REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
29/05/2018	Journal	05/29/2018

4. TITLE AND SUBTITLE
Split-Night Polysomnography Overestimates Apnea-Hypopnea Index in High-Risk Professions

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Rouse, Jessica K

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

8. PERFORMING ORGANIZATION REPORT NUMBER
17881

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release. Distribution is unlimited.

13. SUPPLEMENTARY NOTES
Journal of Sleep Research

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Clarice Longoria
					19b. TELEPHONE NUMBER *(Include area code)*
					210-292-7141

Split-Night Polysomnography Overestimates Apnea-Hypopnea Index in High-Risk Professions
SN-PSG Overestimates AHI in High-Risk Professions

Jessica K Rouse, MD[1], Sean R Shirley, MD[2], Aaron B Holley, MD[3] Vincent Mysliwiec, MD[2], Robert J Walter, MD, DHCE[3],
1 Department of Medicine (Internal Medicine Division), phone (210) 220-7156, fax (210) 916-4721, jessica.rouse.mil@mail.mil, 3551 Roger Brooke Drive, JBSA Ft Sam Houston, TX 78234, Brooke Army Medical Center, San Antonio, TX
2 Department of Medicine (Sleep Medicine Division), 2200 Bergquist Dr. Ste 1, Lackland AFB, TX, 78236, Wilford Hall Ambulatory Surgical Center, San Antonio, TX
3 Department of Medicine (Pulmonary Division), 3551 Roger Brooke Drive, JBSA Ft Sam Houston, TX 78234, Brooke Army Medical Center, San Antonio, TX

Abstract:
Our objective was to determine the accuracy of split-night polysomnography (SN-PSG) in a cohort of active duty service members (ADSMs). Retrospective review of ADSMs undergoing full-night diagnostic polysomnography (FN-PSG). FN-PSG data were processed to obtain partial-night data for the first 2 and 3-hours of recording. OSA severity was determined by calculating the AHI of each subject's FN-PSG and SN-PSG. 300 patients, 79% male, with a mean age 37.6±8.4 years, and mean BMI of 28.5±3.3 kg/m^2. 112 patients (37%) would have qualified for a SN-PSG, of which 94 (84%) were appropriately classified and 18 patients (16%) were misclassified. In the relatively young, non-obese ADSM population, the majority did not qualify for a SN-PSG. The 3-hour SN-PSG accurately determined OSA severity in those with moderate-severe OSA; however, some patients with mild OSA would have been misclassified which can result in unnecessary duty limitations. A SN-PSG may not be ideal for this population.

Keywords: Split-Night Polysomnograms, Full-Night Polysomnograms, High-Risk Professions, Obstructive Sleep Apnea, Military Personnel, Active Duty Service Members

Total Words: 2209
Number of References: 18

The authors above declare that there is no conflict of interest.

Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense of its Components.

Introduction:

Untreated OSA has been implicated in innumerable occupational accidents, especially in high-risk professions such as commercial truck drivers, pilots, firefighters, and police officers (Federal Aviation Administration 2016; Barger 2015; Sassani 2004). Additionally, untreated OSA can result in medical-related absences from work or even career termination. Thus, an accurate diagnosis in these high-risk professions is essential. Split-night polysomnography (SN-PSG) is currently utilized in many sleep labs for the diagnosis of OSA, to include commercial motor vehicle drivers (Colvin 2016), aviators (Federal Aviation Administration 2017) and active duty service members (ADSM) (Army 2016). However, it is unknown if SN-PSGs accurately classify the severity of sleep disordered breathing of personnel in these high-risk occupations.

Most studies in general populations suggest that SN-PSGs are accurate for assessing OSA severity (Kim 2015; Chou 2011; Khawaja 2010; Sanders 1991). For example, Khawaja et al. assessed 114 consecutive full-night diagnostic polysomnographies (FN-PSGs) and found the apnea-hypopnea index (AHI) from the first 2 and 3 hours correlated with FN-PSG AHI (Khawaja 2010). However, ADSMs represent a population of high-risk professionals within which the accuracy of SN-PSGs has not been validated (Rogers 2016; J 2017). OSA carries implications for the performance of their military duties and careers; specifically, those with an AHI $\geq$ 15/hour are not deployable without a waiver and can be discharged from military service if not effectively treated. Our hypothesis was that SN-PSGs would accurately diagnose OSA severity when compared to FN-PSG (Kapur 2017).

Participants and Methods:

Study Design

We conducted a retrospective review of 300 consecutive patients who underwent a diagnostic in-lab FN-PSG. All participants were ADSMs referred to a single military sleep disorder center for evaluation of sleep disordered breathing and underwent a FN-PSG. Patients with central sleep apnea and those who did not sleep more than three hours of total sleep time were excluded. The protocol was approved by our institution's Department of Clinical Investigation (Protocol #FWH20160091E). No external funding was utilized to complete this study.

Measured Variables

Baseline demographic and clinically-relevant data were recorded, to include age, gender, and BMI. All FN-PSGs were performed in accordance with American Academy of Sleep Medicine (AASM) standards for Level 1 PSG within an AASM accredited lab (Embla Systems, Sandman Version 9.3). Studies were manually scored by registered polysomnographic technologists and interpreted by board certified sleep medicine physicians utilizing the 2012 AASM scoring guidelines (Berry 2012). Hypopneas were scored as a 30% drop in the nasal pressure from baseline for 10 seconds and associated with either an arousal or drop in oxygen saturation by 3% (Berry 2012). Each patient's AHI was based on this study. Other polysomnographic variables, to include sleep onset latency, rapid eye movement onset latency, total sleep time, sleep efficiency, wake time after sleep onset, sleep stages (N1, N2, N3, REM), arousal index (AI), apnea-hypopnea index (AHI) during REM, AHI during non-REM, number of minutes with spO2 <89%, and oxygen saturation nadir were analyzed.

Calculated Split-Night Apnea-Hypopnea Index

The AASM guidelines for SN-PSGs state that this test is appropriate if AHI ≥15/hour is observed during a minimum of 2 hours of recording time on the PSG and at least 3 hours are available for CPAP titration (Berry 2016). If patients demonstrated an AHI >15/hour in the first 2 hours of the PSG based on their FN-PSG, their data were processed to obtain partial-night data for the subsequent 2-hours (SN-PSG2) and 3-hours (SN-PSG3).

Statistics

Means and standard deviations were used as summary statistics for continuous variables and were analyzed using Student's t-test and ANOVA or Wilcoxon's Test, whichever most appropriate. Categorical data was summarized using percentages and analyzed utilizing Chi-Squared analysis. Paired t-tests were performed to determine if there was an overall bias in comparing sleep metrics across the 3 trials. All statistical analysis was performed using JMP v12.0. Statistical significance was established as p-values <0.05.

Results:

A total of 300 ADSMs were included in the analysis. Within our cohort, 79% were male with a mean age of 37.6±8.4 years and mean BMI of 28.5±3.3 kg/m^2. Of the 300 patients, 72 (24%) did not meet the criteria for OSA (AHI <5/hour), 122 (41%) were diagnosed with mild OSA (AHI 5-14.9/hour), 57 (19%) with moderate OSA (AHI 15-29.9/hour), and 49 (16%) with severe OSA (AHI ≥30/hour).

The SN-PSG2 showed a statistically significant increase in AHI when compared to the FN-PSG (17.6±17.6 vs 16.2±17.2; p-value 0.029), although this finding was not clinically significant. The SN-PSG3 demonstrated no significant difference in AHI (16.7±18.9 vs 16.2±17.2; p-value 0.192) when compared with FN-PSG and was positively correlated with FN-PSG AHI (Figure 1; r=0.92; p-value=0.192). Additionally, in the SN-PSG3, a modest difference in O2 nadir (86.9±5.7 vs. 88.7±5.0; p-value <0.001) and sleep efficiency (85.2±10.3 vs 81.4±16.0; p-value <0.0001) were observed. As expected, there was increased percent REM sleep in FN-PSG compared to SN-PSG2 and SN-PSG3 (14.7±7.2 vs 5.3±7.7 and 7.6±7.6; p-value <0.001 and <0.001, respectively).

There were significant demographic differences between those that qualified for SN-PSG3 and those that did not qualify, including more males (91% vs 72%) and older age (40.8 vs 35.7), (see Table 1). Of our cohort, 112 patients (37%) would have qualified for a SN-PSG based upon the first 3-hour recording (Figure 2). Of those patients, 94 (84%) were appropriately classified as either moderate (47%) or severe (53%) OSA. Of the 18 patients (16%) misclassified, all were classified as moderate OSA based on SN-PSG3, but had mild OSA on FN-PSG. Differences between those misclassified and those who qualified for SN-PSG3 include lower weight (BMI 26.9±4.0 vs 29.0±4.2; p-value 0.0153) and lower AI (28.1±8.8 vs 39.5±21.9; p-value 0.0005).

Discussion:

Although the majority of patients in our study did not qualify for SN-PSG, in those that did qualify, we found good overall correlation with OSA severity between FN-PSG and SN-PSG3. This is consistent with the study by Sander et al. (1991). When comparing baseline demographics between those that qualified for SN-PSG3 versus not qualifying, there were various differences to include a larger percentage of older males in the qualified group which reflects known risk factors for OSA.

Interestingly, all 18 of the patients who were misclassified with moderate OSA by SN-PSG3 were classified as mild OSA by FN-PSG. In those that were misclassified, there was a higher proportion of males, lower BMIs and lower arousal indexes. These misclassifications were an unexpected finding based upon the existing literature. In a study by Fanfulla et al. analyzing 29 consecutive SN-PSGs by calculating the AHI of the first half of the night and comparing it to the FN-PSG, a significant difference was observed in the mean AHI (33/hour vs 40/hour; p-value <0.01) (Fanfulla 1997). This underestimation by SN-PSG was hypothesized to be caused by an increased REM and/or supine sleep typically present in the second half of the PSG (Rogers 2016). Within our cohort, while the percentage of REM sleep was higher in the FN-PSG vs SN-PSG3, there was no difference in the AHI between FN and SN-PSG3. However, the SN-PSG2 did have a higher overall AHI than the FN-PSG. One possible explanation for this unexpected finding is the high prevalence of the low arousal threshold (low ArTH) observed among ADSMs (Smith 2017). In REM sleep, the ventilatory response to chemical and mechanical respiratory loads is attenuated. In a population whose sleep-related breathing events are heavily influenced by the low ArTH, there may paradoxically be a relative respiratory stabilization during REM, leading to slightly lower overall AHI in the FN-PSG (Eckert 2007).

Our study has several potential limitations. First, our results reflect observations from a retrospective collection of available data rather than a prospective,trial. As such, our study design may limit the validity of our findings. However, we included consecutive patients, which minimizes the potential for bias. Likewise, our cohort was limited to an ADSM population who tend to be younger, have lower BMIs, and less cardiovascular comorbidities than civilian-counterparts with OSA. Thus, our findings may be limited to only similar populations.

Conclusion:

Within a cohort of ADSMs undergoing polysomnography, our study assessed the diagnostic accuracy of SN-PSGs. We observed that SN-PSG accurately determined moderate or severe OSA severity when the qualifications were met for SN-PSG testing. These results are consistent with multiple prior studies which revealed good overall agreement between SN-PSGs and FN-PSGs in determining the AHI (Kim 2015; Chou 2011; Khawaja 2010; Sanders 1991; Rogers 2016). Within our cohort, the 3-hour protocol was more accurate than the 2-hour. However, in patients with mild OSA, there was a potential to misclassify their OSA severity as moderate disease. While this does not affect treatment per se, this misclassification can impact their military career. The use of split night polysomnography in the military and similar high risk occupations requires further study.

References:

Army, U.S., *Army Regulation 40-501: Medical Services Standards of Medical Fitness*. 2016: Washington, DC. p. 152.

Barger, L.K., et al., *Common sleep disorders increase risk of motor vehicle crashes and adverse health outcomes in firefighters.* J Clin Sleep Med, 2015. **11**(3): p. 233-4

Berry, R.B., 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): p. 597-619.

Berry, R.B., Brooks, R., Gamaldo, C.E. et al, American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and asociated events: rules, terminology and technical specifications, version 2.3. 2016, American Academy of Sleep Medicine: IL.

Chou, K.T., et al., The minimum period of polysomnography required to confirm a diagnosis of severe obstructive sleep apnoea. Respirology, 2011. 16(7): p. 1096-102.

Colvin, L.J. and N.A. Collop, *Commercial Motor Vehicle Driver Obstructive Sleep Apnea Screening and Treatment in the United States: An Update and Recommendation Overview.* J Clin Sleep Med, 2016. **12**(1): p. 113-25.

Eckert DJ, Jordan AS, Merchia P, Malhotra A. Central sleep apnea: Pathophysiology and treatment. Chest. 2007 Feb;131(2):595-607.

Fanfulla, F., et al., Obstructive sleep apnoea syndrome: is the "half-night polysomnography" an adequate method for evaluating sleep profile and respiratory events? Eur Respir J, 1997. 10(8): p. 1725-9.

Guide For Aviation Medical Examiners, F.A. Administration, Editor. 2017. p. 463.

J, A.C., J.J. Knapik, and H.R. Lieberman, Trends and factors associated with insomnia and sleep apnea in all United States military service members from 2005 to 2014. 2017. 26(5): p. 665-670.

Kapur, V.K., 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): p. 479-504.

Khawaja, I.S., et al., Diagnostic accuracy of split-night polysomnograms. J Clin Sleep Med, 2010. 6(4): p. 357-62.

Kim, D.K., et al., Rethinking AASM guideline for split-night polysomnography in Asian patients with obstructive sleep apnea. Sleep Breath, 2015. 19(4): p. 1273-7.

Obstructive Sleep Apnea (OSA): Overview for the Aerospace Community, A.M.E. Division, Editor. 2016, Federal Aviation Administration Civil Aerospace Medical Institute Oklahoma City, OK.

Rogers, A.E.S., Shauna; Hunt, Devin J.; Oh, Gi-Taik; Clark, Leslie L., Obstructive Sleep Apnea and Associated Attrition, Active Component, U.S. Armed Forces, January 2004–May 2016, in Medical Surveillance Monthly Report. 2016. p. 24.

Sanders, M.H., et al., Diagnosis of sleep-disordered breathing by half-night polysomnography. Am Rev Respir Dis, 1991. 144(6): p. 1256-61.

Sassani, A., et al., *Reducing motor-vehicle collisions, costs, and fatalities by treating obstructive sleep apnea syndrome.* Sleep, 2004. **27**(3): p. 453-8.

Smith PR, Sheikh KL, Costan-Toth C, Forsthoefel D, Bridges E, Andrada TF, Holley AB. Eszopiclone and Zolpidem Do Not Affect the Prevalence of the Low Arousal Threshold Phenotype. Journal of Clinical Sleep Medicine. 2017 Jan 15;13(1):115-119.