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Obstructive sleep apnoea suspicion in lung cancer patients in Indonesia

Andika Chandra Putra[1,2,*], Agus Dwi Susanto[1], Elisna Syahruddin[1]

[1]*Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia-National Respiratory Center Persahabatan Hospital, Jakarta, Indonesia*
[2]*Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas YARSI-YARSI General Hospital, Jakarta, Indonesia*

Abstract

English:

Background: *Obstructive sleep apnoea (OSA) is often underdiagnosed and can cause various complications.*
Objective: *This study aimed to find prevalence and correlation between OSA cases in lung cancer patients.*
Methods: *This was a cross-sectional study of 151 lung cancer patients. We interviewed and assess the risk of OSA in lung cancer patients by using the Berlin questionnaire, Epworth Scale, and STOP-BANG questionnaire.*
Results: *Out of 151 patients, 121 (80.13%) patients were identified as having a low risk of OSA and 30 (19.87%) patients as high risk of OSA. Most patients with a high risk of OSA were identified with the Epworth Sleepiness Scale (53 patients). Most patients with a low risk of OSA were identified with the Berlin questionnaire (120 patients). The result shows no significant difference ($P > 0.05$) between age and risk based on the three questionnaires we used. A significant difference ($P < 0.05$) was found between body mass index (BMI), body height, and OSA risk based on the Berlin and STOP-BANG questionnaires.*
Conclusions: *There is a correlation between sleep apnoea and lung cancer as a risk factor and a consequence of poor sleep in the lung cancer population.*

Keywords

obstructive sleep apnoea • lung cancer • Berlin questionnaire • Epworth Sleepiness Scale questionnaire • STOP-BANG questionnaire

Estimarea riscului de sindrom de apnee in somn la pacientii cu cancer pulmonar in Indonezia

Rezumat

Romanian:

Cadru general: *Sindromul de apnee obstructiva in somn (OSA) este adesea subdiagnosticat si poate provoca diferite complicatii.*
Obiective: *Acest studiu a avut drept obiectiv stabilirea prevalentei OSA in randul pacientilor cu cancer pulmonar si a corelatiilor existente intre cele doua afectiuni.*
Metode: *Este un studiu cross-sectional efectuat pe 151 pacienti cu cancer pulmonar care au fost intervievati pentru evaluarea riscului de asociere a OSA cu ajutorul chestionarului Berlin, a scalei Epworth si a chestionarului STOP-BANG.*
Rezultate: *Din cei 151 de pacienti, 121 (80.13%) aveau risc scazut de OSA si 30 (19.87%) aveau risc crescut de asociere a OSA. Majoritatea pacientilor cu risc crescut de OSA au fost identificati cu ajutorul scalei de somnolenta Epworth (53 pacienti). Majoritatea pacientilor cu risc redus de OSA au fost identificati prin chestionarul Berlin (120 pacienti). Nu a existat o diferenta semnificativa statistic ($P > 0.05$) intre varsta si riscul de OSA la cele trei chestionare utilizate. Diferente semnificative statistic ($P < 0.05$) au fost gasite intre Indexul de Masa Corporala (BMI), talie si riscul de OSA stabilit prin chestionarele Berlin si STOP-BANG.*
Concluzii: *Exista o corelatie intre riscul de OSA si cancerul pulmonar ca factor de risc si o consecinta a calitatii reduse a somnului la acesti pacienti.*

Cuvinte-cheie

sindrom de apnee obstructiva de somn • cancer pulmonar • chestionarul Berlin • scala de somnolenta Epworth • chestionarul STOP-BANG

Corresponding author: Andika Chandra Putra
E-mail: andikapulmo@gmail.com

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Introduction

Lung cancer is the most common malignant disease found in the world and one of the leading causes of cancer death. According to WHO, every year there are 1.2 million new lung cancer patients or 12.30% of all malignant tumours; this number is expected to continue to increase, likely reaching an anticipated 12 million cases in 2030 (1). The American Cancer Society estimated that the incidence of lung cancer in the United States in 2017 is 225,000 new cases (2). In Indonesia, the incidence of lung cancer is 11.60% and the number of new cases is 34,696 (3). According to data from the Department of Pulmonology and Respiratory Medicine Universitas Indonesia-Persahabatan Hospital Jakarta, the incidence of lung cancer has increased more than five times in the past 10 years. Lung cancer has a poor prognosis compare to other types of cancer.

The link between lung cancer and obstructive sleep apnoea (OSA) has received attention in cohort studies, and currently available evidence revealed that OSA is associated with increased lung cancer death (3). OSA is a breathing disorder during sleep characterised by episodes of stopping of breath for at least 10 s/episode (4). A decrease in a tidal volume exceeding 50% but below 75% of the baseline with 10 s of cessation of airflow is called hypopnoea. The pathophysiology of OSA is comprised of a combination of apnoea and hypopnoea (5). OSA is often underdiagnosed; in untreated patients, OSA can cause various cardiovascular, metabolic, neuroendocrine, and inflammatory complications. In this study, we investigated and examined OSA suspicion in lung cancer patients (6).

Material and methods

This study design was a cross-sectional study of lung cancer patients. Data sources were obtained directly using a questionnaire instrument to examine OSA in lung cancer patients. Data were collected by consecutive sampling technique and included 151 patients in this study. Subjects were interviewed and followed by using the Berlin questionnaire, Epworth Sleepiness Scale (ESS), and STOP-BANG questionnaire to assess the risk of OSA in lung cancer. In addition, the Persahabatan Hospital Research Ethics Committee approved this research (reference 65/KEPK-RSUPP/08/2019). All subjects who participated were required to submit a written informed consent statement. Statistical analysis was undertaken by using the chi-square test, with statistical significance being defined by $P < 0.05$.

Results

Subject demographics

The mean age of the subjects was 55.5 (± 10.96) years and most of them were male (87 subjects, 57.60%). The mean ± standard deviation (SD) body weight of the subjects was 56.24 (± 9.40), height 160.64 (± 7.09), and body mass index (BMI) 21.77 (± 3.14) (Table 1). There is a frequency risk factor of OSA based on the Berlin questionnaire, Epworth Sleepiness Scale, and STOP-BANG questionnaire. Among these three questionnaires, the Berlin questionnaire has a low probability in showing a high risk factor of OSA, and the highest high risk to have OSA was found when subjects were examined by the ESS questionnaire (Table 2).

Berlin questionnaire

In the Berlin questionnaire, the number of lung cancer patients who had low risk to have OSA is 120 of 151 (79.48%) patients, followed by patients with high risk of OSA who

Table 1. Demographic variables of 151 lung cancer patients at Persahabatan Hospital, Jakarta.

Variables	Subjects (*n* = 151)
Sex	
Male (%)	87 (57.60)
Female (%)	64 (42.40)
Age (years) (±SD)	55.5 (±10.96)
Weight (kg) (±SD)	56.24 (±9.40)
Height (cm) (±SD)	160.64 (±7.09)
BMI (kg/m^2) (±SD)	21.77 (±3.14)

BMI, body mass index; SD, standard deviation.
Data are presented as *n* (%) or mean (SD).

Table 2. Frequency risk factor of OSA based on the Berlin, ESS, and STOP-BANG questionnaires.

Model of questionnaire	Risk factors of OSA	Frequency (*n*)	Percentage (%)
Berlin	Low risk	120	79.48
	High risk	31	20.52
ESS	Low risk	98	64.90
	High risk	53	35.10
STOP-BANG	Low risk	104	68.87
	High risk	47	31.13

ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnoea.

Table 3. Demographic variables of subjects' risk factor OSA based on Berlin questionnaire.

Variables	Berlin questionnaire		
	Low risk (*n*)	High risk (*n*)	*P* value (OR)
Sex			
Male	60	27	0.00 (6.75)
Female	60	4	
Age (years)	55.12 (10.98)	57 (10.90)	0.39
Weight (kg)	55.74 (8.13)	58.16 (13.22)	0.33
Height(cm)	160.03 (7.24)	163 (6)	0.03
BMI (kg/m^2)			0.00
Underweight	10 (62.50)	6 (37.50)	
Normal	78 (83)	16 (17)	
Overweight	17 (89.50)	2 (10.50)	
Obesity I	15 (78.90)	4 (21.10)	
Obesity II	0 (0)	3 (100)	

BMI, body mass index; SD, standard deviation.
Data are presented as *n* (%) or mean (SD).

amounted to 31 of 151 (20.52%). The male higher risk factor for OSA demonstrated an OR value of 6.75, which means that male patients had a 6.75-times higher risk of OSA based on the Berlin questionnaire. Concerning the BMI, it is ascertained that the most common category is the normal one, both in low-risk and high-risk factor OSA. The mean age of patients with low risk OSA is 55.12 with an SD of 10.98, and that corresponding to high risk OSA is 57 with an SD of 10.90. A significant difference ($P < 0.05$) is ascertained between sex, body height, BMI, and risk factor of OSA in lung cancer patients, based on the Berlin questionnaire (Table 3).

Epworth sleepiness scale

Based on ESS questionnaire, 98 of 151 (64.90%) patients had a low risk of having OSA and 53 of 151 (35.10%) patients had a high risk of having OSA (Table 4). The male predominance was observed both in low risk and high risk factors of OSA with the OR value 2.53, which means that male patients had a 2.53-times greater risk of developing OSA based on the ESS questionnaire. Concerning BMI, it is ascertained that the most common category is the normal one, both in low-risk and high-risk factor OSA. The mean age of patients with low risk OSA is 54.52 with an SD of 10.85, and that corresponding to high risk OSA is 57.32 with an SD of 11.02. A significant difference ($P < 0.05$) is ascertained between sex and risk factor of OSA in lung cancer patients based on the ESS questionnaire.

STOP-BANG questionnaire

Using the STOP-BANG questionnaire, it was ascertained that the number of lung cancer patients characterised by a low risk of increase in the intensity and frequency of symptom-onset of OSA is 104 of 151 (68.87%) patients, which is significantly greater than the number of patients with a high risk of OSA, amounting to 47 of 151 (31.13%). The male predominance could be observed both in low risk and high risk factors of OSA

Table 4. Demographic variables of subjects' risk factor OSA based on ESS questionnaire.

Variables	ESS		
	Low risk (*n*)	High risk (*n*)	*P* value (OR)
Sex			
Male	49	38	0.01 (2.53)
Female	49	15	
Age (years)	54.52 (10.85)	57.32 (11.02)	0.13
Weight (kg)	56.21 (9.03)	56.28 (10.13)	0.96
Height (cm)	160.33 (7.16)	161.23 (6.97)	0.45
BMI (kg/m^2)			0.46
Underweight	8 (50)	8 (50)	
Normal	65 (69.10)	29 (30.90)	
Overweight	13 (68.40)	6 (31.60)	
Obesity I	10 (52.60)	9 (47.40)	
Obesity II	2 (66.70)	1 (33.30)	

BMI, body mass index; SD, standard deviation.
Data are presented as *n* (%) or mean (SD).

Table 5. Demographic variables of subjects risk factor OSA based on the STOP-BANG questionnaire.

Variables	STOP BANG		
	Low risk (*n*)	High risk (*n*)	*P* value (OR)
Sex			
Male	46	41	0.00 (8.61)
Female	58	6	
Age (years)	54.87 (10.94)	56.91 (10.97)	0.28
Weight (kg)	54.94 (7.68)	59.11 (11.99)	0.03
Height (cm)	158.94 (6.53)	164.40 (6.87)	0.00
BMI (kg/m^2)			0.02
Underweight	9 (56.20)	7 (43.80)	
Normal	67 (71.30)	27 (28.70)	
Overweight	16 (84.20)	3 (15.80)	
Obesity I	12 (63.20)	7 (36.80)	
Obesity II	0 (0)	3 (100)	

BMI, body mass index; SD, standard deviation.
Data are presented as *n* (%) or mean (SD).

with the OR value 8.61, which means that male patients had an 8.61-times greater risk of developing OSA based on the STOP-BANG questionnaire. Concerning BMI, it is ascertained that the most common category is the normal one, both in low-risk and high-risk factor OSA. The mean age of patients with low risk OSA is 54.87 with an SD of 10.94, and that corresponding to high risk OSA is 56.91 with an SD of 10.97. A significant difference ($P < 0.05$) was observed between sex, weight, height, BMI, and risk factor of OSA in lung cancer patients based on the STOP-BANG questionnaire (Table 5).

Discussion

This study aimed to ascertain the prevalence and correlation between OSA suspicion cases and lung cancer by using

three questionnaire instruments (Berlin, ESS, and STOP-BANG questionnaires). Results showed that there is a risk factor of OSA in lung cancer patients, both high risk and low risk. From the questionnaire, prevalence of patients with low risk OSA is higher than that of patients with high risk OSA. Sleep apnoea is the emergence of sleep disturbances at the respiratory associated with the upper airway during sleep marked by stopping breathing (apnoea) or decreased ventilation (hypopnoea). OSA is the most common respiratory tract disorder during sleep with the absence of airflow despite ventilation efforts marked by contraction of the respiratory muscles (diaphragm) (7). OSA is a highly prevalent disorder characterised by repetitive upper airway obstructions during sleep that lead to intermittent hypoxia (8).

Out of 151 lung cancer patients, there were 121 with low risk OSA, and 30 with high risk OSA. One of the most specific signs of OSA is intermittent hypoxia, which is reported damage to the tissue and systemic level. Hypoxia in cells provides adaptive responses to transcription factors, namely hypoxia-inducible factor (HIF-1). HIF-1 activates transcriptions of genes that play a role in angiogenesis, invasion, and metastasis to stem cell maintenance related to cancer. HIF-1 is also associated with an increase in reactive oxygen species produced during the reoxygenesis period that caused tumorigenesis (9). Hypoxia has a frequent occurrence in most solid tumours, and the presence of low intra-tumoural oxygen tension has been considered as a major modifying factor underlying cancer progression, metastasis, and angiogenesis (10). It means that OSA in lung cancer patients can increase metastases and poor prognosis of lung cancer. The male predominance is higher than the female, and possible explanations for this predominance include effects on upper airway muscles and collapsibility, differences in body fat distribution, and different pharyngeal anatomy (11). The mean age of patient's risk factor for OSA is >50 years. This result was similar to previous studies reporting an increased prevalence of OSA in patients aged 50–59 years (12).

Our findings showed that based on the Berlin questionnaire, a significant difference is ascertained between sex and increased risk factor of OSA. That is to say, males have a higher risk of developing OSA. Significant differences were also found between BMI and risk factor of OSA. OSA assessment with the Berlin questionnaire consists of three categories (overall 10 question items) related to the risk of having sleep apnoea. Risk classification of sleep apnoea is based on response to the individual questions. Category 1 consists of five question items regarding snoring symptoms. Category 1 is positive if the total score is ≥2 points. Category 2 consists of four question items. Category 2 is positive if the total score is ≥2 points. Category 3 consists of one question item. Category 2 is positive if the answer is yes or if the BMI of the patient is >30 kg/m^2. High risk OSA is based on the Berlin questionnaire if there are two or more categories where the score is positive, and low risk OSA if there is only one or no positive category (7).

Based on the ESS questionnaire, a significant difference is ascertained between sex and risk factor OSA, with the male predominance being higher than the female. This result was similar to studies by Doshi et al. (13) using the ESS questionnaire to assess risk factor OSA, which showed a significant difference between male and female patients. There is no significant difference between other characteristic demographics (age and BMI) in terms of increasing the risk factor of OSA based on the ESS questionnaire. OSA assessment with ESS questionnaire consists of eight questions. Each question has a score of 0–3 according to having dozed off or fallen asleep in the course of activities. The total score can range from 0 to 24. A score of 0–10 represents the normal range of sleepiness and a score of ≥11 represents sleepiness, which could be a sign of OSA (14).

Based on the STOP-BANG questionnaire, there is a significant difference between sex and the increase in risk factor of OSA with the male predominance. In a study by Teng et al. (15), using the STOP-BANG questionnaire in OSA screening showed a significant statistic with $P < 0.001$ between male and female patients. OSA assessment with the STOP-BANG questionnaire consists of eight questions, which are the main characteristics of OSA, such as snoring, tiredness, stopping breathing, blood pressure, BMI, age, neck circumference, and male gender. A low risk of OSA was inferred if the answer was 'yes' to none of the questions, to up to two questions. An intermediate risk of OSA was inferred if the answer was a 'yes' to three or four questions, and a high risk if 'yes' to five to eight questions (16). Another study conducted by Doshi et al., using the STOP-BANG questionnaire, showed that there was a significant difference between male patients and female patients ($P < 0.0001$). Another significant difference was found between BMI and risk factor of OSA, in a study by Doshi et al. (13), where there was a significant difference in patients with high BMI values ($P < 0.04$).

OSA is often underdiagnosed and it can increase poor prognosis of cancer. Assessment of the OSA risk factor using a standardised questionnaire can help in early diagnosis. From the results of this study, it can be seen that there is a risk factor for OSA in lung cancer patients based on the Berlin, ESS, and STOP-BANG questionnaires. It was also found that the characterisation of patients' OSA risk factor, such as the variables sex, age, and BMI, had statistical significance in the risk of developing OSA.

Based on this study, it is opined that the best tool for detecting OSA cases in lung cancer patients is the ESS questionnaire.

Lung cancer patients with high risk of OSA are more likely to be suspected of having OSA using the ESS questionnaire, which means the risk of underdiagnosed OSA in lung cancer patients can be reduced.

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Conflict of Interest

The authors declare that no competing interests exist.

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