

Validation of Filipino Version of Berlin Questionnaire as Screening Instrument for Obstructive Sleep Apnea as Correlated with Overnight Polysomnography

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Abstract

Background: The Berlin questionnaire is a validated instrument used to identify individuals at risk of OSA. The Berlin questionnaire has been translated to different languages including Filipino however, it was not correlated with overnight polysomnography, the gold standard for diagnosing OSA.

Objective: The general objective of this study is to validate the Filipino version Berlin Questionnaire (Filipino BQ) against standard overnight polysomnography among patients seen at sleep clinic.

Main Outcome Measures: Risk stratify patients for occurrence of obstructive sleep apnea based on their Berlin score and correlate Berlin score with Respiratory Disturbance Index during polysomnography.

Methods: All patients ≥ 18 years old suspected with OSA seen at Sleep Clinic for full night diagnostic or split night study from October 2016 to May 2017 who are Filipino language literate were requested to participate in this study. The PSG was staged and scored according to the American Academy of Sleep Medicine guideline by two sleep specialists who had no knowledge of the questionnaire results. Descriptive statistics, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of Filipino version of Berlin Questionnaire were computed.

Results: A total of 110 subjects were included in the final analysis in the study. The overall median age was 44 years (IQR = 25), range from 20 to 87 years. Most subjects were male (66.4%). Median neck circumference was 42 cm (IQR = 7.75), range from 32 to 56 cm while median BMI was 31.4 kg/m² (IQR = 10.3), range from 17.4 to 57.7 kg/m². Using diagnostic cut off of RDI > 5, the Filipino BQ had a sensitivity of 82.07%, specificity of 75%, positive predictive value of 98.6% and negative predictive value of 13.64%. When using different diagnostic thresholds, RDI > 15 and RDI > 30, the sensitivity was 87.50% and 87.21% respectively, and the specificity was 71.43% and 45.83% respectively

Conclusion: The Filipino BQ has a good correlation with PSG in the diagnosis of OSA. The Filipino Berlin Questionnaire demonstrated good sensitivity and therefore may be used in selecting or prioritization of patients suspected of obstructive sleep apnea who should undergo PSG to confirm diagnosis of OSA.

Keywords: Berlin Questionnaire; Obstructive Sleep Apnea; Polysomnography

Abbreviations: AHI: Apnea Hypopnea Index; BQ: Berlin Questionnaire; OSA: Obstructive Sleep Apnea; PSG: Polysomnography; RERA: Respiratory Effort Related Arousal; RDI: Respiratory Disturbance Index

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Introduction

Obstructive sleep apnea (OSA) is a common but under recognized medical disorder and affects 2% of women and 4% of men. It is estimated that nearly 80% of men and 93% of women with moderate to severe sleep apnea are undiagnosed. [1]

The relatively high prevalence of undiagnosed OSA along with its short-term and long-term complications requires a reliable screening tool for a quick prediction of OSA. This tool would enable clinicians to detect the possibility of OSA during initial clinics visits and determine those patients at high risk in need of further assessment or immediate therapeutic treatment. [2]

The gold standard diagnostic test for OSA is the overnight in-laboratory polysomnography and requires an overnight stay in the hospital with trained staff who are capable of monitoring and interpreting the data throughout the night. This process is expensive and time consuming, hence many researchers have explored the use of clinical predictors or questionnaires to help identify high risk patients. [3]

The Berlin questionnaire (BQ) is a validated instrument used to identify individuals at risk of OSA. It was an outcome of the Conference on Sleep in Primary Health Care held in 1996 in Berlin, Germany. Questions selected was based from literature reviewed and factors or behaviors that persistently correlated to the presence of sleep-disordered breathing were included in the questionnaire. [4] The Berlin questionnaire consists of 10 items on snoring, nonrestorative sleep, sleepiness while driving, apneas during sleep, hypertension, and body mass index. Several studies on translation and validation of Berlin questionnaire to different languages had been made namely: Hindi, Persian, Greek, Korean, Malay, Thai and Turkish. [5, 11-13, 15-17]

Berlin questionnaire has been translated in Filipino and was administered to 40 individuals able to understand both English and Filipino in different communities within Metro Manila and it showed high construct validity. [6] Although validation of the translated version was done, it was not correlated with overnight polysomnography, the gold standard for diagnosing OSA.

The study primarily aimed at validating the Filipino version Berlin Questionnaire against standard overnight polysomnography among patients seen at sleep clinic. This will specifically risk stratify patients for occurrence of obstructive sleep apnea based on their Berlin score and be able to correlate Berlin score with Respiratory Disturbance Index during polysomnography.

Materials and Methods

Study Design

The prospective cross-sectional study was conducted among adult patients seen at the Lung Center Sleep Laboratory and Disorders Clinic from October 2016 to May 2017.

Inclusion Criteria

1. All patients \geq 18 years old suspected with OSA seen at Sleep Clinic for full night diagnostic or split night study who signed the informed consent
2. Filipino language literate

Exclusion Criteria

None

Study Instrument

Demographic characteristics, (age, sex, neck circumference, blood pressure, BMI and Mallampati score) were collected from patients' document files. Eligible patients were asked to fill out the Filipino version of Berlin Questionnaire after giving their informed consent.

The Berlin Questionnaire (BQ) is composed of three categories of symptoms, five questions are related to snoring and cessation of breathing in category 1, four questions related to daytime sleepiness in category 2, and question on hypertension in category 3. The validated Filipino BQ version will be administered to all patients enrolled. The overall BQ score will be determined as follows: scores from the Category 1 and 2 were positive if with frequent symptoms (> 3–4 times/week), and the score from Category 3 was positive if there was a history of hypertension or a BMI > 30 kg/m². Patients are scored as high-risk for OSA if they had a positive score on two or more categories, while those who scored 1 or none as low-risk. [4]

Polysomnography

All patients underwent overnight video-synchronized polysomnography. The PSG recordings include 6-channel electroencephalography (EEG), 2 channel electrooculography (EOG), 3 channel submental electromyography (EMG), respiratory movements via chest and abdominal belts, airflow both via nasal pressure transducer and oro-nasal thermistor, oxygen saturation by oximeter finger probe, and leg movements via both tibial anterolateral electrodes. The polysomnographic study was staged and scored according to the American Academy of Sleep Medicine guideline. Respiratory event will be scored as apnea if there was a drop in the peak signal excursion by $\geq 90\%$ of pre-event baseline using an oronasal thermal sensor and the duration of the 90% drop in sensor signal is ≥ 10 seconds. Respiratory event will be scored as hypopnea if there was a drop in the peak signal excursion by $\geq 30\%$ of pre-event baseline using nasal pressure sensor and the duration of the 30% drop in sensor signal is ≥ 10 seconds associated with > 3% oxygen desaturation or arousal. [7]

Diagnosis of OSA is confirmed using the overnight PSG if there are greater than 5 obstructive events per hour (apneas, hypopneas, and respiratory event related arousals) in a patient who reports any of the following symptoms- sleepiness, nonrestorative sleep, fatigue or insomnia symptoms, wakes up with breath holding, gasping, or choking, habitual snoring, breathing interruptions or both, or is diagnosed with hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 Diabetes Mellitus; or if there are 15 or more predominantly obstructive events even in the absence of sleep related symptoms. [8] OSA severity is defined as mild for RDI ≥ 5 and < 15, moderate for RDI ≥ 15 and ≤ 30 and severe for RDI > 30/hr. [9] The PSG was staged and scored by two sleep specialists who had no knowledge of the Filipino version of Berlin questionnaire results.

Statistical Methods

All valid data from evaluable patients were included in the analysis. Summary statistics were presented in tables and reported as median (IQR) for continuous outcome variables with skewed distributions and n (%) for qualitative or discrete variables. Chi-square test of association was used to determine association between Berlin Questionnaire score and Respiratory Disturbance Index during polysomnography. Sensitivity, specificity, positive predictive value and negative predictive value were computed. Statistical significance was based on p-value ≤ 0.05 . Data processing and analysis were done using STATA v13.

Results

A total of 127 eligible subjects met the criteria but only 110 patients were included in the final analysis in the study. The 17 subjects were lost to follow up and did not undergo the overnight polysomnography test. The overall median age was 44 years (IQR = 25), range from 20 to 87 years. Most subjects were male (66.4%). Median neck circumference was 42 cm (IQR = 7.75), range from 32 to 56 cm while median BMI was 31.4 kg/m² (IQR = 10.3), range from 17.4 to 57.7 kg/m². Median blood pressure was 130 mmHg systolic and 80 mmHg diastolic. Mallampati scores were mostly Grade 3 (33.6%) and Grade 4 (45.5%).

Of the 110 subjects, 100 (91%) had positive score in Category 1, 57 (52%) had positive scores in Category 2, and 79 (72%) had positive scores in Category 3.

Characteristic	n = 110
Age in years, median (IQR)	44 (25)
Sex, n (%)	
Male	73 (66.4%)
Female	37 (33.6%)
Neck circumference, median (IQR)	42 (7.8)
Body Mass Index (BMI, kg/m ²), median (IQR)	31.4 (10.3)
BMI, n (%)	
Normal (18.5-24.9)	21(19.09)
Overweight (25-29.9)	31(28.18)
Obese (≥ 30)	58 (52.73)
Blood pressure (BP, mmHg), median (IQR)	
Systolic	130 (20)
Diastolic	80 (10)
BP, n (%)	
Hypertensive	58(52.73)
Non hypertensive	52(47.27)
Mallampati score, n (%)	
Grade 1	8 (7.3%)
Grade 2	15 (13.6%)
Grade 3	37 (33.6%)
Grade 4	50 (45.5%)
Respiratory disturbance index, n (%)	
Normal (RDI < 5)	4 (3.6%)
Mild (5 ≤ RDI < 15)	10 (9.1%)
Moderate (15 ≤ RDI < 30)	10 (9.1%)
Severe (RDI ≥ 30)	86 (78.2%)
Berlin Questionnaire, n (%)	
Low Risk	22 (20.0%)
High Risk	88 (80.0%)

IQR: interquartile range, RDI: respiratory disturbance index

Table 1: Characteristics and clinical profile of patients seen at sleep clinic.

Using a cut-off of more than 5 events per hour of total sleep time, 96.4% (106 of 110) had obstructive sleep apnea (OSA) based on respiratory disturbance index as determined by polysomnography. Of these patients, 81.1% had severe OSA (86 of 106) and 9.4% (10 of 106) had mild or moderate OSA based on RDI >15 and >30 events per hour respectively. Based on score of the Filipino version of the Berlin questionnaire, 80% were at high risk for sleep apnea while 20% at low risk. A significant majority of patients with severe OSA were classified at high risk for sleep apnea according to BQ (68.18%; p < 0.0001).

Berlin Questionnaire	Polysomnography				p-value
	Normal (RDI < 5)	Mild (5 ≤ RDI < 15)	Moderate (15 ≤ RDI < 30)	Severe (RDI ≥ 30)	
	n = 4	n = 10	n = 10	n = 86	
Low Risk	3 (2.73%)	7 (6.4%)	1 (0.91%)	11 (10.0%)	0.000*
High Risk	1(0.91%)	3 (2.7%)	9 (8.18%)	75 (68.18%)	

RDI: Respiratory Disturbance Index

Table 2: Obstructive sleep apnea (OSA) determined by polysomnography vs. Berlin questionnaire (BQ) score

*Significant at 5% level

Among those patients diagnosed with OSA, 82.08% were at high risk of having sleep apnea (regardless of severity) based on the Filipino version of the Berlin Questionnaire (p = 0.005).

Berlin Questionnaire	Polysomnography		p-value
	Normal	Mild/Moderate/Severe	
	n = 4	n = 106	
High Risk	1 (25.0%)	87 (82.08%)	0.005*
Low Risk	3 (75.0%)	19 (17.92%)	

Table 3: Obstructive sleep apnea (OSA) determined by polysomnography vs. Berlin questionnaire (BQ) score

Data presented as n (%)

*Significant at 5% level

The present study showed that the Filipino BQ had a sensitivity of 82.07%, specificity of 75%, positive predictive value of 98.86% and negative predictive value of 13.64% at RDI > 5. When using different diagnostic thresholds, RDI ≥ 15 and RDI >30, the sensitivity was 87.50% and 87.21% respectively, and the specificity was 71.43% and 45.83% respectively (Table 4).

	RDI > 5	RDI ≥ 15	RDI ≥ 30
Sensitivity	82.07 (73.17-88.60)	87.50 (78.80-93.09)	87.21 (77.85-93.13)
Specificity	75 (21.94-98.68)	71.43 (42.00-90.41)	45.83 (26.17-66.76)
Positive predictive value	98.86 (92.96-99.94)	95.45 (88.13-98.53)	85.23 (75.70-91.59)
Negative predictive value	13.64(3.59-35.96)	45.45 (25.07- 67.33)	50.00 (28.80-71.20)

PPV: positive predictive value; NPV: negative predictive value; RDI: respiratory disturbance index

Table 4: Sensitivity, specificity, PPV and NPV of Filipino version of Berlin-F Questionnaire using RDI categories.

Data presented as % (95% CI)

Discussion

In the Philippines, there is still no prevalence data for obstructive sleep apnea. As the study of sleep medicine advances and more patients are being diagnosed with OSA, clinicians will need a screening tool to be able to recognize this condition.

The demographic data showed that there were more men than women with a median age of 44 years, which is similar to studies done in Asian countries. [13,15,17] More than half of the subjects are obese and hypertensive with increased neck circumference and higher Mallampati scores. This clinical profile is similar to those of other Asian countries. A Korean study in 2015 found that old age and large neck circumference were significant for predicting the presence of obstructive sleep apnea, whereas hypertension and large neck circumference were independent variables for predicting severity of obstructive sleep apnea. [18]

The present study using the RDI threshold of > 5 , demonstrated a sensitivity of 82.07% specificity of 75%, positive predictive value of 98.86% and negative predictive value of 13.64%. This implies 98.86% of patients at high risk actually had OSA while low risk patients had 13.64% chance of actually being OSA free. Among those classified as low risk, 17.92% turned out to be positive for OSA. The threshold of $RDI \geq 5$ was used as a cut-off for defining OSA, since our study was performed to validate the questionnaire in subjects at risk for OSA, and subjects enrolled are those who were referred to the sleep clinic with symptoms related to sleep disordered breathing. The sensitivity and specificity of Berlin Questionnaire have ranged from 63% to 86% and 49% to 95% respectively, with BQ as the only screening instrument for OSA that has been validated in general practice, hospital, and sleep clinic. [20] Different study populations and different PSG methods or cut off points for OSA diagnosis might be the factors of these varying results. [15]

The Original Berlin questionnaire had a sensitivity of 77%, specificity of 89%, and a positive predictive value 71%. This study was done in a primary setting and the questionnaire was validated through home portable sleep monitoring. [14] In contrast with the present study which utilized a sleep laboratory monitored PSG involving patients from sleep clinic. This may account for the difference in sensitivity and specificity.

The sensitivity of the Filipino BQ is consistent with the findings of other translated Berlin Questionnaires (Table 5). However, there was observed difference between studies regarding the use of gold standard Respiratory Disturbance Index (RDI) vs. Apnea-Hypopnea Index (AHI). AHI is the number of apneas and hypopneas per hour of sleep while RDI is the number of apneas, hypopneas, and respiratory effort-related arousals (RERAs) per hour of sleep. [7] Most of the questionnaires have utilized AHI (Thai BQ, Malay BQ, Persian BQ, Korean BQ, Greek BQ, and Hindi BQ) as the gold standard for the diagnosis of OSA. This is of great importance in this regard as RDI is broader than AHI. [16]

	Sensitivity	Specificity
Filipino Berlin*	82.06	75
Original Berlin*(14)	86	77
Persian Berlin*(16)	81.7	100
Thai Berlin ***(12)	87	75
Malay Berlin ***(13)	92	17
Korean Berlin***(15)	69	83
Greek Berlin***(11)	76	40
Hindi Berlin***(17)	86	58

Table 5: Sensitivity and Specificity of different versions of validated Berlin Questionnaire (AHI/RDI > 5).

*RDI used as gold standard

**AHI used as gold standard

In the systematic review by Seneratna et al, Berlin questionnaire's diagnostic utility varied by study population, definition of hypopnea used, and apnea-hypopnea index threshold used. Furthermore, they found that the sensitivity of Berlin questionnaire for detecting clinically relevant OSA in the sleep clinic population ranged from 57% to 91% when hypopnea was defined as 3% oxygen saturation and from 68% to 90% when hypopnea was defined as 4% oxygen saturation, showing a good sensitivity of Berlin Questionnaire regardless of the hypopnea definition used in the gold standard. [14]

The third category of Berlin questionnaire is related to patient's self-reported history of hypertension or the presence of obesity. This study followed the original instruction of a cut off value of BMI ≥ 30 kg/m². In comparison, Kang, *et al.* in 2012 have utilized the World Health Organization Western Pacific Regional Office recommendation of a modified BMI cut off value of ≥ 25 kg/m² to define obesity in the Korean BQ. [15,19] If the same value will be applied to the present study, this may affect the sensitivity and specificity of the Filipino BQ as BMI also factors into the scoring. Sensitivity increased to 89.62% to 93.75% from 82.07%-87.05% while specificity decreased to 57.14% to 75% from 71.43% to 75% if the cut off value of ≥ 25 kg/m² to define obesity will be applied.

A highly sensitive test means that there are few false negative results, and thus fewer cases of disease are missed. The specificity of a test is its ability to designate an individual who does not have a disease as negative. A highly specific test means that there are few false positive results. In terms of obstructive sleep apnea, a high sensitivity of a screening test is favored over specificity. Although the cost of sleep studies for the resulting false positives from the Berlin questionnaire is high, the cost of missing the true cases of undiagnosed OSA with its known serious consequences should also be considered. [14]

The sensitivity increased gradually as the RDI threshold increased. This was also observed in the Thai version and Korean version of the BQ, wherein sensitivity increased from 87% to 96.2% and 69% to 89% respectively (AHI > 5 to > 30). [12,15] Although, the specificity did not follow this trend (Table 4). This high sensitivity but decreasing specificity across increasing RDI threshold suggests that the Filipino BQ may be used to screen OSA symptoms but may be poor in confirming clinical OSA, hence overnight PSG is still recommended to diagnose the condition. The sensitivity of the Filipino BQ has no difference between diagnostic cut-off of RDI >15 and RDI ≥ 30 , hence cannot be utilized to identify severity of OSA.

Despite many validation studies conducted for Berlin questionnaire, there have been few high-quality studies that have assessed the utility of these questionnaires in the primary care setting or general population. In a Norwegian population based study in 2010, they found that BQ performed sub optimally as a screening test for OSA in a low-prevalence population, hence cannot be recommended as a screening tool in the general population. [20] However, utility of the BQ in the practitioner's office or clinic with higher estimates of OSA prevalence may provide benefit in identifying patients at high risk. High risk patients such as those with cardiovascular risks and special population group such as commercial truck drivers may be targeted rather than the general adult population as they are more likely to benefit from treatment for OSA that may not only improve alertness but also help control associated diseases. [21]

The study was limited by its smaller sample size of 110, involving patients of one sleep center. The findings therefore do not represent the general population. The Filipino BQ is sensitive in detecting the presence of OSA, but has a low negative predictive value hence risk grouping should be viewed with caution.

Conclusion

The Filipino Berlin Questionnaire has a good correlation with PSG in the diagnosis of OSA. This study showed that risk grouping was useful in prediction of RDI. The Filipino Berlin Questionnaire demonstrated good sensitivity and may be used in selecting or prioritization of patients suspected of obstructive sleep apnea who should undergo PSG to confirm diagnosis of OSA. Although it is very useful, it should not be utilized as a single tool to diagnose obstructive sleep disordered breathing.

Further study should be done with large sample size and in a non-specialized center to determine the utility of the questionnaire to the general population. However, with the current evidence of increased utility of Berlin questionnaire in identifying patients at high risk for OSA in specific population, targeted screening should also be considered.

Conflict of interest

There are no conflict of interest.

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