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Observational Study

High Risk for Obstructive Sleep Apnea and Risk of Hypertension in Military Personnel: The CHIEF Sleep Study

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Abstract

BACKGROUND

Background: Epidemiological studies have revealed an association between obstructive sleep apnea (OSA) and hypertension in the general population, while the association in military personnel was rarely investigated.

AIM

To examine the association between high risk for OSA and hypertension by phenotypes in military young adults.

METHODS

A total of 746 military personnel, aged 27.9 years, were included in the cardiorespiratory fitness and health in armed forces (CHIEF)-sleep study in Taiwan in 2020. Antihypertensive medications were not used by the subjects. High risk for OSA was assessed using the Berlin Questionnaire. Hypertension was defined using the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) and the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines. The cutoff levels of

systolic and diastolic blood pressure (SBP and DBP) for the 2017 ACC/AHA- and JNC 7-based guidelines were 130/140 mmHg and 80/90 mmHg, respectively. Hypertension phenotypes included isolated systolic and diastolic hypertension (ISH, high SBP only and IDH, high DBP only) and combined hypertension (both high SBP and DBP). Multivariable logistic regression analysis with adjustment for demographics, lifestyle and metabolic biomarkers.

RESULTS

The prevalence of high risk for OSA, JNC 7-based hypertension and 2017 ACC/AHA-based hypertension were 8.0%, 5.2% and 22.0%, respectively. Those with a high risk for OSA had a higher probability of JNC 7-based overall and combined hypertension (odds ratios (ORs) and 95% confidence intervals: 2.82 (1.07, 7.42) and 7.54 (1.10, 51.54), although the probabilities of ISH and IDH were unaffected by a high risk for OSA (ORs: 1.96 and 2.35, respectively, both p >0.05). In contrast, no associations for any hypertension phenotypes were found according to the 2017 ACC/AHA criteria.

CONCLUSION

A high risk for OSA was associated with severe hypertension and combined hypertension among Asian military young adults.

INTRODUCTION

Obstructive sleep apnea (OSA) has the potential to engender grave adverse consequences, notably an amplified vulnerability to cardiovascular diseases and neurocognitive morbidities [1, 2]. OSA is characterized by recurrent episodes of respiratory airflow cessation related to upper-airway collapse during sleep, leading to decreased oxygen saturation [3]. A recent systematic review noted the dearth of data regarding the prevalence of OSA in the Asian population [4]. Epidemiological surveys have shown a significant association between OSA and hypertension in both general

population samples and clinic-based cohorts [1, 5-8]. Hypertension represents a prominent risk factor for cardiovascular diseases and all-cause mortality [9]. Reports indicate that the prevalence of hypertension in Asia is comparable to that observed in Western countries; however, there exists a notable disparity in the awareness of hypertension, with significantly lower levels in Asian populations compared to their Western counterparts [10]. There may be more individuals with undiagnosed hypertension in the Asian population with certain sleep-related disorders.

However, insufficient emphasis has been placed on examining the associations between OSA and hypertension in young adults. As the relationship between OSA and hypertension is characterized by its intricate and multifaceted nature, OSA and obesity usually coexist and exhibit overlapping pathophysiological mechanisms [11]. Epidemiological surveys provide evidence supporting the associations between obesity and hypertension, as well as OSA and obesity [3, 5, 12, 13]. To our knowledge, the prevalence of hypertension in young adults is much lower than that in middle-aged and older individuals. Whether obesity is a moderator between OSA and hypertension remains unclear in young adults.

The purpose of this study was to determine the prevalence of high OSA risk and its association of hypertension with various phenotypes in military young personnel who have rarely been investigated before in Taiwan. In addition, the roles of age, central obesity and night sentry duty in modifying the association between OSA and hypertension were examined.

MATERIALS AND METHODS
Study population

In the ancillary Cardiorespiratory Fitness and Health in Armed Forces (CHIEF) sleep study implemented in Taiwan in 2020, a sample of 746 military personnel, with an average age of 27.9 years, was recruited. Significantly, individuals with

antihypertensive medication use were intentionally excluded from the study protocol. The assessment of the risk for OSA was undertaken using the well-validated Berlin Questionnaire [14, 15]. The study design was approved by the Mennonite Christian Hospital Ethics Committee (No. 16-05-008) in Hualien, Taiwan, and was performed in accordance with the Helsinki Declaration, as revised in 2013. All participants were informed of the nature of the study and gave written informed consent.

Individuals at high risk for OSA

Participants at high risk for OSA in this investigation were defined according to the Berlin Questionnaire [14, 15], which consists of three distinct sections. The first section is used to evaluate snoring behavior, the second is used to evaluate fatigue, tiredness, and daytime sleepiness symptoms, and the third is used to investigate the presence of obesity or hypertension. In Sections 1 and 2, a persistent symptom reported more than 3-4 times per week is indicative of high risk for OSA. In Section 3, a historical diagnosis of hypertension or a body mass index (BMI) ≥30.0 kg/m^2 is considered as criteria suggestive of high risk for OSA. Individuals are classified as high risk for OSA if they meet the high-risk benchmarks in at least two of the questionnaire's three sections.

Definitions of hypertension and phenotypes

Hypertension was defined based on the diagnostic guidelines included in both the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) [9] and the recommendations from the American College of Cardiology (ACC) and American Heart Association (AHA) in 2017 [16], thereby ensuring a uniform and methodical approach to categorization and subsequent data analysis. In this study, the resting blood pressure (BP) of each participant was measured once over the right upper arm in a sitting position by an automatic device through the oscillometric method (FT201 Parama-Tech Co., Ltd, Fukuoka, Japan) [17-20]. The cutoff values for systolic and diastolic BP for hypertension, as specified by the 2017 ACC/AHA and JNC 7 guidelines, were established at 130/140

mmHg and 80/90 mmHg, respectively. Within the context of these guidelines, hypertension phenotypes were classified as combined hypertension (marked by elevated levels of both SBP and DBP), isolated systolic hypertension (ISH, identified by elevated SBP only), and isolated diastolic hypertension (IDH, identified by elevated DBP only).

Confounding factors for OSA and hypertension

Participants were asked about their smoking and alcohol consumption status (active vs. former/never) [21, 22] and cardiorespiratory fitness (assessed by 3000-m run performance in 2020) [23-25]. Sentry duty at night was evaluated by times per month. Abdominal obesity was defined as a waist circumference ≥90 cm for men and ≥80 cm for women [26]. Fasting blood samples were obtained to measure metabolic risk factors, i.e., a lipid panel test, fasting glucose and serum uric acid [27-30].

Statistical analysis

Statistical evaluations were executed utilizing SPSS software for Windows (SPSS Inc., Chicago, IL, USA). To compare subjects with high risk for OSA and those without, the chi-square test was used for categorical data, and analysis of variance (ANOVA) was used for continuous data. Multiple logistic regression analysis was used to determine the associations between high risk for OSA and hypertension phenotypes, i.e., combined hypertension, ISH and IDH. Model 1 was the unadjusted model. Model 2 was adjusted for age, sex, smoking, alcohol intake and 3000-m run time. Model 3 was additionally adjusted for total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides and uric acid. Model 4 was further adjusted for BMI. Subgroup analysis was performed based on age (≥30 years vs. <30 years), abdominal obesity status and night sentry status. The covariates in the models were selected due to their potential as risk factors for both hypertension and OSA and a p value <0.20 between the two groups. A p value of <0.05 was considered indicative of statistical significance.

RESULTS

Table 1 shows the clinical profiles of participants with high risk for OSA (*n* = 60, 8.0%) and those without (*n* = 686, 92%), based on the responses to the Berlin Questionnaire. The mean age of the high-risk OSA group was significantly higher than that of their counterparts (30.45 years vs. 27.67 years). The high-risk OSA group had higher BMI, waist circumference systolic and diastolic BP levels and ran slower than their counterparts. The prevalence of JNC-7-based hypertension was higher in the high risk for OSA group, whereas no difference between the high risk for OSA group and the counterparts was observed. In addition, the prevalence of all hypertension phenotypes was higher in the high-risk OSA group, while only combined hypertension was higher in the high-risk OSA group. The high-risk OSA group had a lower high-density lipoprotein level and higher serum triglycerides and uric acid levels than their counterparts.

Table 2 demonstrates the results of multivariable logistic regression analyses of high risk of OSA for various hypertension phenotypes according to the JNC 7-based guidelines. In Model 1, the odds ratio (OR) of all hypertension phenotypes was greater than 2.75, in which only overall (ISH, IDH and combined) and combined hypertension were significantly associated with a high risk for OSA. The associations of overall and combined hypertension with high risk for OSA remained significant with adjustments for the potential covariates in Models 2-4 [ORs: 2.82 (95% confidence interval (CI): 1.07-7.46) and 7.54 (95%CI: 1.10-51.54), respectively, in Model 4].

Table 3 shows the results of multivariable logistic regression analyses of high risk for OSA for various hypertension phenotypes using the 2017 ACC/AHA-based guidelines. Combined hypertension was the only phenotype significantly associated with a high risk for OSA [OR: 2.53 (95%CI: 1.10-5.79)], whereas there were no associations for ISH,

IDH and overall hypertension (ORs: 1.06, 0.67 and 1.38, respectively). However, the associations for all hypertension phenotypes were not significant in Models 2-4.

Table 4 reveals the results of the associations of JNC 7- and 2017 ACC/AHA-based hypertension with high risk for OSA in subgroup analyses based on age, abdominal obesity and night sentry duty status. In the subgroup analysis based on age, the association of high risk for OSA with JNC 7-based hypertension was significant in participants aged ≥30 years [OR: 4.55 (95%CI: 1.50-13.78)] but not significant in those aged <30 years (OR: 2.07). In the subgroup analysis by abdominal obesity status, the association between high risk for OSA and JNC 7-based hypertension was significant in those without abdominal obesity [OR: 5.83 (95%CI: 1.42-23.95)] but not significant in those with abdominal obesity (OR: 2.01). In the subgroup analysis by the presence of night sentry duty, the association between high risk for OSA and JNC 7-based hypertension was significant in those free of night sentry duty [OR: 5.28 (95%CI: 1.35-20.71)] but not significant in those having at least one occurrence of night sentry duty per month (OR: 2.73). Notably, the association between high risk for OSA and 2017 ACC/AHA-based hypertension was not significant in any subgroup analyses based on age, abdominal obesity status and night sentry duty status.

DISCUSSION

The principal findings in this study were that young individuals with a high risk for OSA, as determined by the Berlin Questionnaire, had a higher probability of having hypertension based on the JNC 7 guidelines or stage-2 hypertension based on the 2017 ACC/AHA guidelines but not mild hypertension according to the 2017 ACC/AHA guidelines. In addition, we found that combined hypertension was the most commonly encountered hypertension phenotype associated with a high risk for OSA among young military adults.

In this study, young individuals identified as high risk for OSA exhibited a higher prevalence of traditional cardiovascular risk factors in addition to elevated BP, such as abdominal obesity and dyslipidemia [17-19]. The clinical characteristics of our study population were in line with the general consensus in the literature regarding the comorbidities of OSA and cardiovascular diseases among adults, regardless of age [31]. The Berlin Questionnaire has been commonly used to define young adults at high risk for OSA and has been validated in many studies (31, 32). The validity has also been investigated in a Korean study of young military subjects by Lee et al. that included a similar age group cohort. [31]. In that Korean study [31], the prevalence of high OSA risk (8.1%) was very close to our finding (8.0%), and Lee et al found that in a Korean military sample, 90% of these young subjects with a high risk for OSA by the Berlin questionnaire had an apnea-hypopnea index (AHI) ≥5 events/hour. Similarly, the prevalence of high OSA risk in a sample of young Thai adults was 6.3% [32], which was also close to our finding (8.0%).

The association between high risk for OSA and JNC 7-based hypertension, also corresponding to stage-2 hypertension on the basis of the 2017 ACC/AHA guidelines, in young adults has been found consistently in the Thailand study mentioned above [32]. The results of the Thailand study [32] were also consistent with our study in some aspects, including that the association strength of high risk for OSA was stronger for JNC 7-based hypertension than an elevated BP level, defined as systolic BP ≥120 mmHg or diastolic BP ≥80 mmHg, with adjustments for demographic and lifestyle factors (ORs: 2.55 and 2.38, respectively). In addition, the strength of the association of high risk for OSA was greater for ISH than IDH (ORs: 3.03 and 2.78, respectively). In contrast, the association of high risk for OSA with combined hypertension as the lowest among the phenotypes in the Thailand study [32] was inconsistent with our study findings. The reason for the differences in the association between high risk for OSA and various hypertension phenotypes was unclear but is possibly because our study subjects were recruited from a specific sample of military personnel who were at a greater stress and

workload than the general population. Mechanisms for more severe hypertension and uncontrolled BP levels have been postulated by activation of the neurohormonal system and increased psychological stress, which are related to intermittent nocturnal hypoxemia [33, 34].

In previous studies, obese and elderly individuals with OSA were found to be at higher risk of hypertension [32, 35]. Obesity has been recognized as a crucial risk factor for OSA, possibly due to obesity related to structural changes, *e.g.*, long uvula, low lying palate and tongue indentation in a supine position during sleep [31]. In the general population of young adults [32], obesity was found to be a mediator between a high risk for OSA and hypertension. However, our study showed inconsistent results that military subjects with younger ages and those without abdominal obesity had a greater strength of the associations compared to their older and obese counterparts, despite both having a nonsignificant p value for interaction (data not shown). The inconsistent findings in our study may be reasoned by the possibility of the existence of substantial confounders, *e.g.*, night sentry duty in military subjects, which may cause sleep disturbance and result in an increased risk of hypertension. In addition, in Asian adults, OSA is not uncommon in those without obesity who may have a relatively flat face and oral cavity anatomical adaptations to long-term supine sleep since childhood [36], possibly reducing the importance of obesity in the association between a high risk for OSA and hypertension.

In this study, there were some limitations, *e.g.*, the cross-sectional nature, which precludes establishing causality, and the self-report questionnaires, which may be subject to bias. Additionally, our sample was restricted to military subjects who may have regular on-demand work at night, which may confound sleep quality, limiting the generalizability of our study findings. Finally, an objective assessment of OSA, such as polysomnography, was lacking, and some subjects may have been misclassified, leading to bias. Polysomnography should be used to define OSA for its relationship

with hypertension risk in future studies. In contrast, our study had some strengths. Our study population was obtained from the military and had similar living circumstances, *e.g.*, diet and training status, possibly minimizing the naïve bias. Second, since our health examinations were comprehensive, the adjustments in the models were believed to be accurate.

CONCLUSION

Our findings suggest that in Asian military young adults, high risk for OSA, as assessed by the Berlin Questionnaire, accounted for 8.0 % of the population and was associated with a higher probability of uncontrolled BP levels, defined by the JNC 7 criterion. Notably, the association was not related to obesity or older age. As the specific population of Asian military subjects we studied, how night activity confounded the association in the military requires further study.

ARTICLE HIGHLIGHTS

Research background

Previous studies have revealed an association between obstructive sleep apnea (OSA) and hypertension in the general population, whereas the association in military personnel was rarely investigated.

Research motivation

Military personnel have some risk factors for both OSA and hypertension, *e.g.* night duty which are rarely seen in the general population.

Research objectives

To investigate the association between high risk for OSA and hypertension by phenotypes in military young adults.

Research methods

A total of 746 military personnel, aged 27.9 years, were included in the cardiorespiratory fitness and health in armed forces (CHIEF)-sleep study in Taiwan in 2020. Antihypertensive medications were not used by the subjects. High risk for OSA was assessed using the Berlin Questionnaire. Hypertension was defined using the 7th Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) and the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines. The cutoff levels of systolic and diastolic blood pressure (SBP and DBP) for the 2017 ACC/AHA- and JNC 7-based guidelines were 130/140 mmHg and 80/90 mmHg, respectively. Hypertension phenotypes included isolated systolic and diastolic hypertension (ISH, high SBP only and IDH, high DBP only) and combined hypertension (both high SBP and DBP). Multivariable logistic regression analysis with adjustment for demographics, lifestyle and metabolic biomarkers.

Research results

The prevalence of high risk for OSA, JNC 7-based hypertension and 2017 ACC/AHA-based hypertension were 8.0%, 5.2% and 22.0%, respectively. Those with a high risk for OSA had a higher probability of JNC 7-based overall and combined hypertension (odds ratios (ORs) and 95% confidence intervals: 2.82 (1.07, 7.42) and 7.54 (1.10, 51.54), although the probabilities of ISH and IDH were unaffected by a high risk for OSA (ORs: 1.96 and 2.35, respectively, both p >0.05). In contrast, no associations for any hypertension phenotypes were found according to the 2017 ACC/AHA criteria.

Research conclusions

High risk for OSA, as assessed by the Berlin Questionnaire, accounted for 8.0 % of the military population and was associated with a higher probability of uncontrolled BP levels, defined by the JNC 7 criterion. Notably, the association was not related to obesity or older age.

Research perspectives

For military personnel, polysomnography should be used to define OSA for its relationship with hypertension risk in future studies. In addition, night activity confounded the association in the military personnel requires further study.

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