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Is There Evidence of Early Vascular Disease in Patients with Obstructive Sleep Apnoea Without Known Comorbidities? Preliminary Findings

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Abstract: We evaluated early atherosclerotic lesions in 20 non-smokers with newly diagnosed Obstructive Sleep Apnoea (OSA) and without known comorbidities by measuring common carotid artery intima media thickness (CCA-IMT), transcranial Doppler ultrasound (TCD), and ankle brachial index (ABI). These were compared with 20 healthy age- and BMI-matched controls. In OSA patients, CCA-IMT was not significantly higher vs. controls (0.74±0.17 vs. 0.66±0.12 mm, p=0.201) and it was positively correlated with neck circumference (r=0.466, p=0.039), arousal index (r=0.663, p=0.001), gamma-glutamyl transpeptidase activity (r=0.474, p=0.035) while it was negatively correlated with Forced Expiratory Volume in 1 sec (r=-0.055, p=0.012). No difference was noted between patients and controls in terms of vascular stenosis on TCD examination, while asymptomatic peripheral artery disease was found in one patient with OSA. In conclusion, OSA patients without known comorbidities exhibit a non-significant increase in CCA-IMT without further evidence of vascular disease, but additional experience in a larger patient series is needed.

Keywords: Ankle-Brachial Index, Atherosclerosis, Intima-Media Thickness, Obstructive Sleep Apnoea, Transcranial Doppler, Vascular disease.

INTRODUCTION

Obstructive Sleep Apnoea (OSA) is associated with increased risk for cardiovascular disease (CVD) [1-3] and cerebrovascular morbidity [4, 5]. Oxygen desaturation accompanying apneic events, negative intra-thoracic pressure, arousals induced by upper airway obstruction, and repeated activation of the sympathetic system could cause an abnormal activation of neural, humoural, thrombotic, metabolic and inflammatory responses, thereby promoting atherosclerosis [6-8].

Common Carotid Artery Intima-Media Thickness (CCA-IMT) is a useful parameter to evaluate the severity of early atherosclerosis [9, 10] and the overall vascular disease risk [11, 12]. Several studies have documented a link between increased CCA-IMT and OSA [13-16]. Transcranial Doppler ultrasound (TCD) is a simple non-invasive procedure that investigates intracranial flow with multiple indications in several clinical conditions [17]. The Ankle-Brachial-Index (ABI) is a practical, widely used and reliable diagnostic tool for peripheral arterial disease (PAD); it is also useful for the screening of CVD [18, 19].

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This preliminary case-series study aimed to examine early atherosclerotic lesions in patients with recently diagnosed OSA free from other known comorbidities. Early vascular lesions were assessed by CCA-IMT, ABI and TCD. To our knowledge, this is the first study that combines CCA-IMT, TCD and ABI measurements for the evaluation of vascular disease in OSA patients.

MATERIALS AND METHODOLOGY

PATIENTS

The study included 20 patients (16 males and 4 females) referred to our sleep laboratory and 20 healthy subjects (16 males and 4 females) who were used as controls. All subjects were non-smokers and underwent laboratory and clinical examination. Information regarding previous medical history, tobacco smoking and alcohol consumption was obtained. Height, weight, body-mass index (BMI) [BMI = weight (kg)/height^2 (m)], neck circumference, hip circumference, waist circumference and waist/hip ratio were measured using a standardised protocol [20]. Briefly, neck circumference was calculated at the cricothyroid level, waist circumference in the midpoint between the 12th rib and the iliac crest, and hip circumference was measured at the level of the greater trochanter.

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Electrocardiogram and arterial blood pressure (BP) measurement were performed. Arterial blood gases were analysed. Venous blood samples were obtained the morning after polysomnography (PSG) after 8 h fasting, during which only water intake was permitted. Levels of total cholesterol, triglycerides, high- and low-density lipoprotein were measured by enzymatic colorimetric methods, fasting glucose was determined by enzymatic method, while C-reactive protein, gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured by an immunoturbidimetric method (Olympus AU640™, Olympus Diagnostica GmbH, Hamburg, Germany). Pulmonary function tests were performed as well (Screenmate, Erich Jaeger GmbH & Co., Hochberg, Germany).

Somnolence was evaluated by the validated Greek version of the Epworth Sleepiness Scale (ESS) [21], a self-administered questionnaire estimating the risk of falling asleep in a variety of situations [maximum score: 24; score> 10: excessive daytime sleepiness (EDS)] [22].

Diabetes was defined as fasting glucose levels ≥ 126 mg/dL or glycated haemoglobin (HbA1c) ≥ 6.5% [23]. Arterial hypertension was defined as: either systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg, both measured on 3 separate occasions, or medical history of documented high arterial BP and use of antihypertensive treatment [24]. Exclusion criteria were as follows: mixed or central apnoeas, chronic obstructive pulmonary disease, cardiac failure or myocardial infarction, kidney disease, cerebrovascular disease, cancer, various causes of daytime sleepiness and any psychiatric or neurological disorder or any other acute medical condition.

All subjects gave their informed consent and the study was approved by the institutional ethics committee.

CCA-IMT

CCA-IMT was assessed by high-resolution B-mode ultrasonography, as previously described [25]. The left and right common carotid arteries were examined in the anterolateral, posterolateral and mediolateral directions. All subjects were examined in the supine position, with the head turned 45° from the site being scanned. Both carotid arteries were scanned longitudinally to visualise the IMT in the distal wall of the artery. The best images of the distal wall were

Table 1. Anthropometric, Clinical and Laboratory Measurements of OSA Patients

Variables	Mean ± standard deviation (Range)
Age (years)	50.8 ± 12.4 (28-72)
Males/females	16/4
Body weight (kg)	101.8 ± 20.6 (57-139)
BMI (kg/m^2)	34.3 ± 7.2 (24.8-50.4)
Alcohol (drinks/week)	1.20 ± 1.00 (0-3)
Neck circumference (cm)	42.6 ± 4.1 (35-50)
Waist circumference (cm)	118.2 ± 13.1 (97-137)
Hip circumference (cm)	114.7 ± 10.3 (101-142)
Waist to hip ratio	1.03 ± 0.06 (0.9-1.2)
Total cholesterol (mg/dl)	202 ± 46 (133-298)
LDL-cholesterol (mg/dl)	116 ± 44 (27-183)
HDL-cholesterol (mg/dl)	46 ± 9 (33-60)
Triglycerides (mg/dl)	202 ± 172 (65-856)
Glucose (mg/dl)	95 ± 10 (80-116)
GGT (mg/dl)	33 ± 24 (2-101)
CRP (mg/dl)	0.46 ± 0.51 (0.08-1.82)
Systolic blood pressure (mmHg)	119.5 ± 9.0 (100-135)
Diastolic blood pressure (mmHg)	76.0 ± 6.8 (60-85)
FEV_1 (% predicted)	91.0 ± 19.9 (54-132)
FVC (% predicted)	87.5 ± 20.3 (47-131)

Abbreviations: BMI, Body Mass Index; CRP, C-Reactive Protein; FEV_1, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; GGT, Gamma-Glutamyl Transferase; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; OSA, Obstructive Sleep Apnoea.

used to determine the CCA. Using cine-loop function, an optimal longitudinal freeze-frame image in the end-diastolic state was measured manually by calipers. CCA-IMT was defined as the mean of the right and left IMT of the common carotid artery, calculated from 5 measurements on each side, which were taken 10 mm proximal to the carotid bifurcation. The lumen/intima leading edge (I line) to media/adventitia leading edge (M line) method, which has been previously validated anatomically [26] was used. Subjects with evidence of plaques (defined as a focal structure encroaching into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value) at the site of CCA-IMT measurements were excluded from further evaluation. The reproducibility of CCA-IMT measurements between and within our sonographers has been previously established [25].

ABI

On the day before PSG, ABI was measured using a handheld 8 MHz Doppler device (MiniDop EX-100Vx, Hadeco, Japan) [27]. Systolic BP was measured in both the dorsalis pedis and posterior tibial artery, and the higher of these pressures was divided by the higher of the 2 brachial systolic BPs to calculate the ABI. Peripheral artery disease (PAD) was defined as ABI ≤0.90, while ABI >1.0 was considered normal. Subjects with elevated ABI (>1.30) suggestive of poorly compressible leg arteries [28] were excluded.

PSG

Overnight PSG (Alice® 4, Philips Respironics, Murrysville, PA, USA) was performed from 22:00 to 06:00 hours, as previously described [29]. A standard montage of electroencephalogram, electro-occulogram, electromyogram and electrocardiogram signals was used. Pulse oximetry was registered and airflow was detected using combined oronasal thermistors. Thoracic cage and abdominal motion were also recorded using inductive plethysmography. Apnoeas, hypopnoeas, and electroencephalogram recordings were manually scored according to standard criteria [30]. Apnoea was defined as complete cessation of airflow for at least 10 sec. Hypopnea was defined as a 50% reduction in airflow for at least 10 sec in combination with oxyhaemoglobin desaturation of at least 4% or an arousal registered by the electroencephalogram [30]. Apnoea-hypopnea index (AHI) was established by the number of apnoeas and hypopneas per hour of PSG-recorded sleep time [30]. Oxygen desaturation index was defined as the number of oxyhemoglobin desaturations of at least 3% per hour of PSG-recorded sleep time. OSA was defined as AHI ≥5 accompanied by daytime symptoms [31]. OSA was graded as mild (AHI: 5-15/h), moderate (AHI: 15-30/h), and severe (AHI >30/h) [31]. Patients with purely central apnoeas were excluded.

TCD

TCD was carried out the day before PSG using a standardised protocol by a neurologist with special training and experience in cerebrovascular ultrasound [32-34]. An insonation depth of 45 mm or more was employed for the identification of proximal (i.e. M1) middle cerebral artery (MCA) flow signals and depths of 30 to 45 mm for presumed distal MCA flow signals (M2MCA). After the identification of

Table 2. Sleep ESS, CCA-IMT, ABI and TCD Measurements of OSA Patients

Variables	Mean ± standard deviation (Range)
ESS (score)	12.50±5.88 (2-24)
AHI (events/hour)	48.68±20.99 (10.8-78.5)
avSpO$_2$ (%)	90.62±3.04 (81-94)
minSpO$_2$ (%)	73.90±11.12 (36-88)
TST with SpO$_2$<90% (%TST)	96.67±73.63 (19.5-276.5)
Sleep efficiency (%TST)	79.38±13.59 (52.6-96.8)
Stage 1 (%TST)	23.95±15.87 (5.9-60.8)
Stage 2 (%TST)	55.99±21.58 (1.6-89.3)
Stage 3+4 (%TST)	8.28±10.53 (0-38.9)
REM (%TST)	8.60±7.24 (0-23.2)
Arousal index	40.57±17.27 (8.2-75.2)
Mean CCA-IMT (mm)	0.74±0.17 (0,48-1.06)
Right ABI	1.10±0.13 (0.8-1.3)
Left ABI	1.10±0.14 (0.7-1.3)
TCD (intracranial stenosis %)	0.00

Abbreviations: ABI, Ankle-Brachial Index; AHI, Apnoea Hypopnoea Index; avSpO$_2$, average oxyhaemoglobin saturation during sleep time; CCA-IMT, Common Carotid Artery Intima Media Thickness; ESS, Epworth Sleepiness Scale; minSpO$_2$, minimum oxyhaemoglobin saturation during sleep time; OSA, Obstructive Sleep Apnoea; REM, Rapid Eye Movement; TCD, Transcranial Doppler; TST, Total Sleep Time.

both proximal M1MCA and proximal A1 anterior cerebral artery (ACA) signals at the depth of approximately 65 mm (range 58-70 mm), the probe was aimed inferiorly and slightly posteriorly and flow signals of the terminal internal carotid artery (TICA) were obtained at a depth of 60-70 mm [32]. Posterior cerebral artery (PCA) intracranial atherosclerotic disease was detected using an insonation depth of 58-70 mm with posterior angulation of the probe during transtemporal insonation [32, 33]. An insonation depth of 40-79 mm and of 80-105 mm was used for the identification of vertebral (VA) and basilar artery (BA) steno-occlusive disease, respectively, during transforaminal or suboccipital insonation [32, 33].

The following mean flow velocity (MFV) cut-offs were used for identification of ≥50% stenosis according to the SONIA (stroke outcomes and neuroimaging of intracranial atherosclerosis) trial criteria [35]: MCA: MFV >100 cm/sec; TICA: MFV >90 cm/sec; VA: MFV >80 cm/sec; and BA: MFV >80 cm/sec. Given that ACA and PCA atherosclerosis were not evaluated in the SONIA trial, we used a set of previously validated criteria for the detection of intracranial atherosclerosis in these vessels [32, 33]. Primary TCD findings in ACA stenosis (≥50%) included a focal and significant mean MFV increase (MFV ≥80 cm/sec and ≥30% difference compared with the contralateral ACA segment) at a depth of 62-75 mm [32]. Similarly, a cut-off of >80 cm/sec was used for identification of ≥50% PCA stenosis [33]. Subjects with absent temporal windows were excluded.

STATISTICAL ANALYSIS

Analysis was carried out using SPSS (Statistical Package for Social Sciences, Chicago, Illinois) v.15.0. Normality was assessed by Kolmogorov-Smirnov test. For normally distributed values, descriptive results were expressed as mean ± SD. Pearson's correlation coefficients were used to examine the association between variables. Analysis of Variance (ANOVA) and Student's t-test were used to examine differences between groups. Reported p-values are two-tailed and significance was defined at $p<0.05$.

RESULTS

The study population comprised 32 males and 8 females with age ranging from 28 to 72 years old (mean 50.80 ± 12.37 years old). All subjects were non-smokers. Their anthropometric, clinical and laboratory characteristics are summarised in Table **1** while the results from PSG, ESS, ABI, TCD and CCA-IMT measurements are reported in Table **2**. Regarding severity (based on AHI), OSA was mainly moderate-to-severe (1 patient with mild OSA, 5 patients with moderate OSA and 14 patients with severe OSA), while 14 out of 20 patients reported EDS (ESS > 10).

In OSA patients, CCA-IMT was not significantly higher vs. controls (0.74 ± 0.17 vs. 0.66 ± 0.12 mm, p = 0.201). No patient exhibited vascular stenosis on TCD, while one patient had asymptomatic PAD (ABI = 0.7).

Mean CCA-IMT in OSA patients was positively correlated with neck circumference (r = 0.466, p = 0.039) and arousal index (r = 0.663, p = 0.001) while it was negatively correlated with FEV_1, expressed as percentage of the predicted value (FEV_1 % pred) (r = -0.551, p = 0.012). Additionally, mean CCA-IMT exhibited a significant positive correlation (r = 0.474, p = 0.035) with GGT activity, while no other correlation was observed between CCA-IMT and other biochemical characteristics. Correlations between CCA-IMT and potential predictors for atherosclerosis are reported in Table **3**.

DISCUSSION

The present study has demonstrated a positive correlation between CCA-IMT and arousal index, neck circumference, and GGT as well as a negative correlation with FEV_1, in patients with newly diagnosed OSA and without known comorbidities. Conversely, intracranial vascular stenosis (studied by TCD) and PAD (evaluated by ABI) showed no association with any index of OSA.

The relationship between CCA-IMT and OSA has been examined in several previous studies [13-16, 36], even though the authors recognise that common cardiovascular risk factors could represent confounding variables [16]. Suzuki *et al*. [14] reported that CCA-IMT was related to AHI, duration of oxygen saturation below 90% and the minimum oxygen saturation. The correlation between OSA-related hypoxemia and CCA-IMT was independently of AHI, indicating that hypoxia could represent an independent risk factor for arterial wall lesions [14]. Importantly, their patients had several comorbidities other than tobacco smoking (47.3% arterial hypertension, 18% dyslipidaemia and 17.4% diabetes mellitus) that can influence the progression of IMT [37-39]. However, after adjustment for confounding factors, the correlation between IMT and severity of OSA remained significant.

Similar findings have been reported by Szabóová *et al*. [40]. Patients with cardiovascular comorbidities and OSA exhibited higher IMT, as compared with the OSA group alone. Nevertheless, when adjusted for age, IMT was normalised. In another study [41], severity of oxygen desaturation and BP status were the best predictors for CCA-IMT and atherosclerotic plaque formation in 83 OSA patients. In a Chinese study of 52 patients with OSA [42], CCA-IMT was significantly higher in the moderate (0.81 ± 0.24 mm) and severe OSA (0.91 ± 0.23 mm) subgroups than in the mild OSA (0.7 ± 0.17 mm) subgroup. Minoguchi *et al*. [43] have also observed increased CCA-IMT in patients with moderate to severe (1.16 ± 0.05 mm, $p < 0.003$) as compared with those with mild OSA (0.71 ± 0.03 mm, $p < 0.0001$). A similar observation has been reported by Saletu *et al*. [44]. However, these results are not confirmed by all studies [36].

In our study, a correlation between arousal index and CCA-IMT was observed. This suggests that sleep fragmentation due to intermittent arousals may result in metabolic and inflammatory deregulation, which, in turn, promotes vascular pathology. Of note, Wattanakit *et al*. [16] found that respiratory disturbance index, and arousal index failed to show a correlation with CCA-IMT after adjustment for additional risk factors for atherosclerosis in 985 subjects from the general population. Importantly, their patients had various risk factors for cardiovascular disease and presented with a mild to moderate OSA with a mean respiratory disturbance index of 8.7 events/h [16]. By contrast, our patients were free from

Table 3. Correlations between CCA-IMT and Studied Parameters as Predictors for Atherosclerosis in OSA Patients

Variables	p	r
Age	0.071	0.412
BMI	0.602	0.124
Neck circumference	0.039	0.466
Waist circumference	0.214	0.29
Hip circumference	0.326	0.231
Waist to hip ratio	0.499	0.161
FEV_1 (% predicted)	0.012	-0.551
FVC (% predicted)	0.050	-0.443
Glucose	0.558	0.139
GGT	0.035	0.474
Cholesterol	0.528	0.150
Triglycerides	0.155	0.330
HDL-cholesterol	0.822	0.054
LDL-cholesterol	0.633	-0.114
CRP	0.684	0.097
ESS	0.733	0.081
Sleep efficiency (%TST)	0.085	0.406
Stage 1 (%TST)	0.59	0.128
Stage 2 (%TST)	0.986	-0.004
Stage 3+4 (%TST)	0.17	-0.32
REM	0.158	-0.328
AHI	0.26	0.264
$avSpO_2$	0.383	-0.206
$minSpO_2$	0.873	0.038
TST with SpO_2<90%	0.44	0.183
Arousal index	0.001	0.663

Abbreviations: AHI, Apnoea Hypopnoea Index; $avSpO_2$, average oxyhaemoglobin saturation during sleep time; BMI, Body Mass Index; CCA-IMT, Common Carotid Artery Intima Media Thickness; CRP, C-Reactive Protein; ESS, Epworth Sleepiness Scale; FEV_1, Forced Expiratory Volume in the first second; FVC, Forced Vital Capacity; GGT, Gamma-Glutamyl Transferase; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; $minSpO_2$, minimum oxyhaemoglobin saturation during sleep time; OSA, Obstructive Sleep Apnoea; REM, Rapid Eye Movement; TST, Total Sleep Time.

known comorbidities. Taken together, the new and the earlier data indicate some correlation between OSA and CCA-IMT, although further information on the most relevant parameters of OSA is still desirable. Of foremost importance appears to be nocturnal hypoxia [13, 14]. At the same time, caution is needed not to underestimate the role of comorbidities. Indeed, it is known that the latter may influence some vascular risk factors [45].

Sleepiness evaluated by ESS was identified as an independent predictor of CCA-IMT in a pre-polysomnographic multiple regression model of an Austrian study [46], a finding not confirmed in our work. Daily somnolence is a major, but still not omnipresent, feature of OSA [46, 47]. It has been shown to be linked with glucose deregulation [47], and its contribution to associated morbidity merits further attention [47].

In previous works, CCA-IMT has been shown to correlate with several biochemical parameters, such as total cholesterol [14], HbA_{1c} [14, 44], C-reactive protein [43, 46], fibrinogen [46], interleukin-6 (IL-6) [43], interleukin-18 (IL-18) [42, 43], and urinary 15-F2t-isoprostane [48]. In our study, we noted a correlation between GGT and CCA-IMT. GGT is known to be associated with arterial stiffness in healthy individuals [49]. Additionally, it has been identified

as a risk factor for all-cause mortality (especially among young subjects) [50], for cardiovascular disease [51, 52] and stroke [52, 53]. Kanbay *et al*. [54] found that elevated GGT was an independent predictor of CVD in OSA patients, and the increase in GGT was proportional to OSA severity. Thus, our finding further supports Kanbay's observations [54], suggesting that GGT is a marker of incipient carotid atherosclerosis in OSA.

We found a significant negative correlation between CCA-IMT and FEV_1, while Zureik *et al*. [55] have also observed a negative but insignificant correlation between IMT and FEV_1 % ($r = -0.13$, $p = 0.17$). Additionally, they found that among male subjects, CCA-IMT was higher in those with than those without bronchial hyper-responsiveness ($p = 0.002$) [55]. This was attributed to the activation of systemic inflammatory mechanisms common to bronchial hyperresponsiveness and arterial injury. In another study [56], CCA-IMT was negatively associated with FEV_1, which, in turn, was associated with development of atherosclerotic plaques. In this context, we have provided additional evidence that FEV_1 reflects concomitant pulmonary and vascular perturbations. Plausible explanations, other than common inflammatory pathways, may include aging-related physiologic changes affecting both respiratory function and arterial wall thickness, as well as reduced arterial wall oxygenation due to chronic hypoxia.

Several studies assessed the correlation between respiratory function and the risk of stroke. A prospective cohort study of 7151 men with a mean follow up of 14.8 years [57] showed that reduced FEV_1 was linked with increased stroke risk even after adjustment for additional CVD risk factors. Men with lower FEV_1 (<3.10 l) had a 50% increase in stroke risk compared with those with higher FEV_1 (≥3.65 l) with a corresponding relative risk (RR) of 1.4 [57]. Similar results were observed in a Danish study [58]. In another prospective study of 379 women with a mean follow up of 26 years [59], middle- and late-life respiratory function was related to cerebrovascular disease shown by brain computed tomography. For an 1-standard deviation decrease in FEV_1, there was increased risk of white matter lesions [odds ratio (OR): 1.46] and lacunar infarcts (OR: 1.42) detected by MRI [59]. In addition, Liao *et al*. [60] have demonstrated a relationship between lower pulmonary function and subclinical CVD detected by MRI. All this data underlines the importance of our reported association between CCA-IMT and FEV_1. It appears, then, that FEV_1 is not by chance associated with CCA-IMT but it is, indeed, a risk marker of stroke, and so it should be measured in OSA patients.

This study failed to show a correlation between OSA and TCD. The small patient number may account for this finding. Foster *et al*. [61] have studied cerebral blood flow in response to hypoxia and the effect of treatment with continuous positive airway pressure (CPAP). Cerebral blood flow in response to isocapnic hypoxia was assessed by TCD in 8 male OSA patients before and after 4 to 6 weeks of CPAP treatment [61]. OSA patients exhibited a diminished response to hypoxia, but this reverted to normal after CPAP treatment [61]. In another study [62], TCD was employed to evaluate the effects of hypoxia and hypercapnia on cerebral circulation in 20 OSA patients compared with 20 healthy subjects. Vascular response to hypoxia and hypercapnia was reduced in OSA patients, while CPAP treatment led to improvement [62]. Morgan *et al*. [63] have demonstrated impaired cerebrovascular responsiveness in patients with sleep-disordered breathing. This prior experience notwithstanding, it should be noted that this study included recently diagnosed OSA patients, in whom intracranial blood flow may not yet have been compromised.

Finally, we found no correlation between OSA and ABI. To the best of our knowledge, this association has not been examined. Kumagai *et al*. [64] have used a similar index, the cardio-ankle vascular index (CAVI), and found that it was correlated with IMT ($r = 0.487$, $p < 0.001$). The absence of any association in our study may, at least partly, be ascribed to the small patient series. Alternatively, new-onset OSA may only be linked with early carotid lesions (as manifested in IMT) but not PAD/generalised atherosclerosis (as manifested by ABI). More studies are needed.

The strengths of this study are the careful evaluation of vascular disease and the inclusion of OSA patients without other known comorbidities, so confounding CVD risk factors were excluded. The limitations are the small patient series and the absence of follow-up. However, we specifically aimed to detect early atherosclerotic lesions in newly diagnosed OSA, and long-term evaluation was beyond the scope of this work.

The clinical implications of this study are that subjects with newly diagnosed OSA without known comorbidities may already exhibit increased CCA-IMT. Although further confirmation and clarification of the underlying mechanisms are desirable, this finding suggests that such subjects need to start regular assessment of carotid pathology. It is also plausible that this assessment should be coupled with patient education about vascular risk factors, appropriate lifestyle modification, and follow-up for early detection of any lesions in other vascular beds, in line with the growing appreciation of the vascular risks posed by OSA [65-67].

Our preliminary findings suggest that subjects with newly diagnosed OSA without known comorbidities exhibit a non-significant increase in CCA-IMT. They have no further evidence of vascular disease affecting the intracranial and the lower-extremity arteries. This knowledge may be seen in the context of improving diagnosis and management of carotid disease, as practised nowadays [68-70]. Additional experience is needed in a larger series.

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CONFLICTS OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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