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Effect of adjunctive corticosteroid therapy on outcomes in pulmonary tuberculosis patients with acute respiratory failure: a cohort study

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ABSTRACT:

Background: Tuberculosis (TB) remains an important and evolving health problem worldwide. Acute respiratory failure, the most severe form of pulmonary tuberculosis, is associated with a high mortality rate. Adjunctive corticosteroid therapy has been reported as an effective treatment in extrapulmonary TB. The aim of this study was to investigate the effect of adjunctive corticosteroid therapy on outcomes in pulmonary tuberculosis patients with acute respiratory failure.

Methods: This retrospective cohort study enrolled newly diagnosed pulmonary tuberculosis patients with acute respiratory failure who were admitted to Siriraj Hospital (Bangkok, Thailand) during January 2011 to December 2013. Patients that received corticosteroid as an adjunctive treatment for pulmonary TB were assigned to the steroid group. The control group consisted of patients that did not receive corticosteroid. Collected data included age, gender, body mass index (BMI), Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, sequential organ failure assessment (SOFA) scores, vital signs, PaO_2/FiO_2 ratio, chest X-ray abnormality pattern, and TB treatment strategies, including antituberculosis agents and adjunct corticosteroid treatment. The primary outcome was hospital mortality rate. The secondary outcomes were hospital length of stay and duration of mechanical ventilation.

Results: Thirty-eight patients were included. There were 18 patients in the steroid group and 20 in the control group. No significant difference was observed between groups for age, gender, BMI, APACHE II score, vital signs, or PaO_2/FiO_2 ratio. Patients in the steroid group had a significantly higher mean SOFA score than controls (5.7±4.5 vs. 3.3±2.6, respectively; p=0.046). Almost all patients in this study (97.1%) had positive culture for M. tuberculosis from sputum. The mean corticosteroid dose was equivalent to hydrocortisone 329.7±146.0 mg/day. Patients in the steroid group had higher hospital mortality than control group patients, but the difference did not achieve statistical significance (66.7% vs. 45.0%, respectively; p=0.21). Adjunctive corticosteroid therapy did not significantly reduce hospital length of stay or duration of mechanical ventilation when compared between the steroid and control groups (12.0±13.3 vs. 14.6±19.3 days, respectively; p=0.636 and 7.2±10.6 vs. 8.0±8.3 days, respectively; p=0.801).

Conclusion: Adjunctive corticosteroid therapy had no significant positive effect on outcomes in pulmonary tuberculosis patients with acute respiratory failure.

Keywords: Adjunctive corticosteroid therapy, Outcomes, Pulmonary tuberculosis, Acute respiratory failure

INTRODUCTION

Tuberculosis (TB) remains an important and evolving health problem worldwide. Globally in 2015, there were 1.4 million new TB cases, and 1.8 million TB-related deaths. Thailand is one of the highest TB-burdened countries in the world, with an estimated 172 new patients per 100,000 population per year, and 13% of these patients have HIV coinfection. The estimated mortality of TB patients with and without HIV coinfection in Thailand was reported to be 8 and 12 per 100,000 population per year, respectively [1].

More than 80% of TB patients have pulmonary involvement, and the most common reason for ICU admission among pulmonary TB patients is acute respiratory failure [2,3]. Acute respiratory failure, including acute respiratory distress syndrome (ARDS), has been reported among 1.5%-18.9% of hospitalized TB patients [4-6]. Mortality among TB patients with acute respiratory failure was reported to range from 62.5% to 81.0% [2,7-9].

Given their anti-inflammatory activity, corticosteroids have been reported as an effective adjuvant therapy for extrapulmonary TB, including tuberculous meningitis and tuberculous pericarditis [10-15]. Data from a recent randomized controlled trial and meta-analysis support the use of steroid to improve outcome in ARDS patients [16,17]. However, whether or not corticosteroid therapy can improve the outcome of pulmonary TB patients with acute respiratory failure has not been established. Accordingly, the aim of this study was to investigate the effect of adjunctive corticosteroid therapy on outcomes in pulmonary tuberculosis patients with acute respiratory failure.

METHODS

This retrospective cohort study enrolled newly diagnosed pulmonary tuberculosis patients with acute respiratory failure who were admitted to Siriraj Hospital (Bangkok, Thailand) during 1 January 2011 to 31 December 2013. Siriraj Hospital is Thailand's largest national tertiary referral center. The study protocol was reviewed and approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand [COA no. 072/2557 (EC3)]. The informed consent was not obtained due to retrospective study nature. The authors declared that the patient's personal data have been secured.

Tuberculosis was diagnosed according to World Health Organization (WHO) definition, which includes identification of Mycobacterium tuberculosis complex from either sputum or bronchoalveolar lavage (BAL) fluid specimen, either by culture or by positive acid-fast bacilli (AFB) stain, with subsequent confirmation of M. tuberculosis by polymerase chain reaction (PCR) [18]. Diagnosis should be based on at least one specimen with confirmed presence of M. tuberculosis, followed by a decision to treat with a full course of anti-TB drugs [19]. Disseminated TB is defined as tuberculous infection involving the blood stream, bone marrow, liver, miliary TB, or 2 or more noncontiguous sites [20-22].

Smear-positive pulmonary TB was defined as at least 2 sputum smears positive for AFB, or one sputum smear positive for AFB with radiographic abnormalities compatible with active pulmonary TB determined by a clinician, or sputum culture positive for M. tuberculosis.

KEY MESSAGES:

- Acute respiratory failure due to pulmonary tuberculosis is associated with a high mortality rate.
- Adjunctive corticosteroid therapy has been proposed as an effective treatment in extrapulmonary TB.
- The result of this study showed that adjunctive corticosteroid had no benefit on outcomes in pulmonary TB with acute respiratory failure patients.

Smear-negative pulmonary TB was defined as sputum smear negative for AFB, but sputum culture positive for M. tuberculosis.

Respiratory failure was defined as a patient who required endotracheal intubation and mechanical ventilation.

We excluded patients aged less than 16 years, those diagnosed with pulmonary TB prior to hospital admission, patients that did not require mechanical ventilation, and cases with an insufficient amount of available information.

Data Collection

Collected data included age, gender, body mass index (BMI), Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, sequential organ failure assessment (SOFA) scores, vital signs, PaO_2/FiO_2 ratio, chest X-ray abnormality pattern, and TB treatment strategies, including antituberculosis agents and adjunct corticosteroid treatment. Patients that received corticosteroid as an adjunctive treatment for pulmonary TB were assigned to the steroid group. The control group consisted of patients that did not receive corticosteroid.

Study Outcomes

The primary outcome was hospital mortality rate. The secondary outcomes were hospital length of stay and duration of mechanical ventilation.

Statistical Analysis

Demographic data were interpreted using descriptive statistics. Continuous variables are expressed as mean ± standard deviation, and categorical variables are presented as number and percentage. Student's t-test or Mann-Whitney U test was used to compare continuous variables between groups, and chi-square test or Fisher's exact test was used to compare categorical variables. We did not perform sample size calculation due to limitation of information about mortality rate of acute respiratory failure associated with pulmonary tuberculosis among those who receive and did not receive steroid treatment. All statistical analyses were performed using the Statistical Package for the Social Sciences version 20 (SPSS, Inc., Chicago, IL, USA). A two-tailed p-value less than 0.05 was regarded as being statistically significant.

RESULTS

One hundred newly diagnosed pulmonary TB patients were admitted to our center during the January 2011 to December 2013 study period. Forty-two of those had acute respiratory failure and required mechanical ventilation. Four of those 42

patients were excluded due to a lack of necessary information. The remaining 38 patients were included in the final analysis. Eighteen patients received adjunctive corticosteroid therapy (steroid group), and 20 patients did not receive adjunctive corticosteroid therapy (control group) (Figure 1).

The baseline characteristics of both groups are shown in Table 1. There were no significant differences between groups relative to age, gender, BMI, APACHE II score, vital signs, or PaO_2/FiO_2 ratio. The average PaO_2/FiO_2 ratio was 187.8±107.4 in the steroid group, and 245.9±106.4 in the control group (p=0.128). Patients in steroid group had a higher SOFA score than patients in the control group (5.7±4.5 vs. 3.3±2.6; p= 0.046).

Treatment strategies and patterns of chest X-ray abnormalities are shown in Table 1. There was no significant difference between groups relative to the proportion of patients who received combination therapy of isoniazid plus rifampicin (77.8% in steroid group vs. 85.0% in control group; p=0.687). Regarding chest X-ray abnormality patterns, most patients had pulmonary infiltration at the upper lobe (72.2% in steroid group vs. 70.0% in control group; p=0.880). The incidence of miliary pattern of pulmonary infiltration was higher in the steroid group, but not significantly so (38.9% in steroid group vs. 15.0% in control group; p=0.144). Multilobar pulmonary involvement was found in 55.6% of patients in the steroid group, and in 65.0% of those in the control group (p=0.741). More than three-quarters of patients (81.2%) in each group met the diagnostic criteria for ARDS.

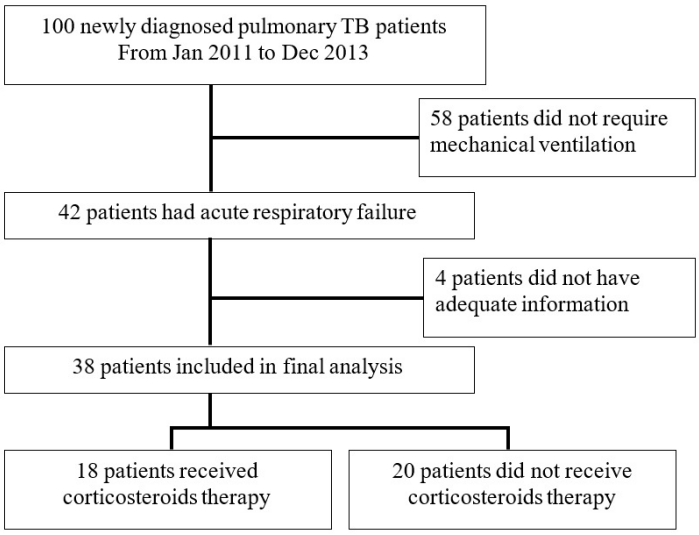

Figure 1. Flow diagram of the study protocol

Confirmation test for diagnosis of pulmonary TB

Almost all patients in this study (97.1%) had positive culture for M. tuberculosis from sputum. Three-quarters (74.3%) of all patients had positive sputum smear for AFB stain. A majority of patients (88.6%) had positive PCR for M. tuberculosis from sputum, and 5.7% of patients had positive PCR for M. tuberculosis from BAL.

Corticosteroid Treatment

Almost half of pulmonary TB patients (47.4%) received corticosteroids as an adjunctive treatment. The mean corticosteroid dose was equivalent to hydrocortisone 329.7±146.0 mg per day. The decision to prescribe corticosteroids was made at the discretion of the attending physician.

Outcomes

Treatment outcomes are shown in Table 2. Patients in the steroid group had higher hospital mortality than control group patients, but the difference did not achieve statistical significance (66.7% vs. 45.0%, respectively; p=0.21). Adjunctive corticosteroid therapy did not significantly reduce hospital length of stay or duration of mechanical ventilation when compared between the steroid and control groups (12.0±13.3 vs. 14.6±19.3 days, respectively; p=0.636 and 7.2±10.6 vs. 8.0±8.3 days, respectively; p=0.801).

DISCUSSION

The results of this study demonstrated that newly diagnosed pulmonary tuberculosis associated with acute respiratory failure is a serious and often fatal condition. The hospital mortality rate in this study was 55%. The administration of corticosteroid, aiming to reduce the inflammatory process that caused lung injury, was unable to improve patient outcomes.

Acute respiratory failure is the most common reason for ICU admission among newly diagnosed Mycobacterium tuberculosis-infected patients, and is associated with a high mortality rate ranging from 62.5% to 81.0% [2,7-9]. The reported predictive factors for the development of acute respiratory failure among pulmonary TB patients include HIV coinfection, large number of acid-fast bacilli on sputum smear, and delayed administration of antituberculosis agents [23].

Although first-line antituberculosis drugs are effective for the treatment of pulmonary TB, a worsening of respiratory symptoms may occur in some pulmonary TB patients after the initial phase of anti-TB treatment. This phenomenon is termed paradoxical reaction [24-26]. A possible explanation for this phenomenon is immunologic restoration, which can lead to the development of new inflammatory lesions. Corticosteroids have been associated with reduced risk of death and disability in tuberculous meningitis [11,12], decreased amount and rate of reaccumulation of tuberculous pericardial effusion [13,14], and faster resolution of pleural effusion in tuberculous pleuritic [15].

In prior study, pulmonary tuberculosis patients who received corticosteroid therapy had a lower mortality rate than those who did not receive corticosteroid therapy (56.7% vs. 77.8%; p=0.046); however, the duration of mechanical ventilation was not significantly different between groups [27]. Another study reported that corticosteroids could be effective for reducing mortality in all forms of tuberculosis, including pulmonary tuberculosis [28]. In contrast, data from a systematic review revealed that adjunctive corticosteroid therapy did not reduce mortality in patients with pulmonary tuberculosis [29].

In the present study, we included only pulmonary tuberculosis patients who required mechanical ventilation and found that patients who received adjunctive corticosteroid therapy had higher hospital mortality than those who did not receive corticosteroids, but the difference did not achieve statistical significance (66.7% vs. 45.0%; p=0.21). Moreover, adjunctive corticosteroid therapy could not reduce hospital length of stay (12.0±13.3 days in patients who received corticosteroids vs. 14.6±19.3 days in those who did not received corticosteroids; p=0.636), or duration of mechanical ventilation (7.2±10.6 days in patients who received corticosteroids vs. 8.0±8.3 days in

Table 1. Baseline characteristics of pulmonary TB patients with acute respiratory failure

Patient characteristics	Control group (n=20)	Steroid group (n=18)	p-value
Age (years), mean±SD	51.1±16.5	42.3±16.2	0.104
Male, n (%)	15 (75.0%)	12 (66.7%)	0.724
BMI (kg/m^2), mean±SD	16.9±3.2	18.9±4.3	0.198
APACHE II score, mean±SD	15.3±7.9	18.9±9.2	0.198
SOFA score, mean±SD	3.3±2.6	5.7±4.5	0.046
PaO_2/FiO_2 ratio, mean±SD	245.9±106.4	187.8±107.4	0.128
MAP (mmHg), mean±SD	70.2±25.8	63.9±19.1	0.421
Temperature (°C), mean±SD	38.5±1.4	38.6±1.7	0.852
Respiratory rate (/min), mean±SD	30.4±7.8	28.9±7.3	0.574
Heart rate (/min), mean±SD	114.7±23.8	120.5±25.7	0.493
Chest X-ray abnormalities, n (%)			0.714
-Multilobar infiltration (≥2 lobes)	13 (65.0%)	10 (55.6%)	
-Miliary pattern	3 (15.0%)	7 (38.9%)	
-Upper lobe infiltration	3 (15.0%)	0 (0%)	
-Cavity lesion	1 (5.0%)	1 (5.6%)	
Received isoniazid + rifampicin, n (%)	17 (85.0%)	14 (77.8%)	0.687

A p-value less than 0.05 indicates statistical significance

Abbreviations: TB, tuberculosis; SD, standard deviation; BMI, body mass index; APACHE II score, Acute Physiology and Chronic Health Evaluation II score; SOFA score, Sequential Organ Failure Assessment score; MAP, mean arterial pressure

Table 2. Treatment outcomes of pulmonary TB patients with acute respiratory failure

Patient outcome	Control group (n=20)	Steroid group (n=18)	Odd ratio (95% confidence interval)	p-value
Primary outcome, n (%)				
-Hospital mortality	9 (45.0%)	12 (66.7%)	1.48 (0.69-3.92)	0.210
Secondary outcomes (day), mean±SD				
-Hospital length of stay	14.6±19.3	12.0±13.3		0.636
-Duration of mechanical ventilation	8.0±8.3	7.2±10.6		0.801

A p-value less than 0.05 indicates statistical significance

Table 3. Summary of the study's population and mortality outcome among corticosteroid and non-corticosteroid treatment for pulmonary tuberculosis

Study	Population	Treatments	Outcomes (Corticosteroid vs non-corticosteroid)
Kim YJ. 2008 (28) Observation	Pulmonary TB with acute respiratory failure	Corticosteroid n=30 Non-corticosteroid n=36	Hospital mortality 56.7% vs 77.8%
	Miliary TB	Corticosteroid n=14 Non-corticosteroid n=10	Hospital mortality 50% vs 70% OR 0.54 (95%CI 0.42-0.67), P=0.001
Critchley J. 2013 (29) Meta-analysis	Pulmonary TB	Corticosteroid n=2,175 Non-corticosteroid n=1,641	Overall mortality 0.016% vs 0.027% Risk ratio 0.77 (95%CI 0.51-1.15), P=0.2
Yang JY. 2016 (30) Retrospective study	Pulmonary TB with acute respiratory failure	Corticosteroid n=70 Non-corticosteroid n=54	90 days mortality 48.6% vs 50.0% Adjusted OR 0.47 (95%CI 0.22-0.98), P=0.049
Tongyoo S. 2021 Retrospective study	Pulmonary TB with acute respiratory failure	Corticosteroid n=20 Non-corticosteroid n=18	Hospital mortality 66.7% vs 45% OR 1.48 (95%CI 0.69-3.92), P=0.21

those who did not received corticosteroids; p=0.801). There was no significant difference in baseline characteristics, antituberculosis treatment, or patterns of chest X-ray abnormalities between groups, except for the mean SOFA score, which was significantly higher in the steroid group (p=0.046). The higher SOFA score predicted higher mortality among patients in the steroid group, which probably did not associate with steroid receiving itself.

A recent cohort study from South Korea designed to investigate the role of corticosteroids in critically ill pulmonary tuberculosis patients with acute respiratory failure reported that adjunctive corticosteroid therapy did not reduce the unadjusted 90-day mortality (odds ratio [OR]: 0.94, 95% confidence interval [CI]: 0.46-1.92; p=0.875). However, when using inverse probability of treatment weighted (IPTW) estimators to adjust for differences between the steroid and non-steroid groups, they found corticosteroid treatment to be independently associated with reduced 90-day mortality (OR: 0.47, 95% CI: 0.22-0.98; p=0.049). However, patients in the steroid group had a higher rate of superimposed infection (32.9% vs. 13.0%; p=0.010) [30].

Having acknowledged a difference in finding between our study and the aforementioned South Korean study, it should be noted that there are some differences in study population baseline characteristics between the two studies. In our study, we enrolled only confirmed pulmonary TB cases (positive culture, or positive AFB smear with positive PCR for M. tuberculosis from sputum or bronchoalveolar lavage fluid), and all of our patients required mechanical ventilation. In contrast, the Korean study also included possible pulmonary tuberculosis cases that had only clinical symptoms and/or signs that were suggestive of tuberculosis, but that had negative sputum culture and negative sputum AFB smear. Moreover, 17.7% of their study population did not require mechanical ventilation. The comparisons between our present study and previous studies were shown in table 3.

This study has some mentionable limitations. First and consistent with the retrospective nature of this study, some patient data was found to be missing or incomplete, such as duration of corticosteroid treatment and ventilator strategy data. Additionally, the inclusion of only definite pulmonary tuberculosis could result in a selection bias. Second, the size of the study population was relatively small. As a result, our study may have lacked sufficient power to identify all significant differences and associations. We were also unable to perform propensity score match analysis, and subgroup analysis for populations at higher risk for mortality. Third, the patients enrolled in this study were from a single center. Fourth, our center is Thailand's largest tertiary referral hospital, which means that we are often referred patients with complicated and intransigent conditions. As such, it is possible that our findings may not be generalizable to patients with the same condition in other settings. Further studies in pulmonary TB patients with acute respiratory failure that include these factors are warranted to more conclusively establish the efficacy of corticosteroids in this patient population.

CONCLUSION

Adjunctive corticosteroid therapy had no significant positive effect on outcomes in pulmonary tuberculosis patients with acute respiratory failure. At current situation, corticosteroid therapy could not be recommended as the treatment of acute respiratory failure associated with pulmonary tuberculosis.

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AUTHORS' CONTRIBUTIONS

(I) Conception and design: All authors; (II) Administrative support: Permpikul C; (III) Provision of study materials or patients: Viarasilpa T; (IV) Collection and assembly of data: Tongyoo S; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

SUPPLEMENTARY MATERIALS

none

REFERENCES

1. World Health Organization, Global Tuberculosis Report 2016.
2. Frame RN, Johnson MC, Eichenhorn MS, Bower GC, Popovich JM Jr. Active tuberculosis in the medical intensive care unit: A 15-year retrospective analysis. Crit Care Med. 1987; 15:1012–4.
3. Silva DR, Menegotto DM, Schulz LF, Gazzana MB, Dalcin PT. Mortality among patients with tuberculosis requiring intensive care: a retrospective cohort study. BMC Infectious Diseases. 2010;10:54.
4. Levy H, Kallenbach JM, Feldman C, Thorburn JR, Abramowitz JA. Acute respiratory failure in active tuberculosis. Crit Care Med. 1987;15:221–5.
5. Agarwal MK, Muthuswamy PP, Shah RS, Addington WW. Respiratory failure in pulmonary tuberculosis. Chest. 1977;72:605-9.
6. Agarwal R, Gupta D, Aggarwal AN, Behera D, Jindal SK. Experience with ARDS caused by tuberculosis in a respiratory intensive care unit. Intensive Care Med. 2005;31:1284-7.
7. Kim JY, Park YB, Kim YS, Kang SB, Shin JW, Park IW, et al. Miliary tuberculosis and acute respiratory distress syndrome. Int J Tuberc Lung Dis. 2003;7:359-64.
8. Penner C, Roberts D, Kunimoto D, Manfreda J, Long R. Tuberculosis as a primary cause of respiratory failure requiring mechanical ventilation. Am J Respir Crit Care Med. 1995;151:867-72.
9. Anekrhananon T, Ratanasuwan W, Techasathit W, Suwanagool S,Dhiraputra C. Multidrug resistant Mycobacterium tuberculosis infections in patients with acquired immunodeficiency syndrome at Siriraj hospital. Siriraj Hosp Gaz. 2002;54:108-14.
10. Didonato JA, Saatcioglu F, Karin M. Molecular mechanisms of immunosuppression and anti-inflammatory activities by glucocorticoids. Am J Respir Crit Care Med. 1996;154:511-5.
11. Thwaites GE, Nguyen DB, Nguyen HD, Hoang TQ, Do TT, Nguyen TC, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med. 2004;351:1741-51.
12. Thwaites G, Fisher M, Hemingway C, Scott G, Solomon T, Innes J, et al. British infection society guidelines for the diagnosis and treatment of tuberculosis of the central nervous system in adults and children. J infection. 2009;59:167-87.
13. Dooley DP, Carpenter JL, Rademacher S. Adjunctive corticosteroid therapy for tuberculosis: a critical reappraisal of the literature. Clin Infect Dis 1997;25:872–87.
14. Trautner BW, Darouiche RO. Tuberculous pericarditis: optimal diagnosis and management. Clin Infect Dis. 2001;33:954-61.
15. Engel ME, Matchaba PT, Volmink J. Corticosteroids for tuberculous pleurisy. Cochrane Database of Syst Rev. 2007;17:CD001876.
16. Tongyoo S, Permpikul C, Mongkolpun W, Vattanavanit V, Udompanturak S, Kocak M, et al. Hydrocortisone treatment in early sepsis associated acute respiratory distress syndrome: results of a randomized controlled trial. Critical Care. 2016;20:329.
17. Meduri GU, Bridges L, Shih MC, Marik PE, Siemieniuk RA, Kocak M. Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature. Intensive Care Med. 2016;42:829–40.
18. World Health Organization. Treatment of tuberculosis: guidelines, 2010.
19. Chaiprasert A. Future trend in laboratory diagnosis of tuberculosis. Siriraj Med J. 2009;61:45-8.
20. American Thoracic Society. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med. 2000;161:1376-95.
21. Sahn SA, Neff TA. Miliary tuberculosis. Am J Med. 1974;54:495–505.
22. Therasakvichya S, Choavaratana R, Sompradeekul S. Disseminated tuberculosis. Siriraj Hosp Gaz. 2002;54:484-8.
23. Bhurayanontachai R, Maneenil K. Factors influencing development and mortality of acute respiratory failure in hospitalized patient with active pulmonary tuberculosis: a 10-year retrospective review. J Thorac Dis. 2016;8:1721-30.
24. Cheng VC, Ho PL, Lee RA, Chan KS, Chan KK, Woo PC, et al. Clinical spectrum of paradoxical deterioration during antituberculosis therapy in non-HIV-infected patients. Eur J Clin Microbiol Infect Dis. 2002;21:803–9.
25. Orlovic D, Smego RA. Paradoxical tuberculous reactions in HIV-infected patients. Int J Tuberc Lung Dis. 2001;5:370–5.
26. Ryu YJ, Koh WJ, Kang EH, Suh GY, Chung MP, Kim H, et al. Prognostic factors in pulmonary tuberculosis requiring mechanical ventilation for acute respiratory failure. Respirology. 2007;12:406-11.

27. Zahar JR, Azoulay E, Klement E, De Lassence A, Lucet JC, Regnier B, et al. Delayed treatment contributes to mortality in ICU patients with severe active pulmonary tuberculosis and acute respiratory failure. Intensive Care Med. 2001;27:513-20.
28. Kim YJ, Pack KM, Jeong E, Na JO, Oh YM, Lee SD, et al. Pulmonary tuberculosis with acute respiratory failure. Eur Respir J. 2008;32:1625-30.
29. Critchly JA, Young F, Orton L, Garner P. Corticosteroids for prevention of mortality in people with tuberculosis: a systematic review and meta-analysis. Lancet Infect Dis. 2013;13:223-37.
30. Yang JY, Han M, Koh Y, Kim WS, Song JW, Oh YM, et al. Effects of corticosteroids on critically ill pulmonary tuberculosis patients with acute respiratory failure: a propensity analysis of mortality. CID. 2016;63:1449-55.