

The Relationship between Six Minutes Walking Distance and Quality of Life in Pulmonary Tuberculosis Sequelae Patients

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ABSTRACT

Background: Tuberculosis is an infectious disease that affects the lung and has high incidence. It could leave sequelae in the patient that has been declared cured. Tuberculosis sequelae results in changes of lung function that could lead to deteriorating of functional capacity and quality of life.

Aim: The study aim to determine the relationship between functional capacity (6MWD) and quality of life (SGRQ) within pulmonary tuberculosis sequelae patients.

Method: This study used cross sectional design and performed on pulmonary tuberculosis sequelae patient in pulmonary clinic of Dr. Sardjito General Hospital and BP4 Yogyakarta. Functional capacity was assessed with six minutes walking distance and assessment of quality of life using SGRQ questionnaire. Distribution of data was tested using the Shapiro-Wilk statistical test. Spearman correlation test and regression test was used to analyze the correlation between 6-minute walking distance test and assessment of quality of life using the SGRQ questionnaire.

Result: The 6 minutes walking distance was 257.02 ± 64.56 m. There were significant negative correlation between 6 minutes walking distance and SGRQ score activity domain ($r = -.333$, $p < 0.05$). The others domains in SGRQ, there were no significant negative correlation at domain symptoms ($r = -.062$), impacts ($r = -.114$), and total ($r = -.135$).

Conclusion: There were negative correlation between the 6 minutes walking distance (6MWD) and SGRQ score. There was significant negative correlation between 6 minutes walking distance (6MWD) and activity domain in the SGRQ score.

Keywords: tuberculosis sequelae, functional capacity, 6MWD, quality of life, SGRQ.

ABSTRAK

Latar Belakang: Tuberkulosis adalah penyakit infeksius yang menyerang paru-paru dan mempunyai angka kejadian yang cukup tinggi. Penyakit ini dapat meninggalkan gejala sisa (sekuele) pada pasien yang sudah dinyatakan sembuh. Sekuele tuberkulosis mengakibatkan perubahan pada paru sehingga pasien dapat mengalami penurunan kapasitas fungsional dan kualitas hidup.

Tujuan: Penelitian ini bertujuan untuk mengetahui hubungan antara kapasitas fungsional (6MWD) dengan kualitas hidup (SGRQ) pada pasien sekuele tuberkulosis paru.

Metode: Penelitian menggunakan analisis potong lintang yang dilakukan pada pasien sekuele tuberkulosis di poliklinik paru RSUP Dr. Sardjito dan BP4 Yogyakarta. Kapasitas fungsional diperiksa dengan uji jalan 6 menit dan penilaian kualitas hidup menggunakan kuesioner SGRQ. Distribusi atau sebaran data diuji menggunakan uji statistik Shapiro-Wilk. Uji korelasi spearman dan regresi digunakan untuk menganalisis hubungan antara hasil uji jalan 6 menit dengan hasil kuesioner SGRQ.

Hasil: Hasil uji jalan 6 menit sebesar $257,02 \pm 64,56$ m. Terdapat hubungan negatif bermakna antara uji jalan 6 menit dengan skor SGRQ domain aktivitas ($r = -.333$, $p < 0.05$). Pada skor SGRQ domain lain, terdapat hubungan negatif tidak bermakna, yaitu domain gejala ($r = -.062$), dampak ($-.114$), dan total ($-.135$).

Kesimpulan: Ada korelasi negatif antara uji jalan 6 menit (6MWD) dengan skor SGRQ. Terdapat juga hubungan bermakna antara uji jalan 6 menit (6MWD) dengan skor SGRQ domain aktivitas.

Kata kunci: sekuele tuberkulosis, kapasitas fungsional, 6MWD, kualitas hidup, SGRQ.

INTRODUCTION

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis and transmitted through the air. The sequelae of tuberculosis is a residue lesion due to histopathology changes in tissues affected by tuberculosis. TB sequelae may affect the functional capacity and quality of life of a person because of complications in lung tissue arising from TB disease. Functional capacity is a person's maximum ability to do physically with the concept of maximal oxygen uptake ($VO_2\max$) is assessed using 6MWD. Quality of life describes how good a person performs daily performance and individual perceptions of the health of physical, psychological, and social aspects. In Post TB patients can be measured with SGRQ.

METHOD

This research used descriptive-analytic observational research design, namely cross sectional study. The study began in May 2013 until the number of samples was met. Place of execution of research at pulmonary clinic Dr. Sardjito and BP4 Yogyakarta. The target population in this study was TB patients who

had been treated for at least 6 months and had been declared cured with smear negative and left sequelae (sequelae) on examination of chest x-ray. Affordable populations are post TB patients who visit the pulmonary clinic of Dr. Sardjito and BP4 Yogyakarta. Patients were included subjects who met the eligibility criteria, i.e post TB sufferers based on anamnesis and physical examination in the medical record, sputum examination with negative smear, chest radiology examination in the presence of fibrosis, aged 18-59 years, have chronic lung disease such as shortness of breath, approving and signing informed consent. Meanwhile, patients who have comorbid such as chronic heart disease, paralysis, facials, scoliosis, lordosis, post thoracic surgery, severe chronic disease, and refusal to follow the study could not be included in the study. The sample was calculated using a large table of samples for correlation research with $\alpha = 0.05$, $\beta = 0.9$, and $r = 0.42$ obtained a sample size of 45. $\alpha =$ level of statistical significance with $\beta =$ expected strength with power = 80% $r =$ correlation coefficient.

Research Tools and Measurement using several ways, there are:

1. Six minute walking distance (6MWD) is done by measuring the farthest distance that can be reached by the patient for 6 minutes.
2. St. Questionnaire George Respiratory Questionnaire (SGRQ) is filled by the patient or a structured interview to the patient.
3. Forms to fill in the patient's identity, vital marking checks, and train test records.
4. Meter to determine the distance in 6MWD.
5. Sphygmomanometer to measure blood pressure.
6. Stethoscope to measure blood pressure
7. Wristwatch or stopwatch to calculate the pulse and respiration rate also 6MWD implementation time.

Research subjects met the inclusion criteria were provided with education, information, anamnesis, and physical examination. All subjects examined 6MWD and filled out the SGRQ questionnaire. Anamnesis results, physical examination, 6MWD examination, and SGRQ questionnaires were recorded in a particular form for each subject with an identification number in each form. Independent variable in this research was 6 minutes walking distance test of patient sequelae pulmonary tuberculosis and dependent variable were life quality of patient.

Operational definition:

1. TB sequelae is a residual lesion due to histopathology changes in tissues affected by tuberculosis (Di Naso et al., 2011).
2. Health-related quality of life describes how well a person performs daily and individual perceptions of physical, psychological, and social health (Guo et al., 2009).
3. Functional capacity is a person's maximum ability to do business physically. The functional capacity or capacity of this exercise uses the concept of measuring the use of oxygen from

maximal uptake (VO₂ max), (Forman et al., and 2010).

4. The 6 minute road test (6MWD) is a test developed to evaluate patients with pulmonary disease (Kosak and Smith, 2005).
5. St. Questionnaire George Respiratory Questionnaire (SGRQ) is an instrument that has been validated to assess the quality of life of patients in some types of lung disease. (Pasipanodya et al., 2007).

The process of data analysis is done by using statistical analysis program (SPSS or STATA). Data analysis was performed to know the correlation of variables with Pearson linear correlation test, and calculated average and standard intersection.

RESULT AND DISCUSSION

The study was conducted from May to June 2013 with the subjects of pulmonary tuberculosis patients who came to BP4 Yogyakarta and pulmonary clinic of RSUP Sardjito.

The subjects were obtained from patients who had been treated for at least 6 months and had been declared cured with smear negative and left sequelae (sequelae) on the examination of chest X-ray images of 46 patients. All patients in the Lung Polyclinic of RSUP Sardjito and BP4 Yogyakarta who were willing to participate in this study were informed consent, anamnesis, and physical examination. If eligibility criteria are met, then the patient will be included in the study. The subjects were given an explanation of the implementation of the 6-minute road test and the completion of the SGRQ questionnaire. All subjects conducted a 6-minute road test with a predetermined time, which was 6 minutes and calculated distance. Quality of life evaluation was done with SGRQ questionnaire, filling questionnaire done by patient accompanied by researcher.

During the research, there were 46 patients of sequelae tuberculosis. There were 42 eligible patients who participated in the study. Table 3

and Table 4 show the basic characteristics of research subjects.

Table 4. Univariate analysis, variables in the form of interval and categorical scales. Distribution and frequency of research subject

Variable	Frequency and distribution
age, year	36.21±1.03
weight, kg	54.70±1.14
height, m	1.62±7.72
Gender, n(%)	
Male	28(66.7%)
Female	14(33.3%)
Smoking status, n(%)	
Active smoker	12 (28.6%)
Passive smoker	10 (23.8%)
Ex-smoker	11 (26.2%)
Non smoker	9 (21.4%)

Male patient with pulmonary tuberculosis are twice bigger than woman, there are twenty-eight (66.7%) of men and fourteen (33.3%) of women (Table 4). This is in accordance with the literature because male patient mostly have smoking habits then making it easier for pulmonary tuberculosis (Smith, 2004). Pasipanodya et al (2010) obtained data that TB patients in Tarrant, Texas who were assessed using Disability-adjusted Life Years (DALYs), obtained men as many as 745 DALYs and women as many as 280 DALYs. Research subjects of patients with sequelae tuberculosis had a mean age of 36.21 ± 1.03 years (table 4). These results fit the literature, that the most female age range of female patients is 30-44 years. However, the average age of most male patients is in the range of 45-59 years (Pasipanodya et al., 2010). Research on 42 patient's sequelae tuberculosis got mean weight equal to 54.70 ± 1.14 kg and mean height of equal to 1.62 ± 7.72 m (table 4).

The proportion of smoking status of patients with pulmonary tuberculosis sequelae was 12 (28.6%) active smokers, ex-smokers 11 (26.2%), 10 (23.8%) and non-smoker was 9 (21.4%). In the study Di Naso et al. (2011) there were 9 active smokers from 15 TB patients with single treatment and 7 active smokers from 12 TB patients with multiple treatment and MDRTB. In Naso et al. (2011), states that the prevalence of smoking does not cause any difference between the two groups. It is also mentioned that smoking is an important factor in the decline in lung function, but its manifestations are not visible. In the study Di Naso et al. (2011) mentioned that there are differences in disturbances suffered by patient's sequelae TB. Saude M (2010) in Di Naso et al. (2011) mentioned that the highest prevalence is a mild restrictive ventilation disorder in patients with cavitation disease and patients without cavitation still have normal function. Zhou C et al., (1995) in Di Naso et al. (2011) mentioned that the higher prevalence is in obstruction disorder (68%). In addition, a study conducted on populations in Brazil with severe pulmonary obstruction found that 15.7% of patients had suffered a sequelae of TB. From these studies, it is known that obstructive and restrictive lung disease in patients with sequelae of tuberculosis is mainly due to the severity and travel of the disease. On the other hand, the effect of smoking on the incidence of obstructive pulmonary disease in patients with sekuele tuberculosis, the risk of smoking increased due to decreased lung function. In addition, it is possible that patients with chronic obstructive pulmonary disease have suffered from previous sequelae of tuberculosis.

Table 5. Univariate Analysis, variable in interval scale. Distribution of 6 minutes walking test and SGRQ score

Variable	Distribution and frequency
6MWD, m	257.02±64.56
SGRQ, score 0-100	
Symptom	20.34±19.97
Activity	16.54±24.42
Impacts	20.02±18.36
Total	19.03±17,63
FVC (% predicted)	79.60±21.07
FVC (L)	2.26±0.81
FEV1 (% predicted)	81.24±17.34
FEV1 (L)	2.02±0.78
Ratio FEV1/FVC	0.90±0.15

The average of 6 minute test result of tuberculosis sekuele patient in this study was 257,02 ± 64,56 m. This result is lower when compared with the results of research conducted by Ralph et al (2013) of 497 m and Sivaranjini et al (2010) 445 ± 56.64 m. This result is also lower when compared with research conducted by Kim et al (2014) of 598 ± 57.92 m with healthy adult research subjects. Mileage can be affected by age, height, weight, body mass index, and race (Kim et al., 2014). The low 6-minute test score is a nonspecific and non-diagnostic value, so other tests can be performed to determine the cause of the disorder, i.e. pulmonary function tests, cardiac function, ankle-arm index, muscle strength, nutritional status, orthopedic function, and cognitive function (Enright , 2003).

All patients performed quality life evaluation with SGRQ questionnaires divided into 4 domains, ie total score, symptom, activity, and impact. Based on the results obtained values of each domain. The mean values for the symptom domain were 20.34 ± 19.97 score points, the domain activity was 16.54 ± 24.42 score points,

the impact domain was 20.02 ± 18.36 score points, and the total SGRQ score was 19.02 ± 1.76 score points (table 5). The SGRQ score indicates the lower the value the better the quality of life (Wiyono et al., 2006). The range of scores for each domain in the SGRQ questionnaire is 0-100. The mean patient symptom domain score was 20.34 ± 19.97 score points. The average domain symptom of 20.34, i.e. 20.34 of 100 points maximum score. This means that the quality of life disorder that occurs equivalent to 20.34%. It is also the same as the score value of the other three domains (activity, impacts, and total score). The subjects of the study were evaluated for lung function using spirometry to assess FEV1 and FVC. Based on the research results, the predicted FVC score is 79.60 ± 21.07%, FVC is 2.26 ± 0.81 L, the predicted FEV1 is 81.24 ± 17.34%, FEV1 is 2.02 ± 0.78 L, and the ratio of FEV1 / FVC was 0.90 ± 0.15 (table 5). According to the American Lung Association (2011), divide the results of spirometry into three, that is normal (FEV1> 80% prediction, FVC> 80% prediction, and FEV1 / FVC ratio> 0.7), obstructive (FEV1 <80% prediction, FVC normal Or down is usually less than FEV1, and FEV1 / FVC> 0.7), and restrictive ratios (FEV1 <80% prediction, FVC <80% prediction, and FEV1 / FVC ratio> 0.7). The results showed that FEV1> 80% prediction, FEV1 / FVC> 0.7, and FVC ratio were close to 80% predicted, so the results were still normal. The results of normal spirometry indicate the patient has symptoms of shortness of breath and often exposed to cigarette smoke or pollution (American lung Association, 2011). Bivariate Analysis, Relationship between 6MWD with SGRQ Score Test analysis begins with the test of normality of the data first. Shapiro-Wilk test and descriptive distribution test to know the distribution of normal distributed data or not. Normally distributed data is a distance test of 6 minutes.

Meanwhile, the four domains of the SGRQ questionnaire were not normally distributed. Therefore Spearman nonparametric correlation test is performed for this data.

Table 6 Bivariate analysis, variable in the form of interval scale. The relationship between the 6 minute road test (6MWD) and the SGRQ score

Variable	Coefficient correlation	p
Symptom	-0.062	0.697
Activity	-0.333	0.031
Impacts	-0.114	0.473
Total	-0.135	0.392

This study analyzed the 6-minute road test scores and the four SGRQ outcomes. The four outcomes, namely domain total score, symptom, activity, and impact. The result of the relationship analysis between the 6-minute road test and the domain activity was $r = -0.333$ and $p = 0.031$ (table 6). The correlation coefficient of $0.2 < r < 0.4$ is the weak category (Dahlan, 2012). These results indicate that the two variables are weakly negative, so the better the 6-min test value the lower the value of the activity domain is statistically significant. That is, the better the mileage then the higher the ability of physical activity of the patient. The results of this analysis are consistent with Chushkin et al. (2012) examined a 6-minute road test as a measure of exercise capacity in patients recovering from tuberculosis and a 6-minute road quality relationship with quality of life (SGRQ). In his research, mentioned that the domain activity ($r = -0.75$, $p < 0.01$), has a strong correlation and statistically significant. Other domain analysis results found a correlation between 6 min (6MWD) sequelae of pulmonary tuberculosis with SGRQ score of symptom domain, impacts, and total score was $r = -0.062$, -0.114 , and -0.135 which all showed very weak correlation strength (Dahlan, 2012). The p values of the three

domains are 0.697, 0.473, and 0.392 (table 6). These conditions indicate that the worse the 6-minute road test value the higher the score for each domain. However, these results have no significant correlation because the $p > 0.05$. The results of this analysis are consistent with the results of a study conducted by Chushkin et al (2012) that the domain symptom, impacts, and total score ($r = -0.54$, $p < 0.01$; $r = -0.72$, $p < 0.01$; $R = -0.73$, $p < 0.01$) have opposite relationship. In this study, the greatest relationship is seen in the domain of activity. Activity domains associated with activities that cause shortness of breath or stunted activity due to spasms (Manual SGRQ, 2008). The 6-minute mileage test is one of the modalities used to measure the capacity of physical functional training (American Thoracic Society, 2002). According to Wiyono et al (2006), functional exercise is the best psychological and physiological intervention for patients with pulmonary disorders especially shortness of breath.

Domain symptom, impact, and total score have the same relationship power but not meaningful. Domain symptoms of the disease associated with respiratory symptoms, frequency, and severity of the symptoms. Spirometry results also show normal values that indicate patients can have symptoms of shortness of breath (American Lung Association, 2011). Meanwhile, the impact domain includes a range of aspects related to social function and psychological disturbance due to respiratory disease. Quality of life is measured through SGRQ scores showing symptoms, physical activity, psychosocial, and total quality of life. The SGRQ score indicates the lower the value the better the quality of life. Therefore, the SGRQ score can still be changed through interventions such as pulmonary rehabilitation so that the quality of life can increase. SGRQ score reduction required of 4% to obtain minimal significant changes (minimally clinically significant change), (Wiyono et al., 2006). In a

study conducted by Yuarsa et al. (2013) also mentioned that the 4% decrease in total score relates to subjective and objective grievance improvements, such as the ability to walk away and decrease complaints shortness before and after the exercise. In addition, each 4% increase in total SGRQ score, mortality risk increased by 5.1% for all cases and the risk of death due to respiration increased by 12.9%. Quality of life consists of several domains, namely physical health, psychological, level of independence, social relations, environment, and spiritual WHO (1997). The physical health domain relates to a 6-minute road test (6MWD) which is also used as a training capacity parameter (Chushkin et al., 2012). According to Enright (2003), in patients with chronic obstructive pulmonary disease given inhaled bronchodilators, oxygen supplementation, and rehabilitation programs may increase 6MWD. In addition, there are several factors that can increase the value of 6MWD, i.e high patients (longer legs), men, high motivation, have taken this test before, taking medication-related illnesses before testing, and oxygen supplementation.

Figure 5, 6, 7, and 8 shows the linearity of both variable correlation, which is 6MWD and symptom score, activity, impact or total score

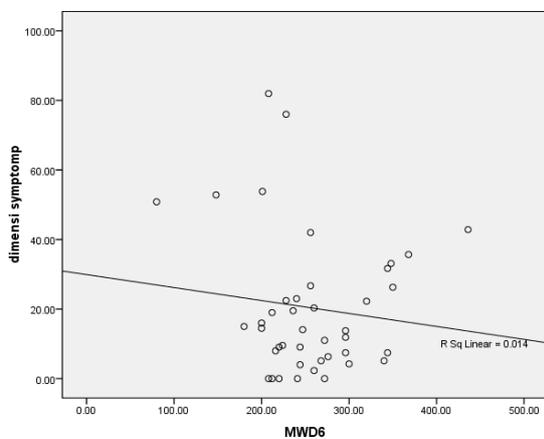
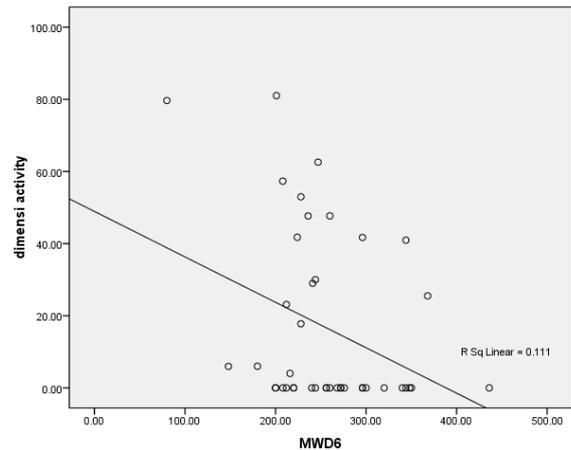


Figure 5. Scatter plot correlation between 6MWD and domain symptom score

Figure 5 shows the scatter plot that collects below the graphic space. No picture of linearity in figure 5. However, there is a relationship that the lower domain symptoms score shows the tendency of better quality of life of the patient and the better the 6MWD.



Picture 6. Scatter plot correlation of 6MWD with domain score activity

Figure 6 shows a scatter plot with linearity tendencies. There was a negative correlation to the scatter plot. That is, the lower the 6 min road test score (6MWD) the higher the activity dimensions score. The higher the score indicates the more severe the physical activity interruption.

In figures 7 and 8 we find a scatter plot with a tendency to spread in the chart space. There was a negative correlation on both scatter plots.

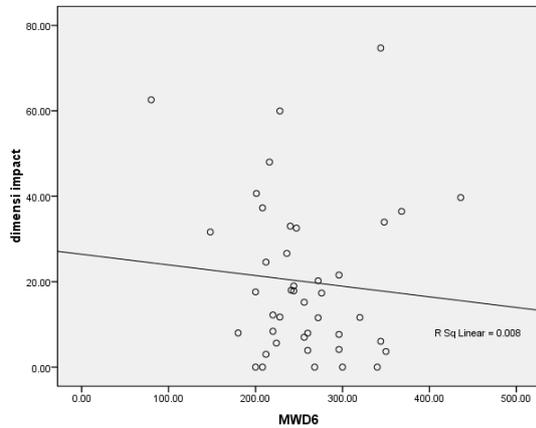


Figure 7. Scatter plot correlation between 6MWD with domain impact score

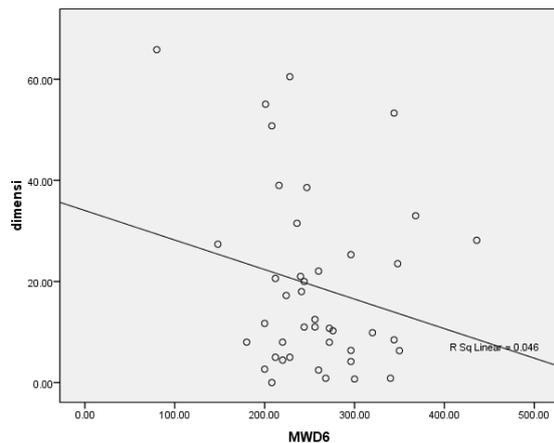


Figure 8. Scatter plot correlation of 6MWD with total SGRQ score

In this study it is found that the distance traveled within 6 minutes affect the quality of life of each domain. A 6-minute road test relationship with four SGRQ outcomes was found to have opposite correlations. This condition shows that the better the mileage the higher the quality of life of the patient. The results of this study were supported by similar studies of patients with sequelae of tuberculosis performed by Chushkin et al. (2012). The study showed a negative relationship between 6MWD and SGRQ domain scores. In this research there

is only one significant relationship, that is 6 minutes road test (6MWD) with SGRQ domain activity score. Therefore, the results of this study have not been able to represent the situation in the general population. In this study, no assessment of factors that could affect the sequelae of tuberculosis suffered by patients such as nutritional intake and environmental conditions of residence. The researchers also did not follow the progress of the patient's illness, so the lung condition prior to TB is unknown because there is a possibility that obstructive pulmonary disease of TB sequelae has existed prior to TB. Such conditions may cause bias. Quality of life is influenced by multifactorials including psychosocial and socioeconomic factors that are not evaluated further in this study. The design of this study was cross sections where data retrieval and observation (exposure and outcome) were viewed at a time so as to be less able to assess a relationship. In addition, the number of samples in this study is relatively small when compared with the number of samples of previous studies that examined the quality of life in patients with pulmonary tuberculosis sequelae.

CONCLUSION

There is a negative correlation between the 6 minute road test (6MWD) with the SGRQ score. There is also a significant relationship between a 6 minute road test (6MWD) with SGRQ domain activity score.

BIBLIOGRAPHY

American lung Association, 2011, Diagnosing Patients With COPD In The Primary Care Setting, Boehringer Ingelheim Pharmaceuticals, Inc, Iowa.
 American Thoracic Society, 2002, 'ATS Statement: Guidelines for the Six Minute Walk Test', Am J Respir Crit Care Med, Vol 166, pp 11-117.

Camelier, A, Rosa, FW, Nascimento, OA, Fernandez, ALG &

Jardim, JR 2007, 'Discriminative Properties and Validity of a Health Status Questionnaire in Obstructive Airway Disease Patients: The Airways Questionnaire 20', *Arch Bronconeumol*, 43(12):662-8.

Chuchkin, M, Aksenova, V, Bogorodskaya, E, Mandrykin, S, Zhutikov, D, Tikhokhod, E, et al. 2012, 'The Six-minutes Walk Test as a Measure of Exercise Capacity in Patient Cured for Pulmonary Tuberculosis', *European Respiratory Society Annual Congress*, 891:1144.

Davies, PDO, Barnes, PF, Gordon, SB 2008, *Clinical Tuberculosis*, 4 edn, Hodder Education, London, UK. Dahlan, MS 2013, *Statistik untuk Kedokteran dan Kesehatan: Deskriptif, Bivariat, Multivariat, Dilengkapi Aplikasi dengan Menggunakan SPSS*, ed 5, Salemba Medika, Jakarta.

DiNaso, FC, Pereira, JS, Schuh, SJ, Unis, G 2011, 'Functional evaluation in patients with pulmonary tuberculosis sequelae', *Journal of pulmonology Portuguese*, 17(5):216-221

Enright, PL, Kronmal, RA, Smith, VE, et al. 1995, 'Reduced vital capacity in elderly persons with hypertension, coronary heart disease, or left ventricular hypertrophy', *Respiratory Care*, 48(8): 738-758.

Fauci, AS, Kasper, DL, Longo, DL, Braunwald, E, Hauser, SL, Jameson, JL, et al. 2008, *Harrison's Principle of Internal Medicine*, 17 edn, The McGraw-Hill Companies, USA.

Guo, N, Marra, F & Marra, CA 2009, 'Measuring health related quality of life in tuberculosis: a systematic review', *Health and Quality of Life Outcomes*, 7(14): 1-11.

Harada, S, Harada, Y, Kitahara, Y, Ishibashi, T, Shinoda, 'Tuberculosis sequelae: clinical aspect', *Kekkaku*, 65(12): 831-8.

Hulley, SB, Cummings, SR, Browner, WS, Grady, DG, Newman, TB 2007, *Designing*

Clinical Research, 3 edition, Lipincott Williams&Wilkins, USA.

Jones, PW & Forde, Y 2008, *The St George Respiratory Questionnaire For COPD Patients (SGRQ-C) Manual*, St George's University of London, London.

Kim, HY, Song, KS, Goo, JM, Lee, JS, Lee, KS, Lim, TH 2001, 'Thoracic Sequelae and complications of tuberculosis', *RadioGraphic*; 21: 839-860.

Kim, AL, Kwon, JC, Park, I, Kim, JN, Kim, JM, Jeong, BN et al. 2014, 'Reference Equations for The Six Minutes Walk Distance in Healthy Korean Adult, age 22-59 years', *TRD*, 76:269-275.

Kosak, M & Smith, T 2005, 'Comparison of the 2-, 6-, and 12-minute walk tests in patients with stroke', *Journal of Rehabilitation Research & Development*, 42(1): 103-108

Machida K, Maekura R., 2005. State of art: sequelae of tuberculosis. *Kekkaku*: 80(10): 665-74.

Megantoro, T 2007, *Hubungan Derajat Keparahan Penyakit Paru Obstruktif Kronik dengan Sesak Nafas (jarak Tempuh Jalan 6 Menit)*, Thesis, Yogyakarta, UGM.

Matheson, L 2003, 'The functional capacity evaluation', In G Anderson & S. Demeter % G. Smith (Eds), *Disability Evaluation*, 2 edn, Mosby Yearbook, Chicago.

Palomino, JC, Leao SC, Ritacco, V, 2007, *Tuberculosis: From Basic Science to Patient Care*, 1 edn, *TuberculosisTextbook.com*

Pasipanodya, JG, Miller, TL, Vecino, M, Munguia, G, Garmon, R, Bae, S et al. 2007. 'Pulmonary impairment after tuberculosis', *Chest*, 131:1817-1824.

Pasipanodya, JG, Miller, TL, Vecino, M, Munguia, G, et al. 2007, 'Using the St. George Respiratory Questionnaire To Ascertain HealthQuality in Persons With Treated Pulmonary Tuberculosis', *CHEST*, vol.132, no.5, pp. 1591-1598,

<http://journal.publications.chestnet.org/> on 10/08/2013

Pasipanodya, JG, McNabb, SJN, Hilsenrath, P, Bae, S, Lykens, K, Vecino, E, et al. 2010, 'Pulmonary Impairment After Tuberculosis and Its Contribution to TB Burden', *BMC Public Health*, vol. 10, pp. 259, <http://www.biomedcentral.com/1471-2458/10/259>

Ralph, A 2010, *Pulmonary Tuberculosis: towards improved adjunctive therapies*, PhD Dissertation, Australia, Menzies School of Health Research, The Australian National University. [fieldsite Timika and environs]

Ralph, AP, Kenangalem, E, Waramori, G, Pontoring, GJ, Sandjaja, Tjira E, et al. 2013, 'High Morbidity During Treatment and Residual Pulmonary Disability in Pulmonary Tuberculosis: Under-Recognised Phenomena', *Plus One*, 8(11):80302.

Rifaat, N, Anwar, E, Ali, YM, Ellaban, A, Hasan, AA 2014, 'Value of pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis', *Egyptian Journal of Chest Disease and Tuberculosis*, 63:1013-1017.

Rubin, R, Strayer, DS, Rubin, E 2012, *Pathology: Clinicopathologic Foundation of Medicine*, 6 edn, Lippincott Williams & Wilkins, Wolter Kluwer Business, Philadelphia.

Sivaranjini, S, Vanamail, P & Eason, J 2010. 'Six Minute Walk Test in People with Tuberculosis Sequelae', *Cardiopulmonary Physical Therapy Journal*, 21(3): 5-10.

Tianusa, N 2003, *Hubungan antara Jarak Tempuh Berjalan dengan Kualitas Hidup pada Penderita Paru Obstruktif Kronik*, tesis, Universitas Sam Ratulangi, Manado.
WHO, 1993, *Global Tuberculosis Control* Geneva: World Health Organization, WHO <http://www.who.int/tb/publications/global_report/1994/en/index.html>

WHO, 1997, *WHOQOL Measuring Quality of Life*, WHO:97-4. WHO, 2007, *Tuberculosis*, WHO <<http://who.int/mediacentre/factsheets/fs104/en/index.html>. Fact sheet No. 104.>

WHO, 2008, *Global Tuberculosis Control*. Geneva: World Health Organization, WHO <http://www.who.int/tb/publications/global_report/2008/en/index.html>

WHO, 2009, *Epidemiology, Global tuberculosis control: epidemiology, strategy, financing*: 6–33.

WHO, 2009, *Tuberculosis Control in the South-East Asia Region*, WHO Regional Office for South-East Asia: 49-54.

WHO, 2010, *Epidemiology, Global tuberculosis control: epidemiology, strategy, financing*: 5–7.

WHO, 2011, *Global Tuberculosis Report*, World Health Organization, Geneva, WHO <http://www.who.int/tb/publications/global_report/2012/en/index.html>

Wiyono, WH, Riyadi, J, Yunus, F, Ratnawati, A & Prasetyo, S 2006, 'The Benefit of Pulmonary Rehabilitation against Quality of Life Alteration and Functional Capacity of Chronic Obstructive Pulmonary Disease (COPD) Patient Assessed using St George's Respiratory Questionnaire (SGRQ) and 6 Minutes Walking Distance Test (6MWD)', *Med J Indones*, vol 15, no. 3, pp.165-72.

Yuarsa, TA, Yunus, F & Antariksa, B 2013, 'Korelasi Penilaian Kualitas Hidup dan Prognosis Penderita Penyakit Paru Obstruktif Kronik dengan CAT, SGRQ dan BODE di Rumah Sakit Persahabatan Jakarta', *J Respir Indo*, 33:8-16.