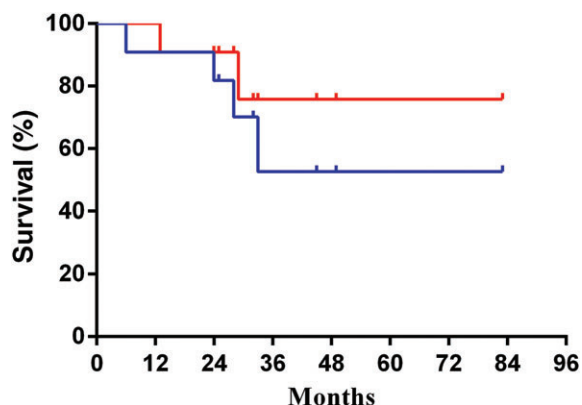


Figure 3 Disease-free and overall survival of patients with malignant solitary fibrous tumors of the pleura. (—) Overall survival and (—) Disease-free survival.

people aged 50–70 years and the male to female incidence ratio is equal. SFTP is reportedly not related to asbestos exposure, but occasional familial aggregation has been reported.^{8–10} We did not find any relationship between SFTP and asbestos or tobacco exposure. External environmental factors may not be related to SFTP occurrence, thus further research based on genetic alternations is needed to explore the cause of SFTP. The malignant proportion of SFTP in our group was 15%, similar to previous results.⁶

The growth of SFTP is often slow and most patients do not display any clinical symptoms. If the tumor is large, patients may experience oppressive symptoms, such as dyspnea and cough. A few patients have presented with paraneoplastic syndrome, such as hypertrophic pulmonary osteoarthropathy and idiopathic hypoglycemia. In our group, most of the patients had no symptoms. The most commonly manifested symptoms are cough, dyspnea, and chest pain. None of the patients in our study had paraneoplastic syndrome.

Previous studies have not reported specific imaging findings of SFTP. A few studies have reported partial pedicle movement of the tumor with respiratory movement or postural changes when partial fluoroscopy or CT scans have been performed. SFTP status cannot be identified by imaging examination at present.¹¹ Pulmonary isotope scanning and tracheoscopy also show no significant results for diagnosis. As complete resection of the tumor is recommended and not difficult to perform for both benign and malignant SFTP patients, in our experience CT-guided puncture before surgery is not necessary in most cases.

Most SFTPs originating from the visceral pleura have clear boundaries. The tumors attach to the normal tissue with a pedicle consisting of many vessels.¹² In our group, 47 (57%) cases originated from the visceral pleura. Benoit Lahon *et al.* reported that malignant tumors are more often symptomatic, large, sessile, and multifocal.¹³ In our study, multivariate analyses revealed that SFTP patients with a larger tumor diameter and a family history of malignant tumors were more likely to have mSFTP. As expected, malignant tumors are usually more aggressive and larger than benign tumors, thus tumor size is a predictor of malignancy. However, our study reports for the first time that a family history of cancer may be another predictor for mSFTP. This conclusion needs to be verified in a larger cohort as our patient sample was limited.

In recent years, researchers have reported that SFTP originates from dendritic stromal cells that express CD34 antigen. Positive vimentin and CD34 expression in immunohistochemistry is highly specific to a diagnosis of SFTP. These immunohistochemical markers are considered important for differentiating pleural solitary fibroma, pleural mesothelioma, and neurogenic tumors.⁸

Complete surgical resection is the preferred treatment for SFTP.¹⁴ Most SFTPs are encapsulated and rarely show conglutination; therefore, even if the tumor is huge, it can be completely removed. Some mSFTPs have extensive pleural metastasis and are difficult to remove completely. There is no separate capsule between the tumor pedicle of SFTP and the normal tissue, thus the tumor presents as an invasive pattern in the pedicle. Therefore, to avoid relapse, we should expand the extent of tumor resection. If the tumor invades the lung parenchyma, chest wall, pericardium, and diaphragm, resection of part of the chest wall, pericardium, diaphragm, and, if necessary, lobectomy or pneumonectomy, is recommended.¹⁰ Thoracotomy is indicated for large masses or tumors that originate in the parietal pleura. VATS shows obvious advantages for resecting smaller lesions. In our cohort, the VATS group required shorter operative duration, experienced less bleeding during surgery, required less chest tube drainage, and rapidly recovered after surgery; thus VATS is safe and reliable for the treatment of selected SFTP patients. In our experience, tumors ≤ 5 cm in diameter and not located in the parietal pleura are good indicators for VATS.

De Perrot *et al.* divided SFTP into four types: benign tumor with pedicle, benign tumor with broad base, malignant tumor with pedicle, and malignant tumor with broad base.⁸ The recurrence rates of these four types of tumors were 2%, 8%, 14%, and 63%, respectively. Approximately 23% of the patients who had a malignant tumor with a broad base died within one year of surgery, while patients with bSFTP rarely relapse after radical surgery. However, recurrence and metastasis rates of mSFTP remain high. mSFTP is

mainly transferred through blood to the brain, bone, and lungs.¹⁴ In our study, no recurrence occurred in the benign group. In the malignant group, four patients had recurrence, two of which were still alive after undergoing a second surgery. Reoperation after local recurrence significantly improved the prognosis of mSFTP.¹³ The factors significantly associated with mSFTP recurrence are sessile morphologic type, resection larger than a wedge, and CD34-negative tumors. Recurrence is significantly associated with a lower survival rate.¹² In our series, local recurrence of mSFTP was also the main cause of death.

This was a retrospective analysis and, as such, has significant limitations in solving the uncertainties regarding SFTPs. However, this study also has some advantages, such as the relatively larger sample size than previous studies and complete surgical information to evaluate the safety and efficacy of VATS for the treatment of SFTP. Our results confirm that radical surgery, including VATS, still plays an important role in the treatment of SFTP.

Acknowledgments

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Disclosure

No authors report any conflict of interest.

References

- Chan JK. Solitary fibrous tumor-everywhere, and a diagnosis in vogue. *Histopathology* 1997; **31**: 568–76.
- Lu C, Ji Y, Shan F, Guo W, Ding J, Ge D. Solitary fibrous tumor of the pleura: An analysis of 13 cases. *World J Surg* 2008; **32**: 1663–8.
- Gengler C, Guillou L. Solitary fibrous tumour and haemangiopericytoma: Evolution of a concept. *Histopathology* 2006; **48**: 63–74.
- Klemperer P, Coleman BR. Primary neoplasms of the pleura: A report of five cases. *Am J Ind Med* 1992; **22**: 1–31.
- Hanan CA, Miettinen M. Solitary fibrous tumor: Histological and immunohistochemical spectrum of benign and malignant variants presenting at different sites. *Hum Pathol* 1995; **26**: 440–9.
- Patsios D, Hwang DM, Chung TB. Intraparenchymal solitary fibrous tumor of the lung: An uncommon cause of a pulmonary nodule. *J Thorac Imaging* 2006; **21**: 50–3.

- 7 England DM, Hochholzer L, McCarthy MJ. Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. 1989; **13**: 640–58.
- 8 de Perrot M, Fischer S, Bründler MA, Sekine Y, Keshavjee S. Solitary fibrous tumors of the pleura. *Ann Thorac Surg* 2002; **74**: 285–93.
- 9 Cardillo G, Carbone L, Carleo F *et al.* Solitary fibrous tumors of the pleura: An analysis of 110 patients treated in a single institution. *Ann Thorac Surg* 2009; **88**: 1632–7.
- 10 Harrison-Phipps KM, Nichols FC, Schleck CD *et al.* Solitary fibrous tumors of the pleura: Results of surgical treatment and long term prognosis. *J Thorac Cardiovasc Surg* 2009; **138**: 19–20.
- 11 Gupta A, Souza CA, Sekhon HS *et al.* Solitary fibrous tumor of pleura: CT differentiation of benign and malignant types. *Clin Radiol* 2017; **72**: 796.e9–796.e17.
- 12 Robinson LA. Solitary fibrous tumor of the pleura. *Cancer Control* 2006; **13**: 264–9.
- 13 Lahon B, Mercier O, Fadel E *et al.* Solitary fibrous tumor of the pleura: Outcomes of 157 complete resections in a single center. *Ann Thorac Surg* 2012; **94**: 394–400.
- 14 Sung SH, Chang JW, Kim J, Lee KS, Han J, Park SI. Solitary fibrous tumors of the pleura: Surgical outcome and clinical course. *Ann Thorac Surg* 2005; **79**: 303–7.