Title Page

- ***Title***: "**Combined Nocturnal Pulse Oximetry and Questionnaire-Based Obstructive Sleep Apnea Screening – A Cohort Study"**
- ***Authors***:

- Saif Mashaqi, MD
*Associate Professor of Medicine
Division of Sleep Medicine,
Sanford Health and Sanford Research. Fargo, ND
e-mail: dr_saif78@hotmail.com

* Associate Professor of Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
Department of Internal Medicine
University of Arizona College of Medicine, Banner University Medical Center
Tucson, AZ
e-mail: saifmashaqi@email.arizona.edu

- Danelle Staebler, MS
Biostatistician, Trauma Research
Sanford Health, Fargo, ND
e-mail: Danelle.staebler@sanfordhealth.org

- Reena Mehra MD, MS, FCCP, FAASM
Professor of Medicine
Director, Sleep Disorders Research, Neurologic Institute
Staff, Respiratory Institute
Staff, Molecular Cardiology Department, Lerner Research Institute
Staff, Heart and Vascular Institute
Cleveland Clinic Lerner College of Medicine of Case Western Reserve University
9500 Euclid Avenue. S-73, Cleveland, OH 44195

- ***Corresponding author***:

- Saif Mashaqi, MD
Division of Pulmonary, Critical Care and Sleep Medicine
Department of Internal Medicine
University of Arizona College of Medicine, Banner University Medical Center
Tucson, AZ
e-mail: saifmashaqi@email.arizona.edu

- This work had been performed at Sanford Health. The corresponding author has moved from Sanford Health to the University of Arizona College of Medicine.
- All authors have seen and approved this manuscript

- Declarations for each author:

  - No off-label or investigational use.
  - No conflict of interest or financial support related to the manuscript.

- The manuscript does not report on any clinical trial.

Combined Nocturnal Pulse Oximetry and Questionnaire-Based Obstructive Sleep Apnea Screening – A Cohort Study

Saif Mashaqi MD[1,3], Danelle Staebler[1], Reena Mehra MD, MS[1]

[1]Sanford Sleep Center - Sanford Research. Fargo, ND
[2]Sleep Disorders Center, Neurological Institute, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio
[3] University of Arizona College of Medicine, Banner University Medical Center, Tucson, AZ

Abstract

Background: Screening for obstructive sleep apnea (OSA) in both inpatient and outpatient settings to pursue diagnostic testing is becoming increasingly relevant, particularly given the estimates of 85-90% of patients with OSA remaining undiagnosed. Albeit many questionnaires are available for OSA screening, the STOP-BANG questionnaire is becoming increasingly used due to ease of use and positive performance characteristics. The utility of nocturnal oximetry, in conjunction with standard questionnaire-based strategies to enhance OSA screening in adults, has yet to be systematically examined.

Research Objectives: To evaluate the utility of nocturnal oximetry measures combined with the standard STOP-BANG questionnaire as a screening strategy for OSA in the hospital setting and outpatient clinics.

Study Design and Methods: We conducted a retrospective cohort study. We reviewed the electronic medical records of 130 patients who were referred to Sanford sleep center from both inpatient and outpatient settings over one year (August 1st, 2016 to August 1st, 2017). Nocturnal oximetry was conducted at home (in the outpatient group) and in the medical wards (in the inpatient group), and the following measures were obtained:

Oxygen Desaturation Index (ODI_{POx}), mean $SaO2_{POx}$ and time spent below 88% SaO2 ($T88_{Pox}$). Apnea-hypopnea index (AHI), mean $SaO2_{PSG}$, and $T88_{PSG}$ from overnight polysomnography (PSG) and STOP-BANG score.

Results: Based upon likelihood ratio testing comparing discriminative ability, a model of (ODI_{Pox} + STOPBANG) was superior and more accurate than STOP-BANG alone in detecting mild OSA in the overall sample (AUC=0.644 [0.549-0.739], *p=0.003*) and inpatient sample (AUC=0.710 [0.582-0.839], *p=0.001*). This approach was also more accurate in detecting severe OSA in full sample (AUC=0.839 [0.763-0.914], *p< 0.0001*), inpatient sample (AUC=0.825 [0.711-0.939], *p< 0.0001*) and outpatient sample (AUC=0.827 [0.699-0.955], *p < 0.0001*). The ODI_{Pox} alone was more accurate than STOP-BANG alone in detecting mild OSA in the overall sample (AUC=0.620 [0.524-0.717], p=0.014) and inpatient sample (AUC=0.704 [0.574-0.835], p=0.002) and severe OSA in full sample (AUC=0.839 [0.764-0.915], *p< 0.0001*), inpatient sample (AUC=0.827 [0.714-0.940], *p< 0.0001*) and outpatient sample (AUC=0.861 [0.771-0.950], *p < 0.0001*).

Conclusion: The use of nocturnal oximetry measures (ODI_{POx}) improved the accuracy of standard OSA screening with the STOP-BANG questionnaire as a screening tool in severe OSA in both inpatient and outpatient settings.

Clinical Implication: Obstructive sleep apnea is a common sleep disorder that impacts many co-morbidities in different age groups. Enhancing affordable screening methods for OSA can facilitate early diagnosis and treatment and subsequently ameliorate morbidity and mortality related to sleep-disordered breathing.

Keywords: nocturnal oximetry, oxygen desaturation index, STOP-BANG, obstructive sleep apnea, screening

INTRODUCTION

Obstructive sleep apnea (OSA) is a common sleep disorder with population-based studies estimating a prevalence of up to 20% in males and 10-15% in females.[1] If left unrecognized and untreated, the chronic repeated exposures of nocturnal intermittent hypoxia, autonomic nervous system fluctuations, and intrathoracic pressure alterations lead to a host of untoward health consequences including cardiovascular disease, neurocognitive decline, mood disorders and a negative impact on the quality of life. [2-5] Despite the adverse impact of untreated OSA on health and well-being, OSA remains sorely under-recognized with data over the last several decades, indicating that a persistent 85-90% of patients with OSA remain undiagnosed.[6] [7] Current screening approaches are suboptimal in part due to inefficient streamlining of patients for diagnostic testing.

The historical gold standard test for the diagnosis of OSA has been attended in-lab polysomnography (PSG). Over the last several years, home sleep apnea test (HSAT) is becoming increasingly used.[8] Despite the increased utilization of HSAT for the diagnosis of OSA-- intended in large part to reduce patient burden and enhance accessibility--, there remains a substantial and unacceptable level of OSA under-diagnosis.

Therefore, enhanced screening methods would allow for more efficient identification of those most likely to have OSA in terms of pursuing diagnostic testing and treatment. Many screening questionnaires tools have been developed to estimate the risk of OSA to inform the clinical approach to be taken for those with high pre-test probability for OSA. Various questionnaires such as the Berlin questionnaire,[9] STOP-BANG,[10,11], and most recently, the NoSAS [12] have been created to assess pre-test OSA probability with validation mainly in community-based samples. The more recently developed NoSAS questionnaire and the SAS score have a higher level of specificity and predictive values and similar sensitivity compared to the STOP-BANG questionnaire. Although NoSAS may have better performance, it requires the additional burden of obtaining the requisite data for the 17-items, which may limit ease of use and practicality.[12,13]

Overnight oximetry is inexpensive, readily available, and straightforward to use; however, compared to the pediatric population, the utility of screening for OSA has not been studied extensively in adults. One study examined the predictive ability of OSA screening questionnaires versus oximetry for CPAP therapy initiation and identified that oximetry performed better than questionnaires (Berlin Questionnaire, Epworth Sleepiness

Scale, and STOP-BANG) in predictive ability without additional benefit of predictiveness with the addition of questionnaire data to oximetry data.[14] We, therefore, conduct a study of both outpatient and inpatient groups to examine the utility of standard OSA questionnaires, nocturnal oximetry and combined data from both approaches in terms of screening for OSA to identify those patients who should pursue diagnostic testing while investigating performance characteristics at varying thresholds of OSA severity. Data generated from this study ideally will help to inform optimal OSA screening approaches utilizing nocturnal oximetry and questionnaires to be implemented by health care providers.

METHODS

Design Overview

We utilized a cohort study design to retrospectively examine data from 248 patients who underwent overnight pulse oximetry followed by an overnight in lab polysomnography at Sanford Sleep Center in Fargo, ND, in the inpatient (non-ICU) and outpatient settings from August 1st, 2016 to August 1st, 2017. The study protocol was approved by Sanford institution's scientific research review committee. (IRB ID STUDY00001070).

Nocturnal oximetry was ordered based on the clinical suspicion of sleep-disordered breathing and conducted in the medical wards (inpatient group) and at home (outpatient group), and all patients who underwent oximetry study were evaluated at the sleep center by a sleep provider. Both overnight oximetry studies and polysomnograms were interpreted by board-certified sleep physicians, and the same protocol was used for oximetry interpretation and referral to sleep medicine. Since the characteristic features of patients in the inpatient and outpatient settings are different, we wanted to test the validity and accuracy of our results in both settings.

Inclusion criteria were adults 18 – 95 years of age who underwent oximetry and PSG with a maximum timeframe of six months between assessments (*mean* 60.4 d for the whole sample, *p=0.61. Range* 5 – 395). Only studies conducted on room air were included. Exclusion criteria were patients with PSG-based central sleep apnea (defined as Central Apnea Index (CAI) > 50% of total Apnea-Hypopnea Index (AHI)), oximetry

data with total recording time less than 5 hours, all split studies given that diagnostic sleep study time less than 4 hours. Five patients (all outpatient) who had home sleep apnea testing (HSAT) were excluded to maintain consistency. Accordingly, 130 patients (66 inpatients and 64 outpatients) were included in the final analytic sample (***Appendix Figure 1***).

Data Collection

Nocturnal pulse oximetry studies were conducted using the Nonin wrist-worn pulse oximeter with Bluetooth wireless technology, Model 3150 (Up to 1080 hours of SaO2, and pulse rate data with a 4-second data collection rate). The following data were collected from nocturnal pulse oximetry: adjusted oxygen desaturation index (ODI_{POx}, $\geq$4 % drop in SaO2), mean $SaO2_{POx}$, and time with SaO2 <= 88% ($T88_{POx}$) (the POx subscript denotes indices are obtained from pulse oximetry). The data were transferred, analyzed, reported, and archived from the oximeter to the PC using nVision software, Version 6.4 (Nonin Medical Inc. Plymouth, MN 55441). The SaO2 signal was averaged over four beats exponentially with a two-beat latency and a 1.5 second delay in display.

Overnight PSGs were conducted using Embla Sandman (Version 10.1.1) and included EEG, EOG, chin, and lower limb EMG, snoring, thermistry, nasal pressure transducer, SaO2, EKG, body position and respiratory inductance plethysmography (RIP) effort belts. The following data were collected: apnea-hypopnea index (AHI), mean $SaO2_{PSG}$, and time SaO2 ≤ 88% ($T88_{PSG}$).

STOP-BANG questionnaires were administered at the time of the office visit or during hospitalization at the time of discharge. This includes (S= Loud **S**noring, T= **T**iredness during the daytime, O= **O**bserved apnea episodes, P= high blood **P**ressure, B= **B**MI $\geq$30, A= **A**ge > 50 years, N= **N**eck circumference > 16 inches in females and 17 inches in males, G= male **G**ender). A score of $\geq$3 is associated with a high risk of OSA and a score $\leq$ 1 is associated with a low risk of OSA.[12]

Variable Definitions

Based upon nocturnal pulse oximetry, an oxygen desaturation event was defined as an event that lasts for more than 10 seconds with an associated 4% drop in oxygen saturation. Adjusted ODI_{POx} was defined as

the total number of desaturation events over total recording time minus the percentage of an artifact. We classified the severity of ODI_{POx} as mild, moderate or severe categories as follows: mild: $ODI_{POx} \geq 5$ and < 15, moderate: $ODI_{POx} \geq 15$ and < 30 and severe: $ODI_{POx} \geq 30$.

In terms of PSG indices, the AHI was calculated using the total number of obstructive apneas (defined as ≥ 90% reduction of the flow for > 10 seconds) and obstructive hypopneas (defined as ≥ 50% reduction in airflow for > 10 seconds with an associated drop in oxygen saturation (SaO2) by ≥ 4%) divided by total sleep time.[15] The AHI was classified into mild, moderate, and severe as follows: mild defined as AHI ≥ 5 and < 15, moderate defined as AHI ≥ 15 and < 30 and severe defined as AHI ≥ 30.

The mean $SaO2_{POx}$ and $SpO2_{PSG}$ and $T88_{POx}$ and$T88_{PSG}$ in both oximetry and PSG are defined as estimate mean of arterial oxygen saturation and the duration where SpO2 was ≤ 88% respectively.

Statistical Analyses

The 130 patients studied were categorized based upon AHI as described above as mild OSA (5 ≤ AHI < 15, n=49), moderate OSA (15 ≤ AHI < 30, n=21), or severe OSA (AHI ≥ 30, n=39). Spearman correlation coefficients were calculated to measure the magnitude and direction of association and direction between ODI_{POx}, mean $SaO2_{POx}$, $T88_{POx}$, and STOP-BANG relative to AHI.

We calculated the accuracy of each oximetry measure (ODI_{POx}, mean $SaO2_{POx}$, and $T88_{POx}$) in detecting OSA at different cut-off ranges (mild, moderate, and severe) relative to PSG measures. Receiver operating characteristic (ROC) analyses were created to evaluate the extent to which oximetry-based measures (ODI_{POx}, mean $SaO2_{POx}$, $T88_{POx}$), and STOP-BANG discriminated between those with mild (5 ≤ AHI < 15), moderate (15 ≤ AHI < 30) or severe (AHI ≥ 30) OSA. The ROC curve was created by plotting the true positive rate (sensitivity) as a function of the false positive rate (1-specificity) at various AHI threshold values. The overall classification was evaluated using the area under the curve (AUC), and cutoff values were determined using Youden's index,[16], which maximizes the summation of the sensitivity and specificity. The area under the curve (AUC) was used to quantify the overall ability of the test to discriminate between those

individuals who have different degrees of OSA and ranges from 0.50 (no diagnostic ability) to 1.0 (perfect diagnostic ability).

We also tested a model that combines oximetry-based ODI to the standard STOP-BANG questionnaire. ROC analyses were performed considering the entire inpatient and outpatient groups separately. Likelihood ratio testing was performed to examine the utility of adding ODI_{POx} to standard STOP-BANG screening.

RESULTS

Demographic Data

Information was collected on demographic characteristics (age and sex), BMI and co-morbid medical conditions which were listed in the problem list section of each patient in the electrical medical record chart as entered by the primary care physician (**Table 1**)

Nocturnal Oximetry Measures and STOP-BANG Relative to Polysomnogram-Based Obstructive Sleep Apnea Severity Thresholds

Results of the performance characteristics of nocturnal pulse oximetry measures (ODI_{POx}, $SaO2_{POx}$, $T88_{POx}$) and the STOP-BANG questionnaire (independent of one another) in terms of diagnostic utility of PSG-based OSA defined by AHI are presented in this section according to different levels of OSA severity (mild: 5 ≤ AHI < 15, moderate: 15 ≤ AHI < 30 and severe: AHI ≥ 30). In each section, salient results of the overall, inpatient, and outpatient samples are provided.

ODI_{POx} showed significant diagnostic utility in discriminating those with mild obstructive sleep apnea for the full and inpatient samples (AUC=0.62 [0.524-0.717] and AUC=0.70 [0.574-0.835] respectively), but not in the outpatient sample. Other oximetry measures (mean $SaO2_{POx}$ and $T88_{POx}$) did not show statistically significant utility in patients with mild OSA in full, inpatient, and outpatient samples. The STOP-BANG questionnaire was not effective in discriminating a mild degree of OSA. (***table 2***)

ODI_{POx} showed statistically significant diagnostic utility in discriminating those with moderate obstructive sleep apnea for the overall sample only (AUC=0.63 [0.512-0.745]). $SaO2_{POx}$ and $T88_{POx}$ did not have

significant diagnostic utility in discriminating moderate levels of OSA. The STOP-BANG questionnaire was not effective in discriminating a moderate degree of OSA. **(*table 2)***

ODI_{POx} and $T88_{POx}$ showed significant diagnostic utility in discriminating those with severe OSA for the full, inpatient, and outpatient samples: AUC=0.84 [0.764-0.915], AUC=0.83 [0.714-0.940] and AUC=0.86 [0.771-0.950] respectively for ODI_{Pox} and AUC=0.69 [0.587-0.793], AUC=0.66 [0.509-0.804] and AUC=0.74 [0.594-0.881] respectively for $T88_{POx}$. Mean $SaO2_{POx}$ did not show significant utility. The STOP-BANG questionnaire was effective in discriminating severe OSA in the full sample only (AUC=0.62 [0.508-0.725]). **(*table 2, appendix table 1, appendix figures 2a-c*).** Positive and negative values for nocturnal oximetry measures (ODI_{Pox} and $T88_{Pox}$) and STOP-BANG are illustrated in **table 4.**

Since nocturnal oximetry and PSG were not conducted simultaneously, we examined BMI changes from the time of oximetry to PSG and found that they did not reach statistical significance (mean difference 0.19, 0.27, and p-value 0.14, 0.45 and 0.21 for full, inpatient and outpatient samples respectively). This reassures that the validity of examining performance characteristics of nocturnal oximetry measures relative to PSG based measures is not compromised by weight change.

Nocturnal Oximetry-Based Oxygen Desaturation Index in Addition to STOP-BANG Relative to Polysomnogram Obstructive Sleep Apnea Threshold Measures

As ODI_{POx} proved to be suitable in discriminating all but moderate sleep apnea, an additional analysis was completed examining the benefit of utilizing both ODI_{Pox} and STOP-BANG data relative to varying PSG-based AHI thresholds. Using a dual combination approach of both ODI_{POx} + STOP-BANG showed significant diagnostic utility in discriminating those with mild OSA for the full and inpatient samples, moderate OSA for the full sample, and severe OSA in the full, inpatient, and outpatient samples. (**Table 3 and Figures 1 a-f**)

Likelihood ratio testing comparing ODI_{POx} + STOP-BANG to isolated STOP-BANG questionnaire use demonstrated that the addition of ODI_{POx} to STOP-BANG is significantly better than STOP-BANG alone for mild (full and inpatient) and severe (full, inpatient, and outpatient), groups. There is no significant addition to the model for moderate sleep apnea or mild sleep apnea for outpatient. (**Table 5)**

Discussion

In this study, we examined the performance of standard OSA screening approaches with STOP-BANG versus nocturnal pulse oximetry data versus a combined approach of both STOP-BANG and nocturnal oximetry in both the inpatient and outpatient settings in those suspected to have OSA based upon clinical judgment. There are several salient findings: 1) ODI from nocturnal oximetry (ODI_{Pox}) had moderate to good discriminative ability in the prediction of mild, moderate and severe degrees of OSA (AUC range of 0.62-0.83)—findings not observed with STOP-BANG, 2) there was an enhanced discriminative ability of ODI_{Pox} in severe OSA versus other OSA categories, 3) mean oxygen saturation (meanSaO2$_{POx}$) and time spent below 88% SaO2 ($T88_{POx}$) did not effectively discriminate OSA in any category except $T88_{Pox}$ for severe OSA, 4) at a mild degree of OSA, ODI_{Pox} performed best in the inpatient sample, and at a severe degree of OSA, it performed the best in the outpatient sample and 5) there is a statistically significant enhancement of OSA discrimination with the addition of ODI_{Pox} to STOP-BANG screening particularly for mild and severe degrees of OSA. These findings are generalizable to those who are older, obese, have cardiovascular risk, and can be extrapolated to women, given that 45% of the overall sample were women. Therefore, these results have external validity and clinical implications for the primary care setting.

Given the ease of use and relatively good performance characteristics, the STOP-BANG questionnaire initially validated in the pre-operative patient population is now being increasingly used in outpatient clinics and the inpatient setting.[17-20] The STOP-BANG screening instrument has a high level of sensitivity, but low specificity, which has led to the development of other tools with enhanced performance characteristics, but with increased complexity and burden of obtaining anthropometric measures[21] Nocturnal pulse oximetry is a simple, cost-effective and objective screening tool for OSA.

The utilization of nocturnal oximetry in the medical literature has been mainly described for inpatients and patients with specific co-morbid conditions. For example, ODI from nocturnal oximetry showed good diagnostic accuracy for moderate and severe OSA in patients hospitalized with acute stroke. The diagnostic accuracy of ODI_{Pox} was examined in relation to respiratory event index (REI) from home sleep apnea test (HSAT) with AUC of 89.3 (84.9-92.8) for mild OSA and 79.9 to 55.5 for moderate and severe OSA

respectively.[22] Our results differed from this study as we observed increased diagnostic utility with an increasing AHI category compared to a reduction in AUC with increasing REI category found in this study of stroke patients. ODI from nocturnal oximetry has also been identified as an accurate tool to detect moderate and severe degrees of OSA in patients with atrial fibrillation (AUC 0.95 (95% CI: 0.929–0.972) and 0.93(95% CI: 0.895–0.968), respectively).[23] With similar findings, nocturnal oximetry (ODI) has been shown to be a useful screening tool for OSA (REI from HSAT) in hospitalized patients with congestive heart failure (AUC 0.88 for REI ≥5 events per hour).[24]

Our study results are consistent with the above results observed in cardiac and cerebrovascular disease, albeit with slightly lower AUC values suggesting perhaps enhanced OSA discriminative ability of ODI_{Pox} in those with underlying comorbidity. The current study supports the strongest ODI_{Pox} discriminative utility in predicting severe OSA only (AUC 0.84 [0.764-0.915]). Across the adult and pediatric literature, it appears that nocturnal pulse oximetry measures alone (especially ODI) are not a good tool to detect a mild degree of OSA.[25] At the same time, the use of standard questionnaires (e.g., STOP-BANG) alone has low specificity. [26,27]This raises the need for a combined model type of approach that utilizes more than one tool and remains easily conducted and cost-effective.

Our study is novel since it is the first study to examine the utility of combining both subjective and characteristic data from STOP-BANG and objective physiologic data from nocturnal oximetry to screen for OSA in adults. The findings support that such a combination overall significantly enhances the diagnostic accuracy of STOP-BANG in mild, moderate, and severe OSA. Interestingly, STOP-BANG alone did not effectively discriminate OSA relative to ODI_{Pox} at any level of OSA severity. This combination approach showed more accuracy in inpatients compared to outpatients, where it discriminates mild and severe OSA in inpatients compared to only severe OSA in outpatients. To our knowledge, there is only one study that examined this model (ODI + STOP-BANG); however, all patients were surgical patients and underwent HSAT—not in-lab PSG, the latter which would offer a more accurate measure of the true degree of OSA. The authors concluded that patients with STOP-BANG scores between 2 and 5 should undergo nocturnal oximetry, where ODI can be used as a surrogate for AHI to avoid delaying surgery.[28]

The findings of this study should be placed into the context of data supporting the non-inferiority of oximetry to PSG in terms of the Functional Outcomes of Sleep Questionnaire (FOSQ); however, other outcomes such as Epworth Sleepiness Scale and positive airway pressure appeared to be worse.[29] It is unclear how STOP-BANG added to oximetry would affect such results.

Other strengths include comparing the performance of oximetry measures to the overnight PSG indices, the latter considered the historical gold standard for the diagnosis of OSA, especially in patients with co-morbid conditions. We used the same definition of oxygen desaturation ($\geq$4% decline in SaO2) in overnight oximetry and PSG. Almost half of the participants in our cohort were females, which enhances the generalization of the results and findings to the entire community.

Limitation of the study is its retrospective nature, therefore making it prone to possible misclassification and selection bias. However, the data collected via PSG and oximetry are objective and do not appear to be substantially impacted by poor data quality compared to a prospective study. Second, the pulse oximetry testing was not conducted immediately around the time of PSG (maximum time frame of six months). This can possibly create weight changes that would compromise an effective interpretation of the data. However, BMI change during this time in the full sample, inpatients, and outpatients was similar with no statistically significant difference, which minimizes this concern. Third, the sleep physician who read the PSG was not consistently blinded to oximetry results and other data.

The results of this study set the stage for hospitalists and health care providers to consider an approach or protocol to evaluate patients at high OSA risk with this combined model, utilizing STOP-BANG and nocturnal pulse oximetry. Patients who score ≥ 3 on STOP-BANG with ODI_{Pox} ≥ 5 events per hour should be considered for diagnostic testing with overnight PSG or HSAT. Further investigation should focus on examining the consistency of findings in a validation study. Further study is also needed to clarify the cost-effectiveness — particularly in relation to the enhanced efficiency offered due to greater OSA discriminative ability of this combination approach in the assessment for OSA risk to inform diagnostic testing pathways.

References

1. Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, Hla KM. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort study. *Wmj.* 2009;108(5):246-249.
2. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol.* 2013;177(9):1006-1014.
3. Marshall NS, Wong KK, Phillips CL, Liu PY, Knuiman MW, Grunstein RR. Is sleep apnea an independent risk factor for prevalent and incident diabetes in the Busselton Health Study? *J Clin Sleep Med.* 2009;5(1):15-20.
4. Vakil M, Park S, Broder A. The complex associations between obstructive sleep apnea and auto-immune disorders: A review. *Med Hypotheses.* 2018;110:138-143.
5. Brunetti V, Ferilli MAN, Vollono C, Della Marca G. Sleep apneas trigger epilepsy. *Sleep Med.* 2017;39:23-24.
6. Chen X, Wang R, Zee P, et al. Racial/Ethnic Differences in Sleep Disturbances: The Multi-Ethnic Study of Atherosclerosis (MESA). *Sleep.* 2015;38(6):877-888.
7. Kapur VK. Obstructive sleep apnea: diagnosis, epidemiology, and economics. *Respir Care.* 2010;55(9):1155-1167.
8. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med.* 2017;13(3):479-504.
9. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med.* 1999;131(7):485-491.
10. Chung F, Subramanyam R, Liao P, Sasaki E, Shapiro C, Sun Y. High STOP-Bang score indicates a high probability of obstructive sleep apnoea. *Br J Anaesth.* 2012;108(5):768-775.
11. Marti-Soler H, Hirotsu C, Marques-Vidal P, et al. The NoSAS score for screening of sleep-disordered breathing: a derivation and validation study. *Lancet Respir Med.* 2016;4(9):742-748.
12. Peng M, Chen R, Cheng J, Li J, Liu W, Hong C. Application value of the NoSAS score for screening sleep-disordered breathing. *J Thorac Dis.* 2018;10(8):4774-4781.
13. Topirceanu A, Udrescu M, Udrescu L, et al. SAS score: Targeting high-specificity for efficient population-wide monitoring of obstructive sleep apnea. *PLoS One.* 2018;13(9):e0202042.
14. Pataka A, Kalamaras G, Vlachogianni E, Argyropoulou P. Combination of oximetry and sleep questionnaires as screening tools for CPAP initiation in patients with obstructive sleep apnea. *Pulmonology.* 2018.
15. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med.* 2012;8(5):597-619.
16. Unal I. Defining an Optimal Cut-Point Value in ROC Analysis: An Alternative Approach. *Comput Math Methods Med.* 2017;2017:3762651.
17. Chia P, Seet E, Macachor JD, Iyer US, Wu D. The association of pre-operative STOP-BANG scores with postoperative critical care admission. *Anaesthesia.* 2013;68(9):950-952.
18. Cowan DC, Allardice G, Macfarlane D, et al. Predicting sleep disordered breathing in outpatients with suspected OSA. *BMJ Open.* 2014;4(4):e004519.
19. Showalter L, O'Keefe C. Implementation of an obstructive sleep apnea screening tool with hypertensive patients in the primary care clinic. *J Am Assoc Nurse Pract.* 2018.
20. Zeng T, Zhang L, Yang Y, Xie F, Zhang D, Hu X. [Screening efficiencies of obstructive sleep apnea screening scales in patients with acute ischemic stroke]. *Zhejiang Da Xue Xue Bao Yi Xue Ban.* 2018;47(2):174-180.
21. Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. *Chest.* 2016;149(3):631-638.
22. Lin SH, Branson C, Leung J, Park L, Doshi N, Auerbach SH. Oximetry as an Accurate Tool for Identifying Moderate to Severe Sleep Apnea in Patients With Acute Stroke. *J Clin Sleep Med.* 2018;14(12):2065-2073.

23. Linz D, Kadhim K, Brooks AG, et al. Diagnostic accuracy of overnight oximetry for the diagnosis of sleep-disordered breathing in atrial fibrillation patients. *Int J Cardiol.* 2018;272:155-161.
24. Sharma S, Mather PJ, Chowdhury A, et al. Sleep Overnight Monitoring for Apnea in Patients Hospitalized with Heart Failure (SOMA-HF Study). *J Clin Sleep Med.* 2017;13(10):1185-1190.
25. Hang LW, Wang HL, Chen JH, et al. Validation of overnight oximetry to diagnose patients with moderate to severe obstructive sleep apnea. *BMC Pulm Med.* 2015;15:24.
26. Chiu HY, Chen PY, Chuang LP, et al. Diagnostic accuracy of the Berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: A bivariate meta-analysis. *Sleep Med Rev.* 2017;36:57-70.
27. Miller JN, Kupzyk KA, Zimmerman L, et al. Comparisons of measures used to screen for obstructive sleep apnea in patients referred to a sleep clinic. *Sleep Med.* 2018;51:15-21.
28. Christensson E, Franklin KA, Sahlin C, et al. Can STOP-Bang and Pulse Oximetry Detect and Exclude Obstructive Sleep Apnea? *Anesth Analg.* 2018;127(3):736-743.
29. Chai-Coetzer CL, Antic NA, Hamilton GS, et al. Physician Decision Making and Clinical Outcomes With Laboratory Polysomnography or Limited-Channel Sleep Studies for Obstructive Sleep Apnea: A Randomized Trial. *Ann Intern Med.* 2017;166(5):332-340.

Table1. **Patient Characteristics**

	Total sample n = 130	Inpatient n = 66	Outpatient n = 64
Age	64.6 ± 14.07	62.2 ±15.4	67.0 ± 12.2
Sex (%)			
Female	59 (45.4)	28 (42.4)	31 (48.4)
Body Mass Index, kg/m^2	33.7 ± 7.3	35.1 ± 8.2	32.3 ± 6.0
Comorbidities (%)			
Hypertension	72 (55.4)	39 (59.1)	33 (51.6)
Diabetes	28 (21.5)	17 (25.8)	11 (17.2)
Coronary Artery Disease	39 (30.1)	27 (40.9)	13 (20.3)
Cerebrovascular Disease	18 (13.9)	16 (24.2)	2 (3.1)
Congestive Heart Failure	27 (20.8)	15 (22.7)	12 (18.8)
Interstitial Lung Disease	1 (0.8)	0 (0.0)	1 (1.6)
COPD	17 (13.1)	5 (7.6)	12 (18.8)
Nocturnal Pulse Oximetry			
ODI $_{Pox}$	21.5 ± 17.5	25.5 ± 19.0	17.5 ±14.9
SaO2 (%) $_{Pox}$	91.5 ± 2.8	91.6 ± 3.2	91.5± 2.5
T88$_{Pox}$	75.5 ± 114.8	84.8 ±120.8	66.1 ±108.5
Polysomnography (PSG)			
Apnea Hypopnea Index	23.5 ± 25.6	27.0 ± 26.6	20.0 ± 24.1
Mean SaO2$_{PSG}$, (%)	92.6 ± 3.1	93.1± 2.5	92.1± 3.6
T88 $_{PSG}$	24.0 ± 5.1	21.3 ± 50.6	26.9 ± 55.9

AHI: apnea-hypopnea index; BMI: body mass index; COPD: Chronic Obstructive Pulmonary Disease, ODI$_{pox}$: oxygen desaturation index on oximetry; T88$_{pox}$: time spent with SaO2 ≤88% on oximetry; T88$_{PSG}$: time spent with SaO2 ≤88% on polysomnography

Table 2. **Receiver Operator Curve (ROC) Analyses of Nocturnal Pulse Oximetry Indices (ODI) and STOP-BANG Questionnaire in mild, moderate, and severe OSA.**

Variable	Sample	N	AUC	SE	Lower Area	Upper Area	p-value
Mild OSA							
Nocturnal Oximetry							
ODI_{Pox}	**Full**	130	0.620	0.049	0.524	0.717	*0.014**
ODI_{Pox}	**Inpatient**	66	0.704	0.067	0.574	0.835	*0.002**
ODI_{Pox}	**Outpatient**	64	0.529	0.073	0.385	0.673	0.691
STOP-BANG							
	Full	130	0.587	0.051	0.488	0.687	0.086
	Inpatient	66	0.568	0.073	0.425	0.712	0.351
	Outpatient	64	0.600	0.072	0.459	0.740	0.165
Moderate OSA							
Nocturnal Oximetry							
ODI_{Pox}	**Full**	130	0.628	0.059	0.512	0.745	*0.030**
ODI_{Pox}	**Inpatient**	66	0.618	0.077	0.467	0.770	0.126
ODI_{Pox}	**Outpatient**	64	0.587	0.097	0.396	0.777	0.374
STOP-BANG							
	Full	130	0.526	0.066	0.396	0.656	0.696
	Inpatient	66	0.583	0.085	0.416	0.750	0.331
	Outpatient	64	0.588	0.092	0.408	0.767	0.338
Severe OSA							
Nocturnal Oximetry							
ODI_{Pox}	**Full**	130	0.839	0.038	0.764	0.915	*<.0001**
ODI_{Pox}	**Inpatient**	66	0.827	0.058	0.714	0.940	*<.0001**
ODI_{Pox}	**Outpatient**	64	0.861	0.046	0.771	0.950	*<.0001**
STOP-BANG							
	Full	130	0.616	0.055	0.508	0.725	*0.035**
	Inpatient	66	0.577	0.078	0.425	0.729	0.319
	Outpatient	64	0.643	0.085	0.476	0.810	0.094

N=sample size; AUC= area under the curve; SE=standard error; ODI=oxygen desaturation index

Table 3. **Obstructive Sleep Apnea Categories and ODI $_{Pox}$+ STOP-BANG Receiver Operator Curve Analyses**

Sample	N	AUC	SE	Lower and Upper Area	p-value
Mild OSA					
Full	130	0.644	0.048	0.549 - 0.739	*0.003**
Inpatient	66	0.710	0.066	0.582 - 0.839	*0.001**
Outpatient	64	0.605	0.072	0.464 - 0.747	0.145
Moderate OSA					
Full	130	0.625	0.060	0.508 - 0.742	0.036*
Inpatient	66	0.614	0.080	0.457 - 0.770	0.154
Outpatient	64	0.607	0.103	0.405 - 0.808	0.301
Severe OSA					
Full	130	0.839	0.039	0.763 - 0.914	*<.0001**
Inpatient	66	0.825	0.058	0.711 - 0.939	*<.0001**
Outpatient	64	0.827	0.065	0.699 - 0.955	*<.0001**

N=sample size; AUC= area under the curve; SE=standard error; ODI $_{Pox}$ =oxygen desaturation index
* p-value <0.05

Table 4. **Positive and Negative Predictive Values for Oxygen Desaturation Index from Nocturnal Pulse Oximetry for Polysomnogram-Based Mild, Moderate and Severe Obstructive Sleep Apnea (Only statistically significant values)**

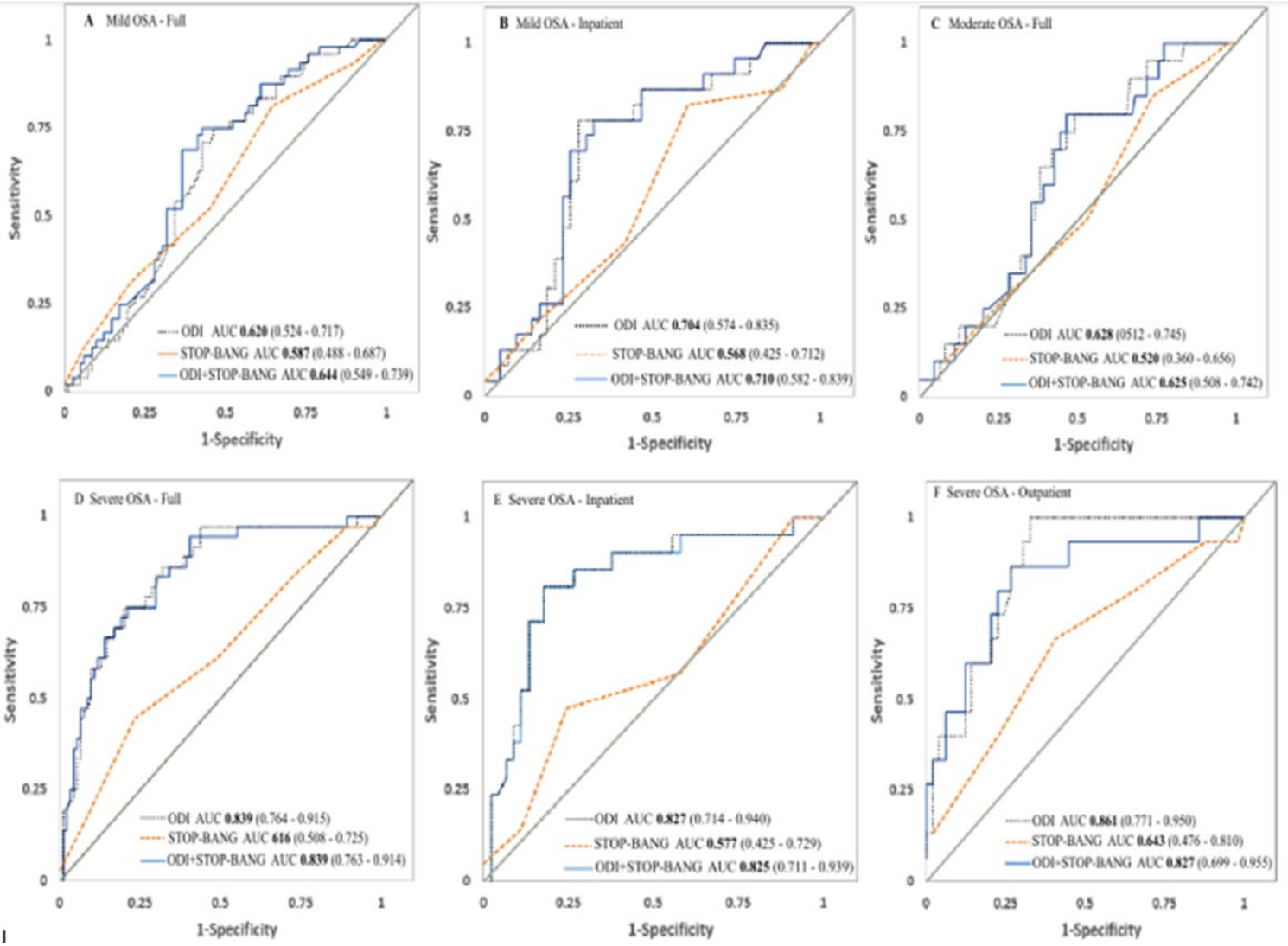
Variable	Sample	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
Mild OSA			
ODI $_{pox}$	Full	0.62	0.68
ODI $_{pox}$	Inpatient	0.61	0.86
Moderate OSA			
ODI $_{pox}$	Full	0.41	0.85
Severe OSA			
ODI $_{Pox}$	Full	0.69	0.81
ODI $_{Pox}$	Inpatient	0.80	0.83
ODI $_{Pox}$	Outpatient	0.26	1.00
Severe OSA			
T88 $_{Pox}$	Full	0.58	0.74
T88 $_{Pox}$	Inpatient	0.57	0.73
T88 $_{Pox}$	Outpatient	0.67	0.73
STOP-BANG			
STOP-BANG	Full	0.44	0.77

Table 5. **Likelihood Ratio Results of STOP-BANG versus ODI $_{Pox}$+ STOP-BANG**

Sample	Log-Likelihood for (STOP-BANG)	Log-Likelihood for (ODI $_{Pox}$+ STOP-BANG)	LR	p-value
Mild OSA				
Full	167.81	160.78	7.03	*0.0080**
Inpatient	84.10	75.95	8.14	*0.0043**
Outpatient	83.60	82.96	0.65	0.4215
Moderate OSA				
Full	111.37	110.00	1.38	0.2409
Inpatient	64.73	64.13	0.60	0.4398
Outpatient	43.80	43.70	0.11	0.7430
Severe OSA				
Full	148.68	115.62	33.06	*<.0001**
Inpatient	80.93	63.45	17.48	*<.0001**
Outpatient	67.00	50.51	16.49	*<.0001**

LR= Likelihood ratio; ODI $_{Pox}$ =oxygen desaturation index; OSA=obstructive sleep apnea
*p-value < 0.05

Figure 1. **Receiver Operator Curve (ROC) Analyses of (ODI $_{Pox}$+ STOP-BANG) versus STOP-BANG versus ODI in mild, moderate and, severe OSA**



I

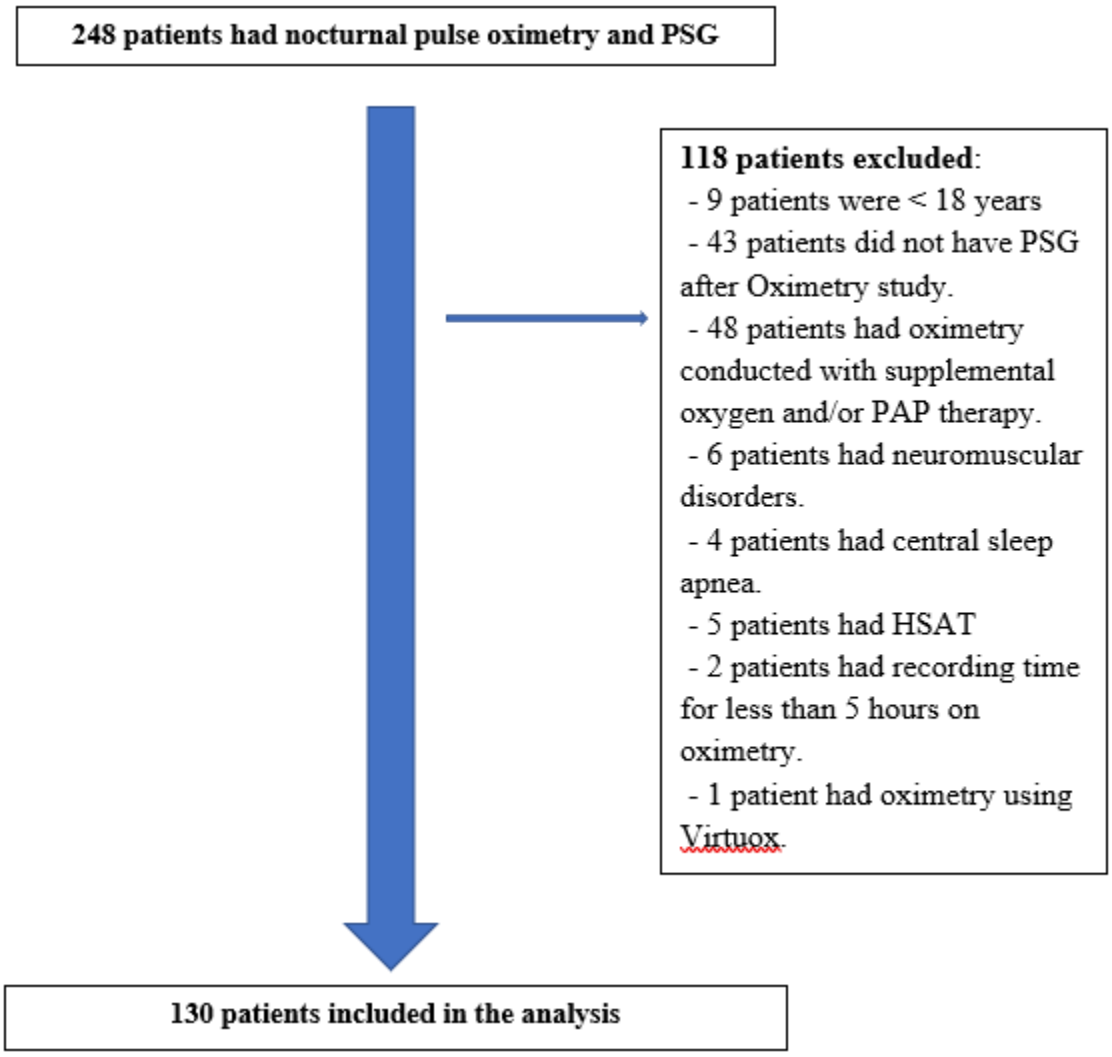
A) Mild OSA in the full group; **B)** Mild OSA in inpatient group; **C)** Moderate OSA in the full group; **D)** Severe OSA in the full group; **E)** Severe OSA in inpatient group; **F)** Severe OSA in the outpatient group; AUC=area under the curve

ODI

STOPBANG

ODI + STOPBANG

Appendix Figure 1. **Study Flow Diagram**

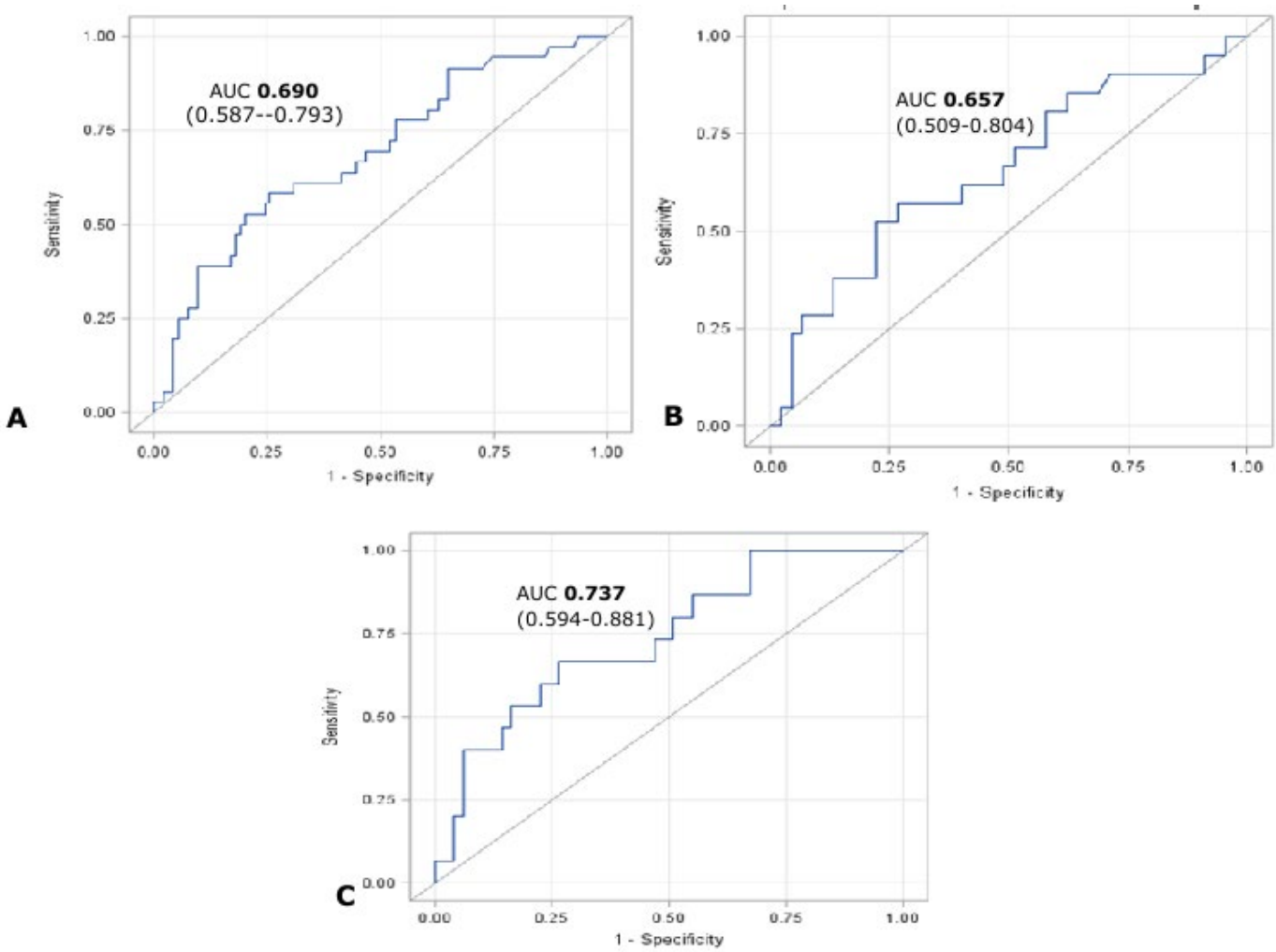


Appendix Table 1. **Receiver Operator Curve (ROC) Analyses of Nocturnal Pulse Oximetry Indices (Mean SPO2 and T88) in Mild, Moderate, and Severe OSA**

Variable	Sample	N	AUC	SE	Lower and Upper Areas	p-value
Mild OSA						
Mean SaO2 $_{Pox}$	**Full**	130	0.566	0.051	0.467 - 0.666	0.193
Mean SaO2 $_{Pox}$	**Inpatient**	66	0.557	0.072	0.416 - 0.698	0.428
Mean SaO2 $_{Pox}$	**Outpatient**	64	0.574	0.075	0.426 - 0.722	0.327
T88 $_{Pox}$	**Full**	130	0.552	0.051	0.452 - 0.652	0.309
T88 $_{Pox}$	**Inpatient**	66	0.600	0.071	0.460 - 0.740	0.163
T88 $_{Pox}$	**Outpatient**	64	0.499	0.074	0.354 - 0.644	0.989
Moderate OSA						
Mean SaO2 $_{Pox}$	**Full**	130	0.606	0.069	0.472 - 0.741	0.122
Mean SaO2 $_{Pox}$	**Inpatient**	66	0.617	0.087	0.446 - 0.788	0.181
Mean SaO2 $_{Pox}$	**Outpatient**	64	0.588	0.114	0.364 - 0.811	0.442
T88 $_{Pox}$	**Full**	130	0.563	0.074	0.418 - 0.707	0.398
T88 $_{Pox}$	**Inpatient**	66	0.581	0.094	0.398 - 0.765	0.386
T88 $_{Pox}$	**Outpatient**	64	0.490	0.124	0.247 - 0.733	0.935
Severe OSA						
Mean SaO2 $_{Pox}$	**Full**	130	0.568	0.061	0.448 - 0.688	0.266
Mean SaO2 $_{Pox}$	**Inpatient**	66	0.531	0.083	0.369 - 0.692	0.710
Mean SaO2 $_{Pox}$	**Outpatient**	64	0.638	0.088	0.466 - 0.810	0.116
T88 $_{Pox}$	**Full**	130	0.690	0.053	0.587 - 0.793	0.000*
T88 $_{Pox}$	**Inpatient**	66	0.657	0.075	0.509 - 0.804	0.037*
T88 $_{Pox}$	**Outpatient**	64	0.737	0.073	0.594 - 0.881	*0.001**

N=sample size; AUC= area under the curve; SE=standard error; T 88=time spent with SaO2 ≤88%

Appendix *Figure 2*. **Receiver Operator Curves for Nocturnal Pulse Oximetry-Based Oxygen T 88 in severe OSA.**



A) Severe OSA in the full group; **B)** Severe OSA in inpatient group; **C)** Severe OSA in the outpatient group; AUC=area under the curve