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CLINICAL REVIEW

Systematic review on noninvasive assessment of subclinical cardiovascular disease in obstructive sleep apnea: new kid on the block!



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SUMMARY

Patients with obstructive sleep apnea (OSA) have a high burden of cardiovascular disease (CVD) but a causal relationship between OSA and atherosclerotic CVD remains unclear. We systematically reviewed the literature analyzing the relationship. A review of the Medline database for studies noninvasively evaluating subclinical CVD in OSA was conducted. A total of fifty-two studies were included in this

Across the studies the prevalence of atherosclerosis, as assessed by coronary artery calcification, carotid intima-media thickness, brachial artery flow-mediated dilation and pulse wave velocity was higher in patients with OSA and correlated with increasing severity and duration of OSA.

This study shows OSA is an independent predictor of subclinical CVD as CVD is more likely to occur in patients with long standing and severe OSA. Further research is however necessary to identify specific OSA populations that would benefit from aggressive screening.

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Introduction

Obstructive sleep apnea (OSA) is a clinical disorder characterized by alternating episodes of apnea and hypopnea. OSA is defined as an apnea/hypopnea index (AHI) of ≥ 5 events/h. The burden is enormous as it affects about 4% of middle-aged men and 2% of middle-aged women [1,2]. OSA affects an estimated 15 million adult Americans [3]. It is estimated that 93% of women and 82% of

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men with moderate to severe sleep apnea syndrome have not been clinically diagnosed [4]. The prevalence of OSA is slated to increase considerably in concert with the global obesity pandemic. This disorder is associated with high rates of morbidity and mortality [5]. Moderate to severe sleep apnea has been described as an independent predictor of mortality [6] and it is well established that these patients have an increased risk of cardiovascular disease (CVD) and cardiovascular death [5,7–9]. However, whether early accelerated atherosclerosis and endothelial dysfunction are the primary drivers of this phenomenon remains to be clearly established [10].

Early recognition of atherosclerotic changes in these patients may significantly impact risk stratification and subsequent risk factor reduction in these patients. Traditional risk stratification has

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	Search Terms	Search Items
1	Sleep Apnea	22986
2	Cardiovascular Disease Risk	3782
3	Inflammation	250243
4	Atherosclerosis	76187
5	Atherosclerosis Progression	646
6	Endothelial Function	10286
7	Outcomes Cardiovascular Disease	14
8	Subclinical Atherosclerosis	1233
9	Coronary Artery Calcium	995
10	Carotid Intima Media Thickness	2863
11	CT Angiography	4701
12	Ankle Brachial Index	2528
13	1 and 2	14
14	1 and 3	457
15	1 and 4	245
16	1 and 5	2
17	1 and 6	84
18	1 and 7	0
19	1 and 8	7
20	1 and 9	0
21	1 and 10	23
22	1 and 11	1
23	1 and 12	4
24	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	334904
25	1 and 24	735
26	2 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12	95613
27	1 and 26	338
28	Limit 27 to Abstracts, English Language and Humans	264
29	Manual Review of 28	52
	I .	

Fig. 1. Search flow chart.

relied on scoring systems such as the Framingham risk score [11]. However, newer modalities that assess coronary artery calcium (CAC), carotid intima-media thickness (CIMT), pulse wave velocity (PWV) and flow-mediated dilation (FMD) provide refined assessment of endothelial dysfunction and subclinical atherosclerosis. The presence of a significant association between OSA and markers of early subclinical CVD would warrant the development of a strategy to consider early detection of these changes in these patients and may promote more aggressive therapeutic approaches. Such an association would also provide evidence for pertinent stakeholders to consider whether OSA warrants being included as one of the risk factors in the algorithms for determination of future risk of CVD events. As a result, in this systematic review, we sought to analyze the relationship between OSA and markers of subclinical CVD.

Methods

An electronic search of the Medline database (National Library of Medicine, Bethesda, MD) was carried out through OvidSP (Ovid, New York, NY) (Fig. 1). We included literature published up to December 2013. The keywords employed for the search were "sleep apnea", "cardiovascular disease risk", "atherosclerosis", "atherosclerosis progression", "endothelial function", "cardiovascular disease outcomes", and "subclinical atherosclerosis". These terms were combined with "coronary artery calcium", "carotid intimamedia thickness", "computed tomography (CT) angiography", and "ankle brachial index". The search was limited to include abstracts and full-text, English language publications from studies in adult human subjects. The search results were reviewed and studies which evaluated the relationship between OSA and markers of

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