

Neck Circumference is Associated with Incidence of Angina Pectoris in a Large Community-Based Population

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Background: Previous studies have found that neck circumference (NC) is associated with cardiovascular disease risk factors. This study investigated the relationship between NC and the incidence of angina pectoris (AP).

Methods: Altogether 4821 participants (2212 males and 2609 females) from the Sleep Heart Health Study (SHHS) with a mean age of 63.4±11.0 years were selected in this study. Anthropometric measurements, including NC, waist circumference (WC), hip circumference (HC), and body mass index (BMI), were collected at baseline. AP was defined as the first occurrence between baseline and 2011. Linear and logistic regression analysis was used to explore the association between NC and incidences of AP.

Results: There was a significant difference in NC between AP and controls in both male (41.1±3.1 cm vs 40.3±3.2 cm; p<0.001) and female (35.2±3.1 cm vs 34.9±2.9 cm; p=0.006). Multivariable linear regression analysis showed that NC (every cm increase) was independently associated with the incidence of AP in both male (odds ratio [OR] 1.067; 95% confidence interval [CI] 1.035–1.100; p<0.001) and female (OR 1.067; 95% CI 1.035–1.101; p<0.001).

Conclusion: NC was significantly associated with the incidence of AP in both male and female. The role of NC in the incidence of AP is worthy of further investigation.

Keywords: angina pectoris, neck circumference, SHHS, obesity, community-based population

Introduction

In recent years, the number of people living with overweight issues and obesity has been increasing around the world.¹ In 2015, a total of 107.7 million children and 603.7 million adults were considered obese.² Common causes of obesity include poor eating habits, inactive lifestyle, sleep quality, genetics, endocrine system functions, psychological factors, and drugs.³ Obesity has become a medical condition that may further cause other diseases and health problems.⁴ A lot of studies have shown that obesity is a risk factor for cardiovascular disease (CVD), hypertension, diabetes mellitus, metabolic syndrome, and cancer.^{5–7} Anthropometric measurements, such as body mass index (BMI), waist circumference (WC), and hip circumference (HC), are typically used as indicators of body fat. Neck circumference (NC), which is correlated with the distribution of upper body subcutaneous adipose tissue, is also an anthropometric marker used to identify overweight and obese individuals.⁸ A previous study demonstrated that NC positively correlated

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with BMI and WC.⁹ In addition, NC was found to be more similar to visceral fat, which is more closely related to cardiovascular risk than subcutaneous fat.¹⁰ An increased NC was also found to be associated with cardiovascular risk factors, such as insulin resistance and metabolic syndrome.¹¹ However, there is no evidence regarding the association between NC and the incidence of angina pectoris (AP). In the present study, we explore the role of NC and the incidence of AP using a large community-based population from the Sleep Heart Health Study (SHHS).

Materials and Methods

Study Population

All the participants in this study were selected from the SHHS (ClinicalTrials.gov Identifier: NCT00005275), which consisted of existing epidemiological studies (including the Atherosclerosis Risk in Communities Study, the Cardiovascular Health Study, the Framingham Offspring and Omni Study, the Strong Heart Study, Tucson Epidemiological Study of Obstructive Lung Disease, the cohort studies of respiratory disease in Tucson, and cohort studies of hypertension in New York). Details of the SHHS design and parent studies have been reported previously.¹² Participants who had missing data regarding AP or NC, or had a history of AP were excluded (Figure 1).

Anthropometric Measurements

BMI was calculated as weight in kilograms divided by the square of the height in meters. WC was measured at the midpoint halfway between the inferior costal margin and the iliac crest. HC was measured at the greatest protrusion of the buttocks. NC was measured with the subject upright and head positioned in the Frankfort Horizontal Plane. An

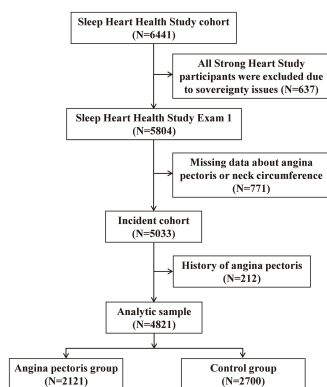


Figure 1 Flow diagram of participant selection.

inelastic tape measure was applied around the neck just inferior to the laryngeal prominence. In the present study, NC was further divided into quartiles in both male (quartile I: ≤ 38.5 cm; quartile II: 38.6 cm–40.5 cm; quartile III: 40.6 cm–42.7 cm; quartile IV: >42.7 cm) and female (quartile I: ≤ 33.0 cm; quartile II: 33.1 cm–35.0 cm; quartile III: 35.1 cm–37.0 cm; quartile IV: >37.0 cm).

AP incidences were extracted from discharge information at local hospitals according to cohort-specific protocols. The definition of AP was based on syndromes of coronary ischemia, ECG findings, exercises stress test, coronary angiography. AP was defined as the occurrence of the first episode during the average follow-up period of 11 years. The apnea-hypopnea index (AHI) was defined as all apnea and hypopnea episodes per hour of sleep accompanied by at least a 4% drop in oxygen saturation. The age, sex, race, education level, marital status, smoking status, alcohol use, prevalence of hypertension and diabetes, and polysomnography (PSG) data of participants were obtained from baseline examination of the SHHS.

Statistical Analysis

Independent sample *t*-tests and chi-square tests were performed to analyse the statistical difference in continuous variables and categorical variables, respectively. Univariate and multivariate logistic regression (or linear regression) analysis was used to analyse the association between anthropometric makers (NC, WC, HC, and BMI) and AP. After adjusting for age, sex, race, education level, marital status, smoking status, alcohol use, hypertension, diabetes mellitus, apnea hypopnea index (AHI), TC, HDL and TG, multivariable logistic regression (or linear regression) was performed to identify independent risk factors and to estimate the odds ratio (OR) and 95% confidence interval (CI). Interaction terms were also constructed between NC and AHI. P-values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS, version 24.0 (SPSS Inc., Chicago, IL).

Results

Participants' Characteristics

The characteristics of the participants with or without AP are shown in Table 1. In this study, 2212 males and 2609 females with a mean age of 63.4 ± 11.0 years were included. Individuals with AP were older, more likely to be married and of Caucasian descent in both male and female. Participants with AP also had longer education

experience, larger NC, WC, and HC, as well as higher BMI in both male and female. In addition, the correlation coefficients (Pearson's correlations) among different anthropometric measurements are showed in [Supplement Table 1](#).

NC and AP

NC in participants with AP was significantly larger than those without AP in male (41.1 ± 3.1 cm vs 40.3 ± 3.2 cm; $P < 0.001$) and female (35.2 ± 3.1 cm vs 34.9 ± 2.9 cm; $P = 0.006$). After adjusting for age, race, educational level, marital status, smoking status, alcohol use, hypertension, diabetes mellitus, AHI, TC, HDL and TG, NC (increased 1 cm) was positively associated with the incidence of AP in male (OR 1.067; 95% CI 1.035–1.100; $P < 0.001$) and female (OR 1.067; 95% CI 1.035–1.101; $P < 0.001$) ([Table 2](#)).

NC was further divided into quartiles in male and female. Participants in the fourth, third, and second quartile were more likely to have a higher incidence of AP than those in the first quartile in both male (53.8%, 49.6%, 46.2% vs 38.0%, respectively) and female (39.4%, 42.7%, 41.0% vs 44.1%, respectively) ([Table 3](#)). The incidence of AP stratified by BMI and AHI in different NC quartiles is shown in [Figure 2](#). Multivariable logistic regression showed that the fourth quartile (OR 1.818; 95% CI 1.397–2.366; $P < 0.001$), third quartile (OR 1.544; 95% CI 1.183–2.014; $P = 0.001$), and second quartile (OR 1.308; 95% CI 1.015–1.685; $P = 0.037$) of NC were risk factors for AP incidence when compared to the first quartile in males. Females in the fourth quartile of NC also had an increased risk of AP (OR 1.513; 95% CI 1.161–1.972; $P = 0.002$) ([Table 3](#)). We further explored the interactions between NC and AHI in the final multivariate logistic regression model. No significant interactions were found in these analyses.

BMI, WC, HC, and AP

We also investigated the relationship between BMI, WC, HC, and AP. Multivariate linear regression analysis revealed that BMI (OR 1.055; 95% CI 1.031–1.079; $P < 0.001$) and WC (OR 1.024; 95% CI 1.014–1.033; $P < 0.001$) were associated with AP incidence in male. In female, BMI (OR 1.054; 95% CI 1.037–1.072; $P < 0.001$), WC (OR 1.047; 95% CI 1.040–1.054; $P < 0.001$), and HC (OR 1.021; 95% CI 1.013–1.029; $P < 0.001$) were also closely related to the occurrence of AP ([Table 2](#)).

Discussion

Obesity is a complex disease and usually increases the risk of diabetes mellitus, hypertension, metabolic syndrome, CVD, sleep disorder breathing (SDB), and cancer.^{5–7,13} BMI, a measure based on height and weight, was used as an indicator for body fat. A BMI greater or equal to 30.0 kg/m^2 was defined as obese, while a BMI between 25.0 kg/m^2 and 29.9 kg/m^2 was defined as overweight. WC and HC were also used to evaluate subcutaneous fat. NC, a relatively novel method in identifying obesity, has been found to be a useful screening tool for cardiovascular risk.¹⁴ Compared to traditional anthropometric measures, such as BMI, WC, and HC, NC has been found to be more closely related to visceral fat, which is strongly associated with cardio-metabolic risks than subcutaneous fat.^{9,15} In addition, NC was less susceptible to the effects of meal and health conditions and could be measured easily in winter compared with WC and HC.¹⁴ However, there is little evidence about the relationship between NC and AP. In the present study, we investigated the association between NC and AP incidence using a large community-based population. Our results demonstrated that increased NC was a risk factor for the occurrence of AP in both male and female.

AP is a symptom of coronary heart disease and is usually caused by cardiac ischemia.^{16,17} Age, smoking, high blood pressure, hyperlipidemia, diabetes mellitus, history of coronary artery disease, stress, and sleeping habits are common AP risk factors. In addition, obesity is also a vital factor in the development of AP.¹⁸ Previous studies have shown that NC is associated with cardiovascular risk factors, such as obesity, systolic blood pressure, cholesterol, hyperuricemia, carotid intima-media thickness, and metabolic syndrome.^{11,19–22} Zhang et al also found that NC was correlated with heart failure in people without SDB.²³ In this study, we explored the role of NC in the incidence of AP and found that the fourth quartile of NC had a substantially higher proportion of participants with AP compared to those in the first quartile in both male and female. These results indicate that individuals with a large NC tended to have an increased risk of AP and that NC may be an essential anthropometric measurement for screening people with AP.

Many studies have shown that large NC was a predictor for SDB.²⁴ Moreover, SDB was also a risk factor for CVD.^{25,26} AHI may be a confounding factor

Table I Characteristics of the Study Subjects

Variables	Total (n=4821)	Men (n=2212)		P value	Women (n=2609)		P value
		Angina (n=1035)	Non-Angina (n=1177)		Angina (n=1086)	Non-Angina (n=1523)	
Age, years	63.4±11.0	64.5±7.1	62.2±12.9	<0.001	63.8±7.7	63.1±13.3	<0.001
Race, n (%)				<0.001			<0.001
White	4182 (86.7)	999 (96.5)	939 (79.8)	–	1040 (95.7)	1204 (79.1)	–
Black	316 (6.6)	29 (2.8)	99 (8.4)	–	42 (3.9)	146 (9.6)	–
Other	323 (6.7)	7 (0.7)	139 (11.8)	–	4 (0.4)	173 (11.4)	–
Education, n (%)				0.001			<0.001
≤15, years	2759 (63.1)	538 (52.4)	591 (59.9)	–	690 (63.8)	940 (73.7)	–
>15, years	1610 (36.9)	489 (47.6)	395 (40.1)	–	391 (36.2)	335 (26.3)	–
Marital Status, n (%)				<0.001			<0.001
Married	3778 (79.8)	954 (92.4)	980 (86.0)	–	867 (80.0)	977 (65.9)	–
Other	959 (20.2)	78 (7.6)	159 (14.0)	–	217 (20.0)	505 (34.1)	–
Smoking status, n (%)				0.008			0.590
Current smoker	478 (9.9)	98 (9.5)	136 (11.6)	–	109 (10.1)	135 (8.9)	–
Former smoker	2093 (43.5)	598 (57.9)	603 (51.3)	–	371 (34.2)	521 (34.3)	–
Never smoker	2240 (46.6)	337 (32.6)	436 (37.1)	–	604 (55.7)	863 (56.8)	–
Alcohol use, n (%)				0.200			0.731
At least 1 drink per day	1952 (43.4)	546 (52.9)	572 (55.8)	–	367 (33.8)	467 (34.6)	–
None	2543 (56.6)	487 (47.1)	454 (44.2)	–	718 (66.2)	884 (65.4)	–
Body mass index, n (%)				<0.001			0.001
≥30, kg/m ²	1489 (31.2)	357 (34.6)	329 (28.1)	–	379 (35.1)	424 (28.4)	–
25–29.9, kg/m ²	2024 (42.4)	501 (48.5)	563 (48.2)	–	390 (36.1)	570 (38.2)	–
18.5–24.9, kg/m ²	1262 (26.4)	175 (16.9)	277 (23.7)	–	311 (28.8)	499 (33.4)	–
Neck circumference, cm	37.6±4.2	41.1±3.1	40.3±3.2	<0.001	35.2±3.1	34.9±2.9	0.006
Waist circumference, cm	97.3±13.7	102.0±12.3	92.2±28.1	<0.001	98.1±14.5	91.2±14.8	<0.001
Hip circumference, cm	105.3±10.4	104.1±10.5	96.0±28.7	<0.001	107.4±11.2	105.5±11.9	<0.001
Hypertension, n (%)	1859 (38.6)	413 (39.9)	449 (38.1)	0.407	411 (37.8)	586 (38.5)	0.775
Diabetes mellitus, n (%)	326 (6.8)	84 (8.1)	87 (7.4)	0.525	71 (6.5)	84 (5.5)	0.276
AHI, n (%)				0.095			0.782
≥30.0, events/h	348 (7.2)	115 (11.1)	125 (10.6)	–	45 (4.1)	63 (4.1)	–
15.0–29.9, events/h	644 (13.4)	202 (19.5)	207 (17.6)	–	96 (8.8)	139 (9.1)	–
5.0–14.9, events/h	1457 (30.2)	370 (35.7)	389 (33.1)	–	302 (27.8)	396 (26.0)	–
<5.0, events/h	2372 (49.2)	348 (33.6)	456 (38.7)	–	643 (59.2)	925 (60.7)	–

(Continued)

Table 1 (Continued).

Variables	Total (n=4821)	Men (n=2212)		P value	Women (n=2609)		P value
		Angina (n=1035)	Non-Angina (n=1177)		Angina (n=1086)	Non-Angina (n=1523)	
SBP	125.2±18.2	124.1±17.3	127.9±17.1	<0.001	122.2±18.7	126.1±18.8	<0.001
DBP	72.4±10.8	72.0±9.9	75.8±11.5	<0.001	69.4±9.5	72.2±11.0	<0.001
TC	206.8±38.4	199.5±34.9	202.4±38.5	0.071	215.5±38.5	209.0±38.3	<0.001
HDL	50.7±15.8	43.7±12.8	43.9±11.4	0.771	58.2±17.8	55.4±14.5	<0.001
TG	151.4±100.6	147.1±98.1	165.4±115.7	<0.001	150.9±92.9	144.3±95.0	0.090

Notes: Results are presented as mean ± standard deviation or n (%). The P values represent the difference between two groups.

Abbreviations: AHI, apnea hypopnea index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

Table 2 ORs and 95% CIs for Neck Circumference Associated with Angina Pectoris in Male and Female

AP	Univariate Models		Multivariable Adjusted ^a		Multivariable Adjusted ^b	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Male (per 1 SD)						
Neck circumference	1.073 (1.044–1.102)	<0.001	1.067 (1.035–1.099)	<0.001	1.086 (1.051–1.121)	<0.001
Waist circumference	1.025 (1.017–1.033)	<0.001	1.023 (1.014–1.032)	0.001	1.031 (1.021–1.041)	<0.001
Hip circumference	1.011 (1.001–1.020)	0.031	1.007 (0.997–1.018)	0.181	1.014 (1.002–1.026)	0.020
BMI	1.045 (1.025–1.065)	<0.001	1.053 (1.031–1.076)	<0.001	1.070 (1.045–1.096)	<0.001
Female (per 1 SD)						
Neck circumference	1.037 (1.010–1.064)	0.006	1.062 (1.031–1.094)	<0.001	1.090 (1.054–1.127)	<0.001
Waist circumference	1.032 (1.027–1.038)	<0.001	1.043 (1.036–1.051)	<0.001	1.050 (1.042–1.058)	<0.001
Hip circumference	1.014 (1.007–1.021)	<0.001	1.019 (1.011–1.027)	<0.001	1.027 (1.018–1.035)	<0.001
BMI	1.028 (1.014–1.042)	<0.001	1.049 (1.033–1.066)	<0.001	1.067 (1.048–1.086)	<0.001

Notes: ^aAdjusted for age, race, education, marry status, smoking status, alcohol use, hypertension and diabetes mellitus. ^bAdjusted for a+ AHI, TC, HDL and TG.

Abbreviations: AHI, apnea hypopnea index; AP, angina pectoris; BMI, body mass index; 95% CI, 95% confidence interval; HDL, high-density lipoprotein; OR, odds ratio; TC, total cholesterol; TG, triglyceride; SD, standard deviation.

Table 3 ORs and 95% CIs for Neck Circumference Quartiles Associated with Angina Pectoris in Male and Female

AP			Multivariable Adjusted ^a		Multivariable Adjusted ^b	
	Persons (N)	Events, n (%)	OR (95% CI)	P	OR (95% CI)	P
Male (per 1 cm)						
Neck circumference	2212	1035 (46.8)				
Q4 (>42.7cm)	552	297 (53.8)	1.818 (1.397–2.366)	<0.001	2.096 (1.580–2.781)	<0.001
Q3 (40.6cm–42.7cm)	502	249 (49.6)	1.544 (1.183–2.014)	0.001	1.645 (1.246–2.170)	<0.001
Q2 (38.62cm–40.5cm)	595	275 (46.2)	1.308 (1.015–1.685)	0.038	1.346 (1.037–1.747)	0.026
Q1 (≤38.5cm)	563	214 (38.0)	1		1	
Female (per 1 cm)						
Neck circumference	2609	1086 (41.6)				
Q4 (>37.0cm)	522	230 (44.1)	1.473 (1.141–1.902)	0.003	1.741 (1.311–2.311)	<0.001
Q3 (35.1cm–37.0cm)	590	242 (41.0)	1.103 (0.869–1.400)	0.420	1.197 (0.927–1.546)	0.167
Q2 (33.1cm–35.0cm)	745	318 (42.7)	1.098 (0.879–1.372)	0.409	1.205 (0.953–1.525)	0.120
Q1 (≤33.0cm)	752	296 (39.4)	1		1	

Notes: ^aAdjusted for age, race, education, marry status, smoking status, alcohol use, hypertension and diabetes mellitus. ^bAdjusted for a+ AHI, TC, HDL and TG.

Abbreviations: AHI, apnea hypopnea index; AP, angina pectoris; 95% CI, 95% confidence interval; HDL, high-density lipoprotein; OR, odds ratio; TC, total cholesterol; TG, triglyceride.

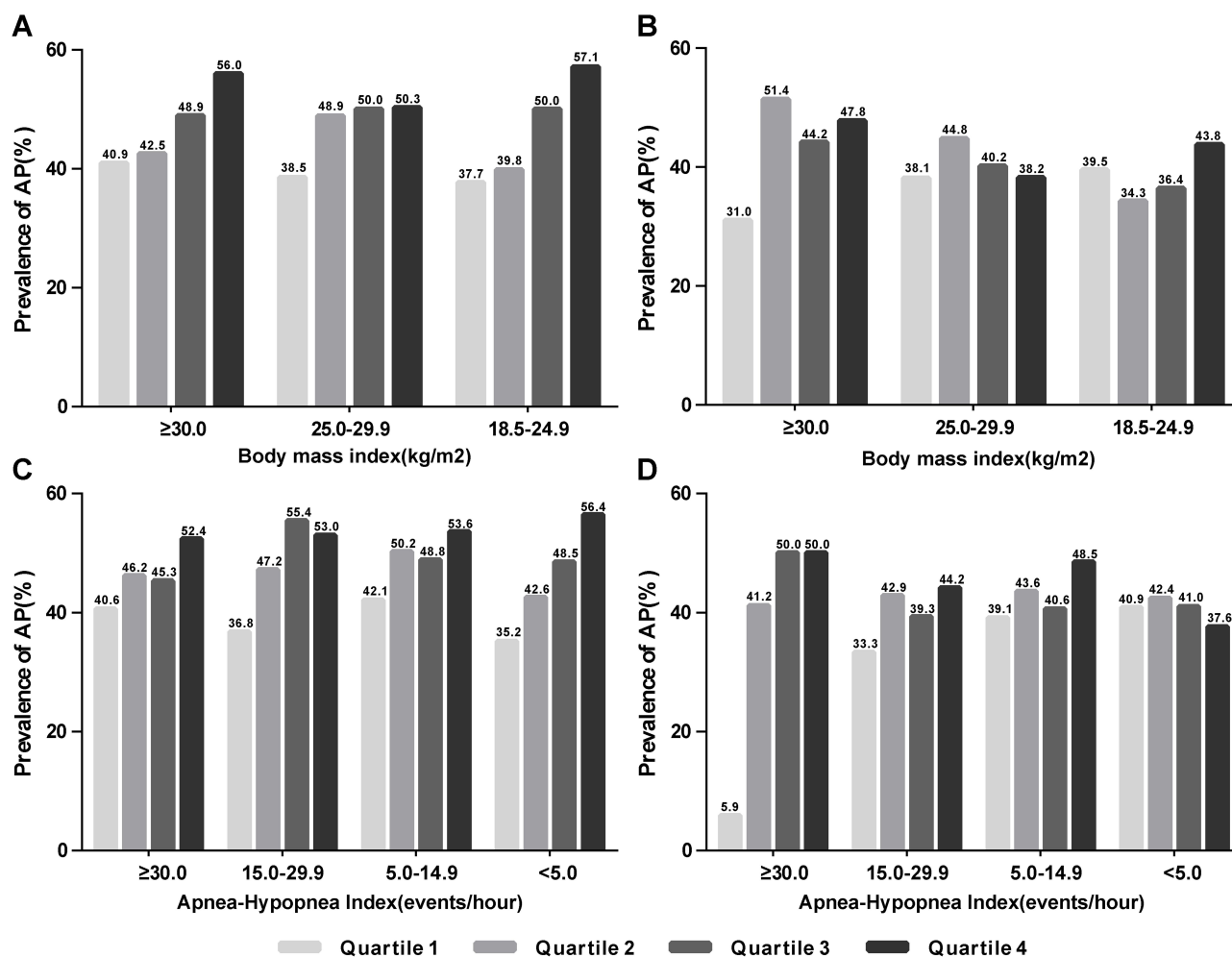


Figure 2 Distribution of AP incidence in NC quartiles stratified by BMI and AHI among males (quartile I: ≤38.5 cm; quartile II: 38.6 cm–40.5 cm; quartile III: 40.6 cm–42.7 cm; quartile IV: >42.7 cm) and females (quartile I: ≤33.0 cm; quartile II: 33.1 cm–35.0 cm; quartile III: 35.1 cm–37.0 cm; quartile IV: >37.0 cm). (A) stratified by BMI in Male; (B) stratified by BMI in Female; (C) stratified by AHI in Male; (D) stratified by AHI in Female.

Abbreviations: AHI, apnea hypopnea index; AP, angina pectoris; BMI, body mass index; NC, neck circumference.

between NC and CVD risk factors.¹⁰ In our study, we investigated the distribution of AP in different NC quartiles stratified by AHI. In male, there was a noticeably high incidence of AP in individuals with larger NC in each subgroup of AHI. This phenomenon is less pronounced in female than in male. We also adjusted AHI in the final multivariate logistic regression analysis. Interaction analysis was also performed between NC and AHI when investigating the role of NC in the incidence of AP. No significant interaction was found in these analyses. The results indicated that NC was significantly associated with AP incidence irrespective of AHI level. Besides, the incidence of AP in NC quartiles stratified by BMI was also different. Males with a large NC obviously tended to have a high incidence of AP in different BMI categories but the trend was not observed in females.

The mechanisms of NC in the incidence of AP remain unknown. However, upper body fat, usually evaluated by NC, is closely related to the level of systemic free fatty acids (FFA).^{10,27} Meanwhile, systemic FFA has been found to be associated with insulin resistance, oxidative stress, triglyceride production, and vascular injury, which are risk factors for CVD.²⁸ In addition, NC was also found to be an anthropometric marker for visceral fat, which was significantly correlated with cardiovascular risk.²⁹ Therefore, NC may be an indicator of the occurrence of AP.

There are several strengths and limitations to the present study. This is the first study to explore the relationship between NC and AP incidence and because our data were based on a community study, our findings can be generalized to a certain extent. However, some limitations still

exist. The dataset of SHHS lacked most of the follow-up time of the first AP episode; thus, we could not investigate the association between NC and AP using the Cox proportional hazards regression models. Besides, the sample size is relatively small in the stratified analysis. In addition, the majority of participants were Caucasian; therefore, our results cannot be generalized to all ethnic groups.

Conclusion

In this study, we investigated the association of NC with AP incidence. Our results showed that individuals with larger NC had an increased risk of AP incidence in both male and female. Thus, NC may be a marker to predict the occurrence of AP.

Clinical Trial Registration

Sleep Heart Health Study Data Coordinating Center; URL: <https://clinicaltrials.gov/ct2/show/NCT00005275?term=NCT00005275&rank=1ClinicalTrials.gov> Identifier: NCT00005275.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest for this work.

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