

# Medical thoracoscopy for tuberculous pleurisy: A retrospective analysis of 575 cases

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## Abstract:

**OBJECTIVE:** The objective of this retrospective study was to assess the efficacy of medical thoracoscopy in diagnosing of tuberculous pleurisy and characterize tuberculous pleurisy with medical thoracoscopy.

**METHODS:** A total of 575 patients with tuberculous pleurisy who underwent medical thoracoscopy were included in the study. Demographic data, clinical manifestations, and routine and biochemical tests on pleural fluid, cultures of pleural fluid, sputum, and pleural biopsy for the detection of *Mycobacterium tuberculosis* and pathological findings were evaluated.

**RESULTS:** Sputum, pleural fluid, and pleural biopsy cultures were positive for *M. tuberculosis* in 12.5%, 19.2%, and 41.9% of patients, respectively. Furthermore, there were significant differences in total positive tuberculosis (TB) tests in the pleural cavity according to patient's age (<18 years old, 50.0%; 18–34 years old, 50.2%; 35–59 years old, 34.8%; >60 years old, 18.6%; and all groups vs. >60 years old,  $P < 0.001$ ). Patients with 18–34 years old were more likely to have granuloma in pleural biopsy specimens when compared to patients >60 years old (77.0% vs. 37.9%). The percentage of patients with high adenosine deaminase (ADA) levels in pleural fluid (>40 U/L), who were <18, 18–34, 35–59, and > 60 years old, was 83.3% (15/18), 72.8% (193/265), 51.2% (88/172), and 34.7% (17/49), respectively (all groups vs. >60 years old,  $P < 0.001$ ).

**CONCLUSION:** Medical thoracoscopy is effective for diagnosing tuberculous pleurisy. Younger patients with tuberculous pleurisy have a higher number of positive TB tests in the pleural cavity, are more likely to have granuloma in pleural biopsy specimens, and have higher ADA levels in the pleural fluid.

## Keywords:

Adenosine deaminase, thoracoscopy, tuberculous granuloma, tuberculous pleurisy

Tuberculosis (TB) accounts for substantial mortality in both developing and developed countries.<sup>[1–3]</sup> *Mycobacterium tuberculosis* is the primary pathogen in TB. It mainly manifests as an infection of the lungs but can cause disease throughout the body.<sup>[1]</sup> A common form of extrapulmonary TB, tuberculous pleurisy, is caused by a delayed-type hypersensitivity reaction to mycobacteria in the pleural cavity.<sup>[4–7]</sup> The pathogenesis of tuberculous pleurisy

involves a T-cell-mediated immune response. Previous reports have shown that RORC2 mRNA expression and the number of CCR4+, CD4+, and CD3+ cells are significantly elevated in patients with tuberculous pleuritis when compared to patients with nonspecific pleurisy.<sup>[7,8]</sup>

The diagnosis of tuberculous pleurisy remains a challenge.<sup>[9]</sup> The gold standard diagnostic is the detection of *M. tuberculosis* in pleural fluid or pleural biopsy specimens, either by smear, culture, or histopathology. Lymphocytic predominant exudate and high adenosine deaminase (ADA) levels

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represent a valuable adjunct in the diagnosis of tuberculous pleurisy, and these may be useful in settings with high TB burden.<sup>[10]</sup>

ADA catalyzes the conversion of adenosine to inosine and plays an important role in the differentiation of lymphoid cells.<sup>[11]</sup> ADA level in pleural fluid has become an important reference index for the diagnosis of tuberculous pleurisy and is widely used in areas with high TB prevalence. However, its value in low-epidemic areas has been questioned.<sup>[7,12]</sup> An ADA level of >40 U/L in lymphocyte predominant pleural fluid is the commonly accepted threshold for the diagnosis of tuberculous pleurisy, with a reported sensitivity and specificity of 92% and 90%, respectively.<sup>[7]</sup>

Biopsy has been considered the decisive tool for the diagnosis of tuberculous pleurisy. Pleural tissues can be obtained by closed pleural biopsy, percutaneous thoracentesis, video-assisted thoracic surgery, open surgical biopsy, or medical thoracoscopy.<sup>[13]</sup> Medical thoracoscopy is a minimally invasive ambulatory procedure performed in nonintubated patients under local anesthesia, which can be used to inspect and obtain a biopsy of the pleural tissue and perform therapeutic interventions.<sup>[14,15]</sup> Medical thoracoscopy is usually reserved for a small number of cases where a diagnosis could not be obtained by closed pleural biopsy. At present, 20%–40% of patients with exudative pleural effusions and suspected tuberculous pleurisy remain undiagnosed. The widespread use of medical thoracoscopy may increase the diagnostic yield for tuberculous pleurisy in these patients. The objective of the present study was to assess the efficacy of medical thoracoscopy in diagnosing tuberculous pleurisy and characterizing tuberculous pleurisy with medical thoracoscopy.

## Methods

### Subjects and study design

This retrospective study included participants with tuberculous pleurisy, who underwent medical thoracoscopy at Shandong Provincial Chest Hospital Affiliated to Shandong University between July 2013 and July 2016. These patients were diagnosed with tuberculous pleurisy according to the following criteria:<sup>[7]</sup> (1) the presence of *M. tuberculosis* in sputum samples, pleural fluid, or pleural biopsy or (2) the presence of tuberculous granulomas in the pleura. Participants with a contraindication for pleural biopsy, human immunodeficiency virus infection, or pleuritis due to other causes were excluded from the study. All participants provided written informed consent. The present study was approved by the Ethics Committee of Shandong Provincial Chest Hospital Affiliated to Shandong University.

### Thoracoscopic procedures

Medical thoracoscopy was performed under local anesthesia using a rigid thoracoscope (R. Wolf GmbH, Knittlingen, Germany). Preoperative monitoring included routine blood tests, coagulation function, hepatitis B virus assay, electrocardiogram, and pulmonary function tests. The patients were positioned in the lateral decubitus posture with the affected side up. The entry point was marked under ultrasound guidance or on the mid- or posterior axillary line at the level of the sixth to seventh intercostal space. The marked area was infiltrated with 2% lidocaine as a local anesthetic. Then, a 1–2-cm incision was made in the skin with a scalpel, followed by blunt dissection of the intercostal muscles with hemostatic forceps. A trocar was inserted vertically to allow the insertion of the thoracoscope. Pleural fluid was aspirated to facilitate the visualization of the pleural cavity. The lung surface, costal pleura, diaphragmatic pleura, sinus phrenicocostalis, and motion of the lungs and diaphragm were examined in detail. Multiple biopsies were taken for laboratory tests, which included a pathological examination and *M. tuberculosis* culture. After the thoracoscopy, liquid and gas in the pleural cavity were removed and a chest tube was placed before wound closure.

### Data collection

The medical records of patients were retrospectively reviewed, and the following data were recorded: gender, age, clinical manifestations (including fever, respiratory distress, chest pain, cough, expectoration, night sweat, fatigue, and emaciation), anti-TB treatment history, comorbidities, routine and biochemical tests on pleural fluid (including cell count and differential protein [PRO], glucose [GLU], lactate dehydrogenase [LDH] and ADA levels, anti-*M. tuberculosis* IgG antibody in pleural fluid and serum, acid-fast bacilli [AFB] in pleural fluid and sputum smear, and the culture of pleural fluid, sputum, and pleural biopsy specimens for the detection of *M. tuberculosis*), radiological manifestations (including the size of the pleural effusion, presence of pleural loculations, and lung infiltrates), and pathological findings.

The total number of positive TB tests in pleural fluid was the sum of the number of AFB-positive pleural fluid smears and *M. tuberculosis*-positive pleural fluid cultures. The number of positive TB tests in the pleural cavity was the sum of the number of AFB-positive pleural fluid smears, *M. tuberculosis*-positive pleural fluid cultures, and *M. tuberculosis*-positive pleural biopsy cultures.

These patients were categorized according to the gross findings under medical thoracoscopy as follows:

predominantly nodular (nodule group), caseous necrosis (necrosis group), or thickening (thickening group). Furthermore, these patients were divided into two groups, according to the ADA levels in their pleural effusions as follows: low-ADA group ( $\leq 40$  U/L) and high-ADA group ( $>40$  U/L). These were determined using the peroxidase method.

**Statistical analysis**

All statistical analyses were performed using the SPSS statistical software package (version 19.0; SPSS, Inc., Chicago, IL, USA). Normally distributed data are expressed as mean  $\pm$  standard deviation. Between-group differences were assessed using the Fisher’s exact test and Mann–Whitney U-test for qualitative and quantitative variables, respectively.  $P < 0.05$  was considered statistically significant.

**Results**

**Baseline characteristics of the study population**

The baseline characteristics of the study population are summarized in Table 1. This study included 575 patients with tuberculous pleurisy. These patients had a mean age of  $35.9 \pm 15.8$  years old. Among these patients, 496 patients (86.2%) were between 18 and 59 years old. Furthermore, among these 575 patients, 445 patients were male, while 130 patients were female. The mean duration of tuberculous pleurisy at the time of thoracoscopy was  $2.5 \pm 3.7$  months. Common symptoms included fever (76.1%), cough (70.3%), respiratory distress (61.2%), chest pain (56.0%), fatigue (42.4%), and night sweats (38.4%). Emaciation was present in 65 patients (11.3%). Furthermore, 179 patients (31.1%) received anti-TB treatment before attending our hospital. Most of the pleural effusions were unilateral (93.2%), with bilateral effusions were only observed in 6.8% of patients. Among the 302 patients (52.5%) with pulmonary TB, 189 patients presented with ipsilateral tuberculous pleurisy, while 22 patients had contralateral pleural effusion.

**Tuberculosis tests**

The mean PRO, GLU, LDH, and ADA levels in pleural fluid were  $47.06 \pm 8.46$  g/L,  $3.94 \pm 2.57$  mmol/L,  $953.90 \pm 1,355.60$  U/L, and  $56.09 \pm 45.66$  U/L, respectively. Monocytes were identified in pleural fluid in 80.4% of patients (230/287), while multinucleated cells were identified in pleural fluid in 19.6% of patients (57/287).

Anti-*M. tuberculosis* IgG antibody was detected in the pleural fluid and serum of 67.2% (313/466) and 63.9% (280/438) of patients, respectively. The pleural fluid and sputum smear were AFB positive in 2.5% (11/445) and 3.7% (15/402) of patients, respectively. Furthermore, the pleural fluid, sputum, and pleural

**Table 1: Clinical characteristics of patients with tuberculous pleurisy**

Clinical characteristics	n (%)
Gender	
Male	445 (77.4)
Female	130 (22.6)
Age (years)	
<18	20 (3.48)
18-34	304 (52.8)
35-59	192 (33.4)
>59	59 (10.3)
Fever (°C)	438 (76.1)
37.3-38.0	130 (22.6)
38.1-39.0	194 (33.7)
>39.1	114 (19.8)
Symptoms	
Cough	404 (70.3)
Expectoration	234 (40.7)
Chest distress	352 (61.2)
Chest pain	322 (56.0)
Night sweats	221 (38.4)
Fatigue	244 (42.4)
Emaciation	65 (11.3)
Previous anti-TB treatment	179 (31.1)
Comorbidities	63 (11.0)
Diabetes	19 (3.3)
Renal	5 (0.9)
Pregnancy	8 (1.4)
Rheumatoid	2 (0.4)
Mental illness	3 (0.5)
Hypertension	26 (4.5)
Pulmonary TB	302 (52.5)
Right side	126 (21.9)
Left side	68 (11.8)
Bilateral	108 (18.8)
Nonpulmonary TB	273 (47.5)
Pleural fluid	
Right side	288 (50.1)
Left side	248 (43.1)
Bilateral	39 (6.8)
Pulmonary TB and pleural fluid	
Ipsilateral	189/302 (62.5)
Contralateral	22/302 (7.2)
Bilateral	91/302 (30.1)

TB=Tuberculosis

biopsy cultures for *M. tuberculosis* were positive in 19.2% (85/442), 12.5% (35/279), and 41.9% (198/473) of patients, respectively [Table 2].

**Thoracoscopic findings**

The gross findings under medical thoracoscopy revealed predominant pleural thickening in 47.3% (273/575) of patients, caseous necrosis in 39.5% (227/575) of patients, and pleural nodules in 13.2% (76/575) of patients. Significantly, more patients in the nodule group (77.0%, 57/74) had granulomatous tissue biopsy samples, compared to patients in the necrosis group (62.2%,

135/217) or thickening group (60.9%, 157/258) ( $P < 0.05$ ). Patients in the nodule group had significantly lower levels of LDH and ADA ( $P < 0.05$ ), and significantly higher levels of GLU in pleural fluid ( $P < 0.01$ ), compared to patients in the necrosis group or thickening group. There were no significant differences in the number of positive AFB pleural fluid smears, pleural fluid cultures, or pleural biopsy cultures among groups [Table 3].

**Table 2: Results of tests used for detecting tuberculosis**

Test	n (%)
Serum positive for anti- <i>M. tuberculosis</i> IgG antibody	280/438 (63.9)
Pleural fluid positive for anti- <i>M. tuberculosis</i> IgG antibody	313/466 (67.2)
Sputum smear, AFB positive	15/402 (3.7)
Pleural fluid smear, AFB positive	11/445 (2.5)
Sputum culture positive for <i>M. tuberculosis</i>	35/279 (12.5)
Pleural fluid culture positive for <i>M. tuberculosis</i>	85/442 (19.2)
Pleural biopsy culture positive for <i>M. tuberculosis</i>	198/473 (41.9)
Total positive tests in the pleural cavity	200/567 (35.3)

AFB=Acid-fast bacilli, *M. tuberculosis*=*Mycobacterium tuberculosis*

### Characteristics of tuberculous pleurisy with and without granuloma

The pleural biopsy specimen revealed granulomas in 63.3% of patients. Patients with granuloma had significantly higher levels of PRO, GLU, and ADA, significantly lower levels of LDH, and predominant monocytes in pleural fluid (88.7% [157/177] vs. 65.3% [62/95]), when compared to patients without granuloma (all,  $P < 0.001$ ). Pleural biopsy cultures obtained from patients with granuloma were more likely to be positive for *M. tuberculosis* (48.1%), when compared to pleural biopsy cultures from patients without granuloma (29.5%) [ $P < 0.001$ , Table 4].

### Characteristics of tuberculous pleurisy according to adenosine deaminase level

Pleural fluid PRO ( $48.3 \pm 7.72$  g/L vs.  $45.18 \pm 9.07$  g/L) and LDH ( $1406 \pm 2137$  U/L vs.  $502 \pm 461$  U/L) levels were significantly higher in patients with tuberculous pleurisy and high-ADA levels ( $>40$  U/L), when compared to patients with tuberculous pleurisy and low-ADA levels

**Table 3: Gross findings on thoracoscopy**

	Nodular	Necrosis	Thickening	P
Pleural fluid PRO (g/L)	49.14±5.55	47.13±8.94	46.43±8.65	0.018
Pleural fluid GLU (mmol/L)	5.13±2.28 <sup>b</sup>	3.82±2.84	3.71±2.33	<0.01
Pleural fluid LDH (U/L)	510±460 <sup>b</sup>	1100±1562	1007±1315	<0.01
Pleural fluid ADA (U/L)	44.56±19.26 <sup>a</sup>	62.97±53.01	53.53±43.32	0.016
Positive TB tests				
Sputum smear, AFB positive	2/50 (4)	9/154 (5.8)	4/194 (2.1)	0.183
Pleural fluid smear, AFB positive	2/61 (3.3)	2/179 (1.1)	7/200 (3.5)	0.305
Sputum culture positive for <i>M. tuberculosis</i>	7/41 (17.1)	20/112 (17.8)	8/123 (6.5) <sup>a</sup>	0.022
Pleural fluid culture positive for <i>M. tuberculosis</i>	7/58 (12.1)	44/183 (24.0)	34/198 (17.2)	0.076
Pleural biopsy culture positive for <i>M. tuberculosis</i>	28/62 (45.2)	76/178 (42.7)	92/228 (40.4)	0.763
TB granuloma in pleural biopsy	57/74 (77.0) <sup>a</sup>	135/217 (62.2)	157/258 (60.9)	0.034
Total positive tests in pleural fluid	9/66 (13.6)	45/197 (22.8)	38/222 (17.1)	0.162
Total positive tests in pleural cavity	30/74 (40.5)	98/223 (44.0)	104/265 (39.2)	0.407

Versus the other two groups, <sup>a</sup> $P < 0.05$ ; <sup>b</sup> $P < 0.01$ . TB=Tuberculosis, PRO=Protein, GLU=Glucose, LDH=Lactate dehydrogenase, ADA=Adenosine deaminase, AFB=Acid-fast bacilli, *M. tuberculosis*=*Mycobacterium tuberculosis*

**Table 4: Characteristics of tuberculous pleurisy with and without granuloma in pleural biopsy**

	Granuloma (n=350)	No granuloma (n=203)	P
Duration of illness (month)	30 (15-60)	30 (20-90)	0.026
Pleural fluid PRO (g/L)	48.22±7.42	44.87±9.82	<0.01
Pleural fluid GLU (mmol/L)	4.20±2.55	3.58±2.60	<0.01
Pleural fluid LDH (U/L)	799±1162	1281±1645	<0.001
Pleural fluid ADA (U/L)	56.91±39.42	54.19±56.39	<0.001
Lymphocytic predominance in pleural fluid	157/177 (88.7)	62/95 (65.3)	<0.001
Positive TB tests			
Pleural fluid positive for anti- <i>M. tuberculosis</i> IgG antibody	192/280 (68.6)	110/168 (65.4)	0.499
Pleural fluid smear, AFB positive	9/271 (3.3)	2/157 (1.3)	0.197
Pleural fluid culture positive for <i>M. tuberculosis</i>	59/270 (21.9)	19/156 (12.2)	0.013
Pleural biopsy culture positive for <i>M. tuberculosis</i>	140/291 (48.1)	49/166 (29.5)	<0.001
Total positive tests in pleural fluid	64/299 (21.4)	21/171 (12.3)	0.013
Total positive tests in pleural cavity	164/350 (46.9)	60/203 (29.6)	<0.001

*M. tuberculosis*=*Mycobacterium tuberculosis*, TB=Tuberculosis, PRO=Protein, GLU=Glucose, LDH=Lactate dehydrogenase, ADA=Adenosine deaminase, AFB=Acid-fast bacilli

(≤40 U/L). Patients with tuberculous pleurisy and high-ADA levels were more likely to have granuloma in pleural biopsy specimens (69.8% vs. 52.3%), a positive pleural fluid culture (26.5% vs. 7.4%), and a positive pleural biopsy culture (51.7% vs. 34.0%) (all,  $P < 0.05$ ). Pleural fluid GLU levels were significantly lower in patients with tuberculous pleurisy and high-ADA levels [ $P < 0.01$ , Table 5].

### Characteristics of tuberculous pleurisy according to patient age

The percentage of patients with high-ADA levels in pleural fluid (>40 U/L), who were <18, 18–34, 35–59, and >60 years old, was 83.3% (15/18), 72.8% (193/265), 51.2% (88/172), and 34.7% (17/49), respectively (all groups vs. >60 years old,  $P < 0.001$ ). Patients with tuberculous pleurisy, who were 18–34 years old, were more likely to have granuloma in pleural biopsy specimens when compared to patients who were >60 years old (77.0% vs. 37.9%). Furthermore, there were significant differences in total positive TB tests in the

pleural cavity according to patient's age [<18 years old, 50.0%; 18–34 years old, 50.2%; 35–59 years old, 34.8%; >60 years old, 18.6%; and all groups vs. >60 years old,  $P < 0.001$ ; Table 6].

## Discussion

The present study assessed the efficacy of medical thoracoscopy in diagnosing tuberculous pleurisy and characterized tuberculous pleurisy with medical thoracoscopy. Most of the patients were male, <34 years old, and had unilateral pleural effusions. These findings were in accordance with a case series from Qatar,<sup>[16]</sup> where the mean age of 100 patients with tuberculous pleurisy was 31.5 years old.

In the present study, monocyte was the main cell type in the pleural fluid. Anti-*M. tuberculosis* IgG antibody was detected in the pleural fluid and serum of 67.2% and 63.9% of patients, respectively. Pleural fluid and sputum smear were AFB-positive in only 2.5% and

**Table 5: Characteristics of tuberculous pleurisy according to adenosine deaminase level (≤40 and >40 U/L)**

	ADA ≤40 U/L (n=191)	ADA >40 U/L (n=312)	P
Pleural fluid PRO (g/L)	45.18±9.07	48.3±7.72	<0.01
Pleural fluid GLU (mmol/L)	4.94±2.23	3.27±2.31	<0.01
Pleural fluid LDH (U/L)	502±461	1406±2137	<0.01
Lymphocytic predominance in pleural fluid	93/113 (82.3)	134/170 (78.8)	0.472
TB granuloma in pleural biopsy	99/189 (52.3)	206/295 (69.8)	<0.01
Underwent decortication	12/191 (6.3)	26/312 (8.3)	0.398
Gross findings on thoracoscopy			
Nodules	30/190 (15.8)	36/309 (11.7)	0.185
Necrosis	66/190 (34.7)	137/309 (44.3)	0.034
Thickening	94/190 (49.5)	136/309 (44.0)	0.235
Positive TB tests			
Serum positive for anti- <i>M. tuberculosis</i> IgG antibody	48/149 (32.3)	85/145 (37.0)	0.345
Pleural fluid positive for anti- <i>M. tuberculosis</i> IgG antibody	104/162 (64.2)	198/293 (70.0)	0.21
Pleural fluid smear, AFB positive	0/161 (0)	10/263 (3.8)	0.012
Sputum smear, AFB positive	3/142 (2.1)	11/212 (5.2)	0.146
Sputum culture positive for <i>M. tuberculosis</i>	7/86 (8.1)	26/156 (16.7)	0.064
Pleural fluid culture positive for <i>M. tuberculosis</i>	11/148 (7.4)	72/272 (26.5)	<0.01
Pleural biopsy culture positive for <i>M. tuberculosis</i>	49/144 (34.0)	136/263 (51.7)	<0.01

*M. tuberculosis*=*Mycobacterium tuberculosis*, TB=Tuberculosis, PRO=Protein, GLU=Glucose, LDH=Lactate dehydrogenase, ADA=Adenosine deaminase, AFB=Acid-fast bacilli

**Table 6: Characteristics of tuberculous pleurisy stratified by patient age**

	Age (years)				$\chi^2$	P
	<18	18-34	35-59	>60		
Pleural fluid ADA >40 U/L	15/18 (83.3)	193/265 (72.8)	88/172 (51.2)	17/49 (34.7)	29.706	<0.001
TB granuloma in pleural biopsy	12/20 (60.0)	221/287 (77.0)	95/188 (50.5)	22/58 (37.9)	52.549	<0.001
Gross findings on thoracoscopy						
Nodule	3/19 (15.8)	39/300 (13.0)	27/192 (14.1)	6/58 (10.4)	0.402	0.940
Necrosis	9/19 (47.4)	120/300 (40.0)	74/192 (38.5)	22/58 (37.9)	0.656	0.883
Thickening	7/19 (36.8)	141/300(47.0)	91/192 (47.4)	30/58 (51.7)	1.301	0.729
Positive TB tests						
Total positive tests in the pleural cavity	10/20 (50.0)	149/297 (50.2)	64/184 (34.8)	11/59 (18.6)	26.45	<0.001

ADA=Adenosine deaminase, TB=Tuberculosis

3.7% of patients, respectively. Sputum, pleural fluid, and pleural biopsy cultures were positive for *M. tuberculosis* in 12.5%, 19.2%, and 41.9% of patients, respectively. Taken together, these findings indicate that the evaluation of biopsy tissues obtained by medical thoracoscopy increases the diagnostic yield of patients with tuberculous pleurisy. The effectiveness and safety of medical thoracoscopy in diagnosing tuberculous pleurisy have been previously reported.<sup>[17-19]</sup> Notably, medical thoracoscopy is a minimally invasive procedure performed under local anesthesia.

Tuberculous pleural effusions are characterized by the formation of tuberculous granulomas. Host immune status directly impacts the early granulomatous response to *M. tuberculosis*.<sup>[20]</sup> As the disease progresses, aberrant immune regulation results in the accumulation of cheesy materials, the formation of a necrotic zone, and the disintegration of the center of the granuloma, which releases *M. tuberculosis* to the pleural cavity where more lesions are formed.<sup>[21,22]</sup> In the present study, granulomas were found in pleural biopsy specimens obtained from 63.3% of patients. Specifically, 77.0% of patients, who were 18–34 years old, presented with granuloma in their biopsy specimens versus 37.9% of patients who were >60 years old. The pleural biopsy culture was significantly more likely to be positive for *M. tuberculosis* in patients with granulomas (48.1%) versus patients without granulomas (29.5%). A previous study demonstrated granulomas in pleural needle biopsy specimens obtained from 80% of patients with tuberculous pleurisy, and the mean age of these patients was  $34.1 \pm 18.1$  years old.<sup>[23]</sup>

In the present study, 83.3%, 72.8%, 51.2%, and 34.7% of patients, who were <18, 18–34, 35–59, and >60 years old, respectively, had high-ADA levels (>40 U/L) in the pleural fluid. ADA levels in pleural fluid are a valuable adjunct in diagnosing tuberculous pleurisy.<sup>[10]</sup> In accordance with the present results, Abrao *et al.*<sup>[24]</sup> reported that pleural fluid ADA level in tuberculous pleurisy was negatively correlated with patient's age.<sup>[25]</sup> These findings may be explained by the relatively weak T-cell-mediated immune response in older patients. Therefore, in older patients, when pleural fluid ADA level is  $\leq 40$  U/L, a diagnosis of tuberculous pleurisy cannot be easily excluded from the study. In the present study, it was found that the number of positive pleural fluid and biopsy cultures and granulomas in biopsy specimens were significantly higher in the high-ADA group compared to the low-ADA group.

The present study was associated with some limitations. First, the present study was performed in a single center. Hence, multicenter studies are needed to validate these results. Second, all data were retrospectively

analyzed. Third, the T-cell enzyme-linked immunospot test for TB (T-SPOT) was not used in this study. This is a relatively new test developed for tuberculous diagnosis.<sup>[26]</sup> Xu *et al.*<sup>[9]</sup> reported that the area under the receiver operating characteristic curve of the T-SPOT test for diagnosing tuberculous pleurisy in the pleural fluid is 0.918.

In summary, medical thoracoscopy is effective for diagnosing tuberculous pleurisy. Younger patients with tuberculous pleurisy have a higher number of positive TB tests in the pleural cavity, are more likely to have granulomas in pleural biopsy specimens, and have higher ADA levels in the pleural fluid.

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### Conflicts of interest

There are no conflicts of interest.

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