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Research paper

Diagnostic accuracy of carotid intima media thickness in predicting coronary plaque burden on coronary computed tomography angiography in patients with obstructive sleep apnoea

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ABSTRACT

Aim: To assess the diagnostic accuracy of common carotid artery intima media thickness (CIMT) for coronary artery disease (CAD) detection in patients with obstructive sleep apnoea (OSA).
Materials & methods: Patients with clinically suspected OSA prospectively underwent polysomnography (PSG), ultrasound CIMT measurement and coronary computed tomography angiography (CTA). An average CIMT of ≥0.9 mm in either common carotid artery designated as a positive test. Coronary CTA was the reference standard for the presence of CAD. Coronary plaque presence, volume, density and type were correlated with CIMT findings.
Results: 35 consecutive male patients were enrolled from sleep clinic. Two patients had no evidence of OSA on PSG (apnoea-hypopnea index [AHI]<5/hr), and were excluded. Of the remaining 33, 18 (54%) had mild-moderate OSA (AHI 5–30/hr) and 15 (46%) had severe OSA (AHI >30/hr). Eight (24%) patients had CAD on coronary CTA. Coronary plaques were predominantly non- or partly calcified, and located in proximal coronary artery segments. Sensitivity, specificity, positive and negative predictive and likelihood ratios for a positive CIMT (≥0.9 mm) in diagnosing CAD were 0.5 (95% confidence interval: 0.76–0.12), 0.96 (1–0.89), 80, 85.7, 12.5 and 0.52 respectively. The adjusted odds ratio was 40.8.
Conclusion: In patients with OSA, CIMT is a highly specific but poorly sensitive test for detecting CAD.

1. Introduction

Obstructive sleep apnoea (OSA) is characterized by episodic hypoxaemia during sleep caused by recurrent upper airway collapse. It is an independent risk factor for atherosclerotic cardiovascular (CV) disease, with an increased lifetime risk of myocardial infarction and cerebrovascular accidents.[1–3] Patients with OSA often have multiple cardiovascular risk factors, such as obesity, hypertension, diabetes and hypercholesterolaemia, further increasing their cardiovascular risk profile.[4] Identification of patients with clinically significant OSA is important, as treatment with nocturnal continuous positive airway pressure (CPAP) has been shown to reduce cardiovascular morbidity and mortality.[5]

Carotid intima media thickness (CIMT) assessed by carotid ultrasonography is a validated tool in the global assessment of a patient's cardiovascular risk profile.[6] A CIMT measurement of >1 mm is associated with a two-fold increased risk of coronary artery disease in men and five-fold increase in women.[7] Patients with severe OSA, but without a history of or risk factors for CV disease, have been shown to have an increased CIMT compared to an age, BMI and gender-matched control cohort.[8]

CIMT does not offer direct evidence of coronary artery disease (CAD). Coronary computed tomography angiography (CTA) allows a rapid, non-invasive direct assessment of the burden of coronary artery disease. It is a validated tool in the assessment of coronary artery disease in the OSA population, and our research group has

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previously shown a higher coronary plaque burden on coronary CTA in patients with more severe OSA.[9] To our knowledge, no study has yet assessed the correlation between CIMT and coronary artery plaque burden in patients with OSA. The primary purpose of this study is to assess the diagnostic accuracy of CIMT for CAD in patients with OSA.

2. Methods

2.1. Patients

Consecutive patients were prospectively recruited from the St Vincent's University Hospital (SVUH) sleep clinic from January 2013 to January 2016. The ethical review board at SVUH approved this study. Patients were enrolled from clinical referrals to a dedicated sleep apnoea clinic and invited to participate in the study if they were male, between the ages of 18–70 years and without a history of known cardiometabolic disease or on any long-term medication. The exclusion criteria included any contraindication to coronary CTA such as a history of anaphylaxis to iodinated contrast or severe renal dysfunction.

After initial enrollment, a full smoking history, baseline clinical measurements (blood pressure, height, weight) and laboratory investigations (fasting cholesterol, triglycerides, high density lipoprotein, low density lipoprotein, glucose, haemoglobin A1c) were obtained. Smoking history was recorded in pack years, with 20 cigarettes a day for one year representing one pack year. All patients underwent an inpatient, attended polysomnography (PSG) to assess for the presence of OSA as per international recommended criteria.[10] Those with an apnoea-hypopnoea index (AHI) of five or more events per hour on PSG analysis were deemed to have OSA, and proceeded to ultrasound measurement of CIMT. Ultrasound measurements were carried out by a single trained technician who was blinded to the results of the PSG and coronary CTA.

2.2. Carotid intima media thickness

CIMT measurement was performed in all patients using recommended international guidelines with a 12 Mhz probe (General Electric, Colorado, USA).[11] Measurements were performed (in millimeters to two decimal places using electronically placed calipers) at the distal common carotid artery, proximal to the carotid bifurcation. Three measurements were performed at each common carotid artery placed approximately 5 mm apart, obtaining an average CIMT for right and left carotid arteries. For the purposes of this study, and based on data from studies on the general and sleep apnoea population, we denoted an average CIMT of $\geq$0.9 mm in either carotid artery as a positive test.[8,12,13]

2.3. Coronary computed tomography angiography protocol

Each patient had coronary CTA performed within 12 weeks of the PSG, and before the commencement of nocturnal continuous positive airways pressure (CPAP) treatment. All coronary CTAs were performed on a 64-slice single-source CT scanner (Siemens Sensation, Forcheim, Germany). Images were acquired with retrospective ECG-gating and collimation of 0.6 mm, gantry rotation of 330 ms, 120 peak kilovoltage (kVp) and a tube current of 800–850 mA. Images were reconstructed with a slice thickness 0.6 mm and slice overlap of 0.3 mm. Beta-blocker premedication (50–100 mg of Metoprolol, Bedford Laboratories, OH, USA) was administered to patients 1 h before image acquisition depending on the heart rate as follows: patients with a resting heart rate of 60–70–bpm were administered 50 mg of metoprolol; those with a heart rate greater than 70–bpm were administered 100 mg metoprolol; no beta blockers were administered to patients with heart rates less than 60 bpm. If the heart rate remained above 65 bpm after beta-blocker premedication, multi-segment reconstruction was utilized. A timing bolus technique was used to ascertain the optimal time to commence image acquisition (20 ml of contrast medium injected at 6 ml/s with a region of interest placed over the ascending aorta). Images were acquired during a single breath hold in mid-inspiration following the administration of sublingual glyceryl-trinitrate for coronary vasodilatation. Iodinated contrast medium (70–90 ml of Iopamidol 340, Bracco Diagnostic, Princeton, NJ, USA) was injected at a rate of 6 ml/s followed by a 20-ml saline bolus chaser injected at 6 ml/s.

Table 1
Baseline characteristics.

Demographic	Mean ± SD
Age (yrs)	44.6 ± 9.6
BMI (kg.m^2)	34.6 ± 6.2
AHI/hr	34.6 ± 25.5
CIMT (mm)	0.72 ± 0.17
Mean coronary artery plaque volume (mm^3)	0.3 ± 0.74
Systolic blood pressure (mmHg)	127.3 ± 11.3
Diastolic blood pressure (mmHg)	77.4 ± 9.3
Fasting Glucose (mmol/L)	5.4 ± 0.5
HbA1c (mmol/mol)	39.9 ± 8.4
Cholesterol (mmol/L)	4.9 ± 0.9
Triglycerides (mmol/L)	1.9 ± 1.1
HDL (mmol/L)	1.1 ± 0.3
LDL (mmol/L)	2.9 ± 08

SD=Standard deviation; BMI = body mass index; AHI = apnoea hypopnea index; CIMT = Carotid intima media thickness; HbA1c = Haemoglobin A1c; HDL = High density lipoprotein; LDL = Low density lipoprotein.

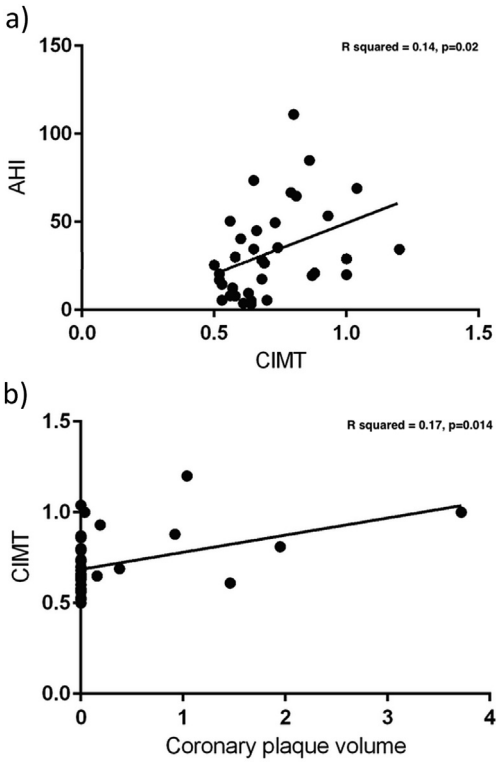

Fig. 1. A) **Apneoa hypopnea index (AHI, hr^{-1}) vs Carotid intimal media thickness (CIMT, mm)**. $R^2 = 0.14$, p = 0.02. B) **Carotid intimal media thickness (CIMT, mm) vs total patient coronary artery plaque volume (mm3)**. $R^2 = 0.17$, p = 0.014.

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