

Coronary Artery Calcium Score and Obstructive Sleep Apnoea

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Abstract

Obstructive Sleep Apnoea (OSA) is a sleep related breathing disorder affecting a significant section of middle aged population. The pro inflammatory state that exists in OSA patients contributes to accelerated atherosclerosis and increased incidence of cardiovascular and cerebrovascular disease. Coronary Artery Calcium (CAC) has emerged as a non invasive tool for assessment of underlying atherosclerosis. It helps predict future cardiovascular events, thereby helping in risk stratification and modifying treatment decisions. The scope of CAC scoring in specific subpopulation of OSA patients remains to be defined.

Keywords: Obstructive sleep apnoea; Coronary artery calcium; Atherosclerosis

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Obstructive Sleep Apnoea (OSA)

Obstructive Sleep Apnoea (OSA) is a sleep related breathing disorder characterised by repeated episodes of upper airway obstruction during sleep. It has been found that as many as 4% of middle-aged men and 2% of women have clinically

significant OSA [1, 2]. The recurrent episodes of upper airway obstruction result in recurrent hypoxia sleep fragmentation and excessive daytime somnolence [1, 3]. Other physiological consequences of OSA include hypercapnia, increased catecholamine secretion due to sympathetic activation, systemic and pulmonary vasoconstriction. OSA has also been associated with systemic inflammation, endothelial dysfunction and accelerated atherosclerosis [4, 5]. Activation of neuroendocrine, vascular and humoral mechanisms contributes to the increased incidence of cardiovascular and cerebrovascular disease in these patient populations. There has been increased emphasis on the early diagnosis of the atherosclerotic disorders in these patients so that appropriate therapy can be initiated early.

Coronary Artery Calcium (CAC) Score

Coronary Artery Calcium (CAC) has emerged as a novel non invasive marker of subclinical atherosclerosis. The American College of Cardiology (ACC) and American Heart Association (AHA) Consensus Panel observed that presence of calcium in the coronary vessel wall was linked to the overall process of atherosclerosis [6]. The electron beam computed tomography has been used to quantify the magnitude of calcium load in the coronary arteries. CAC measurements use low radiation scan, avoids contrast exposure and is reproducible. It has shown to predict the severity of coronary stenosis and the future risk of cardiovascular events [7, 8]. In addition it has prognostic value as well with higher calcium scores being associated with worse prognosis [9]. The 2010 ACC/ AHA guidelines consider measurement of CAC reasonable for cardiovascular risk

assessment in asymptomatic adults at intermediate risk of cardiovascular events (Class IIa). Besides, limited evidence has suggested it to be comparatively more reliable in predicting future cardiovascular events compared to other non invasive markers of atherosclerosis [10].

OSA, Atherosclerosis and CAC Score

OSA patients are predisposed to generalize atherosclerosis [5, 11]. Repeated apnoeic spells associated with hypoxia followed by re oxygenation generates oxidative stress that promotes degenerative changes of the arterial walls. OSA is associated with a pro inflammatory state whereby the plasma levels of soluble cell adhesion molecules; Vascular Endothelial Growth Factor (VEGF), C-reactive protein and fibrinogen are increased [11-15]. The progression of the disease process culminates in an increased cardiovascular morbidity and mortality in such patients. Multiple studies have tried to find an association between the severity of OSA and underlying atherosclerosis as measured by CAC scoring (Agatston score). The scoring is based on electron beam computed tomographic visualisation of the calcification in the coronary arteries and is a product of area and density of calcific plaque burden. Each plaque is assigned a value according to its density measured in Hounsfield Units (HU) (score of 1 for 130–199 HU, 2 for 200–299 HU, 3 for 300–399 HU, and 4 for 400 HU and greater). The value is then multiplied by the area of plaque (square millimetres) to calculate the score for that segment of the artery. Individual scores from multiple tomographic slices of the heart are then added to find out the total score. A CAC score of 1-100 predicts a risk ratio of 2.1, CAC score of 100-400 predicts risk ratio of 5.4 and CAC score of >400 predict a risk ratio of 10 for the development of subsequent coronary heart disease event in asymptomatic individuals [9].

In a prospective study by Arik et al. [16] CAC scoring was performed in 73 patients with OSA who were asymptomatic for coronary artery disease. Apnoea-Hypopnea Index (AHI) levels were weakly correlated with coronary calcium score ($r = 0.342$, $p = 0.003$) and body mass index ($r = 0.337$, $p = 0.004$), moderately correlated with basal oxygen saturation ($r = -0.734$,

$p < 0.001$), and strongly correlated with oxygen desaturation index ($r = 0.844$, $p < 0.001$). However, on further analysis the authors observed that age and AHI independently predicted CAC scores in OSA patients. The authors concluded advanced age and moderate to severe OSA should alert clinicians to the presence of underlying atherosclerosis.

A similar cross sectional observational study was performed by Kepez and co-workers [17]. The investigators evaluated 97 patients with OSA who underwent CAC scoring and were divided into four groups according to the severity of OSA. Interestingly the authors found that the calcium scores of patients increased linearly with the increase in severity of OSA ($p=0.046$). However, age was the only independent variable that predicted the presence of coronary calcification (OR 1.11, 95% CI 1.039-1.188, $p=0.002$).

Weinreich et al. tried to analyse the association of OSA with cardiovascular disease risk factors and subclinical coronary atherosclerosis. In a cross-sectional analysis of the Heinz Nixdorf Recall study Coronary Artery Calcium (CAC) was measured in a subgroup of 1604 subjects who underwent polysomnography. The authors noted that increased AHI was associated with rise in CAC in men aged ≤ 65 years and in women of any age. Doubling of the AHI was associated with a 19% increase of CAC in men aged ≤ 65 years and with a 17% increase in women of any age [18].

Sorajja et al. studied 202 patients with no history of coronary artery disease who underwent electron-beam CT within 3 years of polysomnography. The authors found a strong association between the severity of OSA and presence of atherosclerosis as measured by CAC. Median and mean CAC scores were significantly higher in OSA patients compared to patients without OSA ($p<0.001$). Median, mean and percentile scores of CAC increased with increasing OSA severity [19].

Vrints and co-workers aimed to investigate the effect of 6 months of Continuous Positive Airway Pressure (CPAP) therapy on coronary calcium burden. Twenty eight moderate to severe OSA patients (AHI>20) were included in the study. These patients were free from confounding factors for Coronary Artery Disease (CAD) like smoking, hypertension, diabetes and

hypercholesterolemia. Patients used at least 4 hrs of daily CPAP. Following six months of CPAP, CAC scores remained equal (CACS before CPAP: 68 ± 85 , after CPAP: 71 ± 91), ($p=0.44$). The authors concluded that 6 months of CPAP does not significantly influence the calcific coronary plaque burden in OSA patients [20].

In conclusion, use of non invasive technique for measurement of atherosclerosis has evolved over the last decade in the form of computed tomographic coronary artery calcium scoring. CAC scoring to assess the underlying atherosclerosis on special population subgroup of OSA patients have shown promise. By predicting the future risk of cardiovascular events based on calcific plaque burden it helps in better risk stratification and may modify treatment decisions. The major limitation to its widespread use is its cost. However judicious use of this non invasive marker in patients with moderate to severe OSA with additional cardiovascular risk factors may help in defining the extent of cardiovascular compromise thereby warranting appropriate preventive measures to halt its further progression.

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