

Clinical Research

The accuracy of Aziza's scoring system in limited slice non-enhanced thoracic CT for the diagnosis of adult pulmonary tuberculosis

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ABSTRAK

Latar belakang: Tuberkulosis (TB) masih merupakan penyebab kesakitan dan kematian terbesar di Indonesia. Dibutuhkan alat diagnostik yang cepat dan akurat dalam diagnosis TB paru dewasa terutama pada TB paru dengan bakteri tahan asam (BTA) negatif. Tujuan penelitian ini menentukan akurasi sistem skoring yang disebut skoring Aziza untuk diagnosis TB paru BTA negatif dengan CT scan toraks tanpa kontras potongan terbatas.

Metode: Penelitian ini adalah penelitian prospektif potong lintang. Pemeriksaan CT scan toraks tanpa kontras potongan terbatas diterapkan pada pasien tersangka TB paru untuk selanjutnya dilakukan pengkajian nilai diagnostik menggunakan sistem skoring. Pada penelitian ini standar referensi adalah pendapat 2 dokter spesialis paru untuk menentukan TB paru. Sistem skoring dianalisis menggunakan analisis bivariat, regresi Cox multivariat.

Hasil: Dari 130 pasien tersangka TB paru, didiagnosis 84 pasien TB paru berdasarkan sistem skoring CT scan toraks tanpa kontras potongan terbatas. Selanjutnya dilakukan analisa bivariat dan regresi Cox multivariat. Diperoleh nilai skor 29 atau lebih untuk menegakkan diagnosis TB paru dewasa dengan nilai akurasi 96,2% (95% IK=90,3-97,8%), sensitivitas 96,5% (95% IK=90-98,8% dan spesifisitas 95,6% (95% IK=85-96,8%).

Kesimpulan: Sistem skoring Aziza dengan CT scan toraks tanpa kontras potongan terbatas mempunyai akurasi setara dengan standard referensi untuk menegakkan diagnosis TB paru dewasa.

ABSTRACT

Background: Tuberculosis (TB) is still a major cause of morbidity and mortality in Indonesia. Thus, a fast and accurate method in diagnosing pulmonary TB (PTB) is needed, especially in adult smear-negative-TB cases. The purpose of this study was to determine the accuracy of a novel scoring system (Aziza's score) using clinical data and characteristic abnormalities that are found in the limited slice non-enhanced thoracic CT.

Methods: This was a prospective cross-sectional study. A limited slice non-enhanced thoracic CT was performed to establish a diagnosis of PTB in patients with suspected PTB and to assess the diagnostic value of the scoring system. A reference standard used in this study was the clinical expertise of two pulmonologists. The scoring system was analyzed using bivariate and multivariate Cox regression analysis.

Results: 84 of 130 suspected PTB patients were diagnosed as PTB. They were diagnosed based on pulmonary characteristic abnormalities that were found in the limited slice non-enhanced thoracic CT. The scoring system was analyzed using bivariate and multivariate Cox regression analysis. The total scores which were equal to or more than 29 could diagnose PTB with the accuracy of 96.1% (95% CIs=91.3-98.3), sensitivity of 96.5% (95% CIs=90.1-98.8), and specificity of 95.6% (95% CIs=90.1-98.8). This novel scoring method was named as an Aziza's scoring system.

Conclusion: Aziza's scoring system performed in the limited slice non-enhanced thoracic CT has a higher accuracy compared to the reference standard for the diagnosis of adult PTB.

Keywords: adult PTB, Aziza's scoring system, limited slice non-enhanced thoracic CT

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Pulmonary tuberculosis (PTB) is a worldwide problem. It is one of the leading causes of mortality, especially in developing countries. PTB remains as a major health problem in Indonesia.¹ The gold standard for diagnosing PTB is to find *Mycobacterium tuberculosis* (MTB) through culture, which is difficult to perform and takes a long time.² Nowadays, PTB is most commonly diagnosed by finding the acid-fast bacilli (AFB) in the patient's sputum. However, in more than 50% of PTB cases, the AFB are not found in sputum examination.² Relying upon clinical judgment in diagnosing and treating PTB will still be continued in the daily practice until an easy, fast, and cheap alternative tool is available.^{3,4}

Currently, diagnosis of PTB is still mainly supported by a chest X-ray, especially in smear-negative TB cases. Thus, incorrect radiology expertise could mislead the management of PTB.^{5,6} The high resolution computed tomography (HRCT) is more sensitive (98%) compared to chest X-ray (19–58%) in showing minimal lesions, differentiating between active and non-active lesions, detecting endobronchial dissemination, and diagnosing active smear-negative PTB.^{2,7–15}

It is important to create a standardized system using a scoring system to guide radiologists in reporting computed tomography (CT) findings when diagnosing smear-negative adult PTB. A scoring system could produce a valid and reliable evaluation of chest CT regardless of radiologists' varying experiences and skills, and in turn, help clinicians to make an empirical judgment in treating PTB. The use of a scoring system along with limited slice non-enhanced thoracic CT is as an innovative tool in diagnostic assessment, especially in smear-negative PTB cases.

The purpose of this study was to introduce a new method in diagnosing PTB by a limited slice non-enhanced thoracic CT and report results by using this scoring system. This method could be a faster, cheaper, and more effective alternative to provide an accurate diagnosis of adult PTB compared to the reference standard.

METHODS

The protocol of this study has been approved by the ethical committee of Persahabatan

Public Hospital Jakarta, Indonesia (No. 01/KEPK-RSUP/IX/2012) and all subjects provided written informed consent. In this cross-sectional study, we consecutively collected 130 subjects from September 2012 to June 2013, who were suspected of having PTB based on the clinical symptoms and chest X-ray, but the sputum smear results were negative.

This study was conducted at the Department of Radiology, Persahabatan Hospital, Jakarta. The CT used kilovolt (KV) 120 and miliampere second (mAs) with application cared doses referenced to 100 and dose length product (DLP) ranged from 110 to 123 (Figure 1). A limited slice non-enhanced thoracic CT confined to adult TB predilection areas was performed to the suspected PTB whose sputum smear finding was negative, to reduce the radiation dose. The examined areas were the upper zone, posterosuperior apical lobes (1.2.3 right and 1/2.3 left segments) and inferior lobes (six right and left segments). To assess the spreading of lesion and pleural effusion, part of middle and the lower zone (4.5.7.8.9.10 right and left segments) were also included. The limited slice chest CT was examined by a thoracic radiologist who had 18 years of experience in the field of thoracic imaging.



Figure 1. Limited slice non-enhanced chest CT A) part of upper lung zone; B) part of middle lung zone; C) part of lower lung zone

All statistical analyses were performed using SPSS statistical software, version 20 for windows. The scoring system was calculated using bivariate and multivariate Cox regression analysis since both independent and dependent variables were dichotomous categorical data. The independent variables were age, the history of previous contact with PTB patients, the history of smoking, and nine characteristic lesions in thoracic CT: infiltrate, nodule, tree in bud opacity, consolidation, ground glass opacity, cavity, reverse halo sign, fibro calcification, and pleural effusion.

The reference standard used in this study was the expert opinions of two pulmonologists based on the subject's clinical follow-up. The diagnosis of TB or non-TB was made two months after the antituberculosis agents (ATA) treatment based on the combination of clinical and radiological improvement, and/or positive culture result. If after two month-clinical and radiological findings showed improvement, ATA was continued even though the culture result was negative. If no improvement was shown, further diagnostic assessment had to be implemented.

RESULTS

With this protocol, 84 cases of PTB were diagnosed out of 130 suspected PTB cases. The median age of subjects was 39 years old, ranging from 16 to 86 years old. The gender of the subjects was relatively equal. Only nine subjects had a history of contact with PTB patients. Forty subjects (30.7%) had history of smoking. 102 subjects had clinical symptoms, and the most common symptom was coughing more than two weeks (62.30%). Chest X-ray suggestive of PTB was found in 60 subjects, and the limited slice non-enhanced CT suspect PTB were 84 subjects. The baseline characteristics of the subjects are presented in Table 1.

From limited slice non-enhanced thoracic CT, there were some major lesions related to PTB. The most common lesion was infiltrate (50%), followed by tree-in-bud (47.7%) and nodules (46.2%). The least common lesion was reverse halo sign, which was only found in four subjects (3.1%). The distribution of lesions is presented in Table 2.

The diagnostic value of the limited slice non-enhanced thoracic CT in predicting adult PTB compared to the reference standard is presented in Table 3.

Scoring analysis was performed from the result of bivariate analysis between each criterion and the reference standard to see which criteria could be included in the Cox regression multivariate

Table 1. Subjects' characteristics of suspected PTB (n=130)

Variable	n	%
Age		
<40	50	38.0
>40	80	92.0
Gender		
Men	68	52.0
Women	62	48.0
Symptom		
Yes	102	78.5
No	28	21.5
TB contact		
Yes	9	6.9
No	121	93.1
Smoking		
Yes	40	30.8
No	90	69.2
Chest X-ray		
TB	60	46.2
Non TB	70	53.8
Chest CT		
TB	84	64.6
Non-TB	46	33.4

Table 2. Main lesions PTB subjects based on limited slice non-enhanced thoracic CT (n=84)

Lesion	n	%
Infiltrate	65	50.0
Tree in Bud	62	47.7
Nodules	60	46.2
Fibro calcification	49	37.7
Cavities	32	24.6
Consolidation	31	23.8
Effusion	15	11.5
GGO	12	9.2
Reverse halo sign	4	3.1

GGO= ground glass opacity

analysis. The results of bivariate analysis are presented in Table 4.

Variables included in the Cox regression multivariate analysis were the variables with $p < 0.25$ in the bivariate analysis, i.e., eight major lesions and two demographic factors consisting of infiltrate, nodules, cavities, tree in bud, consolidation, reverse halo sign, fibro calcification, pleural effusion, age, and history of smoking. To create the scoring model, the score of each variable was calculated from the index value of Cox regression analysis by dividing every variable's B/SE value with the lowest B/SE value, the pleural effusion's, as a comparison. Infiltrate had the highest score value (27) with the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 75%, 98%, 98%, and 68%, respectively; likelihood ratio was 33.88. The result of each variable score is presented in Table 5.

The scoring system was then applied to the subjects, and the result was compared with the reference standard in predicting PTB using receiver operating characteristic (ROC) method to acquire the cutoff point with the area under the curve (AUC) of 0.987 (0.969–1.00). A cut off point of 29 provided the most balanced sensitivity of 96.5% and specificity of 95.6% and was decided as the total score limit to differentiate PTB and non-PTB cases.

Scoring analysis

Based on the scoring system, 82 subjects had a total score of ≥ 29 and were diagnosed as having PTB, while from the reference standard, there were 85 subjects diagnosed as having PTB. This showed that subjects with negative findings of sputum and chest X-ray were diagnosed as

Table 3. Diagnostic value of the limited slice thoracic CT compared to the reference standard in predicting adult PTB

	Reference standard					
	TB	Non-TB	Sn	Sp	PPV	NPV
Thoracic CT			0.99	1	1	0.98
TB	84	0				
Non-TB	1	45				

Sn= sensitivity, Sp= specificity, PPV= positive predictive value, NPV= negative predictive value

Table 4. Analysis between each demographic factor and several main lesions found in the limited slice thoracic CT compared with the reference standard in predicting adult pulmonary TB

Variables	Reference standard				p
	Positive		Negative		
	n	%	n	%	
TB contact					0.933
Yes	6	7.10	3	6.70	
No	79	92.90	42	93.30	
Smoking					0.124†
Yes	30	35.30	10	22.20	
No	55	64.70	35	77.80	
Age					0.022*
<40	50	58.80	17	37.80	
≥ 40	35	41.20	28	62.20	
Gender					0.57
Woman	39	45.90	23	51.10	
Man	46	54.10	22	48.90	
Infiltrate					0.001*
Present	64	75.30	1	2.20	
No	21	24.70	44	97.80	
Nodule					0.001*
Present	52	61.20	8	17.80	
No	33	38.80	37	82.20	
Tree in bud					0.001*‡
Present	62	72.90	0	0.00	
No	23	27.10	45	100.00	
Cavities					0.001*‡
Present	32	37.60	0	0.00	
No	53	62.40	45	100.00	
GGO					0.59
Present	7	8.20	5	11.10	
No	78	91.80	40	88.90	
Consolidation					0.001*
Present	30	35.30	1	2.20	
No	55	64.70	44	97.80	
Reverse H.					0.139†
Present	4	4.70	0	0.00	
No	81	95.30	45	100.00	
Fibrocalcification					0.059†
Present	37	43.50	12	26.70	
No	48	56.50	33	73.30	
Effusion					0.065
Present	13	15.30	2	4.40	
No	72	84.70	43	95.60	

* $p < 0.05$; † < 0.25 eligible for multivariate Cox regression analysis; ‡ Fischer exact test bivariate analysis predicting adult PTB

negative-smear PTB after being re-examined using limited slice non-enhanced thoracic CT with Aziza's scoring system. This result was confirmed by two experts. The summary of Aziza's scoring system in limited slice non-enhanced thoracic CT for the diagnosis of adult PTB is presented in Table 6.

Among the 46 patients diagnosed as not having PTB, 18 (13.8%) patients did not have any lesion, 15 (11.5%) patients were diagnosed as having inactive TB lesion, 5 (3.8%) patients were diagnosed as having pneumonia, and 8 (6.2%) patients had other abnormalities.

DISCUSSION

This study has developed a novel scoring system in interpreting limited slice non-enhanced thoracic CT scan in a predilection area of adult PTB, aptly named Aziza's scoring system. The scoring system could produce a valid and reliable evaluation of chest CT regardless of the radiologists' various experiences and skills, and in turn help clinicians to make an empirical judgment in treating PTB. The proposed method is not only simple and feasible, but also has a high accuracy to distinguish between adult PTB and non-PTB, as reflected by AUC of 0.987.

The scoring system included demographic factors and main lesions in CT. The median age of the subjects was 39 years old with a range of

15 to 86 years old. Several studies have found similar results.¹⁶⁻¹⁹ This situation will bring socio-economic impacts for patients, families, and communities because in this age group, the level of social interaction is high. Therefore, it could increase the possibility of transmission and major problems in the future, such as permanent pulmonary disability, multidrug resistant (MDR) TB and post-PTB obstruction syndrome. Our study used the age of 40 as the cut off point, as well as one of the variables predictive of PTB based on scoring.

Table 6. Summary of Aziza's scoring system in limited slice non-enhanced thoracic CT for the diagnosis of adult pulmonary tuberculosis

Variables	Score
Age <40	4
smoking	3
Infiltrate	27
Nodule	13
Tree in bud	22
Cavity	8
Consolidation	15
Reverse	2
Fibrocalcification	8
Effusion	1
Total score	103

Based on the Aziza's scoring system, cut off point ≥ 29 was decided as the total score limit to differentiate PTB and non-PTB based on demographic and the limited slice non-enhanced thoracic TB in a predilection of post primary TB

Table 5. Diagnostic value of each variable score compared to the reference standard

Variables	Score	Sn (%)	Sp (%)	PPV (%)	NPV (%)	LRP	LRN	Accuracy (%)
Age <40	4	59	62	75	44	1.56	0.66	50
Smoking	3	35	78	75	39	1.59	0.83	60
Infiltrate	27	75	98	98	68	33.88	0.25	83
Nodule	13	61	82	87	53	3.44	0.47	68
Tree in bud	22	73	100	100	66	-	0.27	81
Cavity	8	38	100	100	46	-	0.62	59
Consolidation	15	35	98	97	44	15.88	0.66	56
Reverse	2	5	100	100	36	-	0.95	37
Fibrocalcification	8	44	73	76	41	1.63	0.77	53
Effusion	1	15	96	87	37	3.44	0.89	43
Total score	103							

Sn= sensitivity; Sp= specificity; PPV= positive predictive value; NPV= negative predictive value; LRP= likelihood ratio positive; LRN= likelihood ratio negative

Forty subjects smoked, and the remaining ninety subjects did not. According to literature, smoking 15 packs/year and having long duration of smoking pose higher risk for the occurrence of PTB. Epidemiological research in South Africa reported that 50% of mortality rate is associated with smoking habit.²⁰ Most subjects exhibited clinical symptoms, in which the most common one was coughing more than two weeks, as it was found in 81 subjects (62.3%). Similar results have been reported in several studies.^{17,18,21} According to literature, patients with negative smear PTB were generally asymptomatic and usually found accidentally while undergoing chest X-ray.^{2,8} Thus, the clinical symptoms were not included in the scoring as the current study focused on the smear-negative PTB patients.

Aziza's scoring system is used after suspected cases are examined on limited slice non-enhanced thoracic CT scan. The statistically significant abnormalities with $p=0.001$ ($p<0.05$ from chi square test) were infiltrates (75.3%), tree in bud (72.9%), nodules (61.2%), cavity (37.6%), and consolidation (35.3%). Yadav et al² reported slightly different findings where the major abnormalities were centrilobular nodules (91%), consolidation (38%), cavity (48%), tree in bud pattern (88%).² Yeh et al⁷ performed thoracic CT in forty cases of smear-negative TB and reported findings such as centrilobular nodules (51.2%), consolidation (35%), cavity (17.5%), and tree in bud (87.5%). Tree in bud is a sign of endobronchial TB, and a sign of active PTB if it is found in areas of PTB predilection.^{2,7,9,12}

Besides finding abnormalities associated with PTB, thoracic CT scans also find other abnormalities. This study found emphysema in 23 patients (17.7%), bronchiectasis in 16 patients (12.3%), fungal infections in three patients (2.3%) and mass in three patients (2.3%). Other studies have also found non-TB abnormalities in the thoracic CT results.^{9,12} This study demonstrates the superiority of thoracic CT despite performed in non-enhanced limited slices.

The limitation of this study is using clinical follow-up expert opinion as a reference standard. This method could be deemed as subjective, but it is the common clinical practice, even in a specialized hospital. From literature, it is said that a standard reference is the best available method to declare

the patients' disease and to ensure patients not suffering from the disease. Reference standards may be clinical follow-up, a combination of clinical follow-up and laboratory tests.^{22,23}

In conclusion, the Aziza's scoring system performed in limited slice non-enhanced thoracic CT has a high accuracy in diagnosing adult PTB. We propose the Aziza's scoring system as a standard guideline in interpreting limited slice non-enhanced thoracic CT and in diagnosing adult PTB due to its benefit for smear-negative PTB cases and for early PTB case-finding.

Conflicts of interest

The authors affirm no conflict of interest in this study.

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