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REVIEW

Aortic diseases and obstructive sleep apnea

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ABSTRACT

INTRODUCTION: Obstructive sleep apnea (OSA), particularly moderate-to-severe OSA, increases all-cause mortality as well as cardiovascular events, and continuous positive airway pressure (CPAP) therapy can reduce cardiovascular events and mortality. In 2003, it was first shown that patients with thoracic aortic dissection (AD) presented a high prevalence of previously undiagnosed and frequently severe OSA. Since then, a number of authors have investigated the association of aortic diseases (including thoracic and abdominal aortic aneurysm as well as AD) with OSA.

EVIDENCE ACQUISITION: In the present article, we reviewed, with a systematic literature search through May 2015, currently available clinical studies investigating the association of aortic diseases with OSA.

EVIDENCE SYNTHESIS: It is suggested that OSA is highly prevalent in patients with aortic diseases and associated with aortic expansion. Through the nocturnal perturbations of intermittent hypoxia, intrathoracic pressure swings, and increased sympathetic neural activation, OSA patients appear to be at increased risk for vascular changes related to oxidative stress, inflammation, and endothelial dysfunction, which may present as risks for aortic diseases. Despite currently available findings, it remains unclear whether common etiology leads to both OSA and aortic diseases or whether OSA itself causes aortic diseases.

CONCLUSIONS: The following types of studies with long-term follow-up would be required: 1) a prospective cohort study comparing the incidence of aortic diseases in OSA patients with that in non-OSA subjects and 2) a randomized controlled trial determining whether CPAP therapy for OSA reduces the incidence of aortic diseases.

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Key words: Aortic aneurysm - Obstructive sleep apnea - Incidence.

Introduction

Several meta-analyses have recently confirmed that obstructive sleep apnea (OSA), particularly moderate-to-severe OSA, increases all-cause mortality as well as cardiovascular events [1-4] and further that continuous positive airway pressure (CPAP) therapy can reduce cardiovascular events and mortality.[2, 5] In 2003, Sampol *et al.*[6] first showed that patients with thoracic aortic dissection (AD) presented a high prevalence of previously undiagnosed and frequently severe OSA. Since then, a number of authors have investigated the association of aortic diseases (including thoracic [TAA] and abdominal aortic aneurysm [AAA] as well as AD) with OSA. In the present article, we reviewed, with a systematic literature search, currently available clinical studies investigating the association of aortic diseases with OSA.

Evidence acquisition

Databases including MEDLINE and EMBASE were searched through May 2015 using Web-based search engines (PubMed and OVID). Relevant studies were also identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. All references were

downloaded for consolidation, elimination of duplicates, and further analysis. Search terms included "sleep apnea" or "sleep apnoea"; "aorta" or "aortic"; and "aneurysm", "dissection", or "dissecting". Eligible articles were clinical studies investing the association of aortic diseases (including TAA, AAA, and AD) with OSA.

Evidence synthesis

AAA/TAA and OSA

Mason *et al.*[7] investigated the prevalence of OSA in 127 patients (67.9±6 years) with AAA (included in an AAA surveillance program) and a possible association between OSA and rate of AAA expansion determined retrospectively from available ultrasound measurements. A >4% oxygen desaturation index (ODI) of >10 events/hour and apnea-hypopnea index (AHI) of >10 events/hour was found in 40.5% and 41.5% of the patients, respectively. Patients with an ODI of >30 events/hour (median baseline AAA diameter, 41 mm) had a significantly faster yearly AAA expansion rate (median, 2.9 mm/year) than patients with an ODI of 0-5 events/hour (median baseline diameter, 39 mm) (median expansion rate, 1.2 mm/year; P<0.05) and 6-15 events/hour (median baseline diameter, 40 mm) (median expansion rate, 1.3 mm/year; P<0.05) during interval between the first and last AAA measurements of median 18 months. In multivariate regression analysis controlling for cardiovascular risk factors and medications, the ODI of >30 events/hour remained an independent risk factor for AAA expansion (adjusted mean difference [MD] in AAA expansion rate between the highest and the lowest ODI group, 2.9±1.1 (standard error [SE]) mm/year; P=0.009). In patients with AAA, OSA is highly prevalent, and severe OSA may be a causal factor for faster AAA expansion. Limitations discussed by the authors were: 1) not studying patients >75 years; 2) performing the sleep studies once at the end of the AAA monitoring period; 3) relatively small actual number of subjects with severe OSA; and 4) using the simple sleep study technique.[7]

Saruhara *et al.*[8] examined the incidence by location of OSA as a complication in 32/36 patients (72.5±4.9/70.8±6.3 years) with AAA/TAA. The ≥3% ODI was significantly higher in the TAA (17.2±12.8 events/hour; P=0.045) and AAA groups (19.6±12.5 events/h; P=0.003) than control group consisting of 32 patients (68.1±8.7 years) with coronary risk factors who were matched with the aortic disease group for age, gender, and body mass index (BMI) (8.8±5.4 events/hour). The incidence of moderate-to-severe OSA (AHI≥15 events/hour) was significantly higher in the TAA (40.6%; P=0.026) and AAA groups (52.8%; P=0.001) than control group (15.6%), while no significant difference was found between the TAA and AAA groups with respect to these variables. These results suggest that OSA may be one of risks for TAA/AAA. Limitations discussed by the authors were: 1) many of the patients waiting for elective surgery and having an aortic aneurysm that had already enlarged (it was difficult to clarify the correlation between the severity of OSA and the intensity of aneurysm diameter enlargement); 2) evaluating patients not by overnight polysomnography but by a sleep study using a portable respiratory monitor; 3) the majority of the patients already being treated for hypertension (it was difficult to discuss the involvement of OSA in the pathogenesis and progression of aortic disease without considering the pathogenetic role of hypertension); and 4) not measuring inflammatory markers indicative of a correlation between OSA and aortic disease.[8]

Bianchi *et al.*[9] sought to determine the risks for OSA (assessed with the Berlin Questionnaire) and cardiometabolic disease (assessed by several biomarkers, with special focus on the lipid accumulation product [LAP] and the triglyceride-glucose index [TGI], 2 validated screening indicators of cardiometabolic disease related to central obesity and insulin resistance, respectively) in 3020 elderly (73.4±8.7 years) patients with diagnosed small (3.5±0.8-cm) AAA. After adjusting for age effects, the high OSA risk (2 or 3 category points) group (60.6%) showed higher cardiometabolic risk in terms of insulin, hemoglobin A1c, triglycerides, TGI, LAP, and lower physical activity expressed as blocks walked/day during the last year. Cardiometabolic disease and OSA may both amplify risk for AAA expansion. Limitations discussed by the authors were: 1) the sample limiting to patients with only small AAA diameters and 2) not having polysomnography data by which to establish presence/absence or severity of OSA.[9]

AD and OSA

Our search identified 4 case-control studies included patients with AD and subjects without AD. First, by the use of clinical questionnaire and polysomnogra-

phy, Sampol *et al.*[6] studied 19 consecutive patients with thoracic AD (56.1±11.9 years) and 19 hypertensive patients of similar age, sex, and BMI (53.0±9.5 years). Patients with AD presented a higher AHI (28±30.3 *versus* 11.1±10.4 events/hour; P=0.032). Additionally, 7 patients with AD presented an AHI of >30 events/hour *versus* one patient in the control group (P=0.042). Patients with thoracic AD presented a high prevalence of previously undiagnosed and frequently severe OSA. Limitations discussed by the authors were: 1) conducting the sleep study several months after the diagnosis of AD; 2) a case-control study not permitting the authors to elucidate whether OSA is a risk factor for AD; and 3) likely existence of confounding factors (other than the controlled main known variables for the development of both entities) to influence their results.[6]

Second, Saruhara *et al.*[8] examined the incidence by location of OSA as a complication in 27 patients (67.4±7.4 years) with AD. The ≥3% ODI was significantly higher in the AD groups (19.9±16.8 events/hour; P=0.005) than control group consisting of 32 patients (68.1±8.7 years) with coronary risk factors who were matched with the aortic disease group for age, gender, and BMI (8.8±5.4 events/hour). The incidence of moderate-to-severe OSA (AHI≥15 events/hour) was significantly higher in the AD groups than control group (51.9% *versus* 15.6%; P=0.003). Furthermore, no significant differences were found between the thoracic and abdominal AD subgroups with respect to AHI (19.9±17.1 *versus* 11.7±9.4 events/hour) and ≥3% ODI (22.2±17.9 *versus* 13.2±11.8 events/hour) as well as the incidences of moderate-to-severe OSA (55.0% *versus* 28.6%). These results suggest that OSA may be one of risks for AD.[8]

Third, Naito *et al.*[10] compared the prevalence of nocturnal intermittent hypoxia and re-oxygenation (IHR) (expressed as ≥3% ODI) among 29 patients with AD (59.8±11.4 years) with that in 59 control subjects (consecutive patients who received sleep study because of severe snoring) without AD (58.9±13.4 years), and investigated whether there is an independent association between AD and IHR. The percentage of either moderate-to-severe (≥15) or severe (≥30) IHR (55.2% *versus* 15.3%; P<0.001) was significantly higher in the AD than control group (75.9% *versus* 52.5%, P=0.04; or 55.2% *versus* 15.3%, P<0.001). The mean ≥3% ODI of patients with AD was significantly higher than that of control subjects (34.8±23.1 and 19.0±14.1; P=0.003). In multivariate analysis, ≥3% ODI was significantly associated with AD (odds ratio [OR] 1.44; 95% confidence interval [CI]: 1.08 to 1.91; P=0.01). The close association between AD and IHR (a major component of OSA) is suggested. Limitations discussed by the authors were: 1) not examining polysomnography, a well-established examination for sleep study; 2) performing the sleep study in the setting when the patients were receiving the treatment of AD; 3) the exclusion of atherosclerotic diseases in the control group solely based on medical history and impossible ruling out the presence of sub-clinical atherosclerotic diseases in the control group; and 4) the relatively small number of the subjects and impossible performing a sample size calculation because of unknown prevalence of IHR among patients with AD.[10]

Fourth, Zhang *et al.*[11] performed a cross-sectional study in 82 patients with Stanford type-B AD (50.17±11.61 years) and 116 controls matched for confounding factors (53.82±14.78 years). Cases had significantly higher Berlin scores than controls (high risk, 75.6% *versus* 54.3%; P=0.002). Among patients and controls, OSA frequency was 81.7% and 67.2%, respectively (P=0.024). Cases had higher AHI (median, 17.5 *versus* 7.0 events/hour; P=0.001) and mean ≥4% ODI (median, 16 *versus* 7 events/hour; P=0.005) and a lower SaO_2 during sleep (median, 81% *versus* 86%; P=0.038) than controls. In a logistic regression model, OSA was independently associated with Stanford type-B AD (OR=1.063; 95% CI: 1.010 to 1.120; P=0.020). Two patients (36 and 37 years) in the control group developed AD during the prospective study with 19.8±6.3-month follow-up, and both patients had serious OSA (AHI>60 events/hour) and high Berlin risk, respectively. Hence, OSA is highly prevalent and independently associated with Stanford type-B AD. Limitations discussed by the authors were: 1) a cross-sectional study preventing the authors to define a potential causal relationship between OSA and AD assessed by the severity of disease; 2) not assessing some data (high-sensitivity C-reacting protein and aortic diameter); 3) unavailable some polysomnography data (central AHI, obstructive AHI, arousal index, and sleep stage); 4) the relatively small number of subjects in the prospective part and impossible performing a sample size calculation because of unknown OSA incidence and prevalence among AD patients; 5) lack of precise information about patients treated for hypertension and other medical problems interfering with OSA

diagnosis and thus with the relation between OSA and AD; and 6) patient follow-up of only 2 years.[11]

The following 2 studies enrolled exclusive patients with AD. First, Hata *et al.*[12] assessed the relationship between acute AD (AAD) and sleep disorders in a working population. Seventy (50.4%) of 139 <65-year subjects with AAD (54.3±8.5 years) suffered from sleep disorders: insomnia was reported by 35 patients (50%), sleep deprivation by 31 patients (44.3%), and OSA was present in 43 patients (61.4%). The average AHI was 22.0±7.5 events/hour, requiring appropriate treatment. Sixty-six (94.3%) complained of severe mental and physical stress in daily life. Sleep disorders are considered one of the risk factors for the occurrence of AAD at younger active ages.[12]

Second, Yanagi *et al.*[13] assessed the prevalence of OSA in patients with AAD and delineated the characteristics of patients who have AAD with OSA. Of 95 consecutive patients with AAD, the OSA-positive group consisted of 12 patients (12.6%), 8 with type A and 4 with type B dissection. Age was significantly lower in the OSA-positive (47.2±8.5 years) than OSA-negative group (64.9±10.3 years; P<0.001). The male/female ratio was significantly higher in the OSA-positive (12/0) than OSA-negative group (39/44; P<0.001). The BMI was significantly greater in the OSA-positive (29.3±3.6) than OSA-negative group (23.5±4.5; P<0.001). All 12 patients in the OSA-positive group had hypertension. Patients who have AAD with OSA are characterized by being tall, fat, and relatively young men with hypertension, and OSA may be a risk factor for AAD in middle-aged men.[13]

Aortic diameter and OSA

Baguet *et al.*[14] assessed the relationship between OSA, its vascular consequences, and aortic root size in 156 newly diagnosed OSA patients free of cardiovascular disease and medication (49±10 years). In univariate analysis, greater aortic root size was associated with older age (P=0.03) and severity of OSA as expressed by mean nocturnal oxygen saturation (SpO_2) (ρ=-0.20; P=0.015). Moreover, greater aortic root size was associated with higher diastolic blood pressure (BP), measured both clinically (P=0.0005) and by 24-hour ambulatory BP monitoring (P=0.02), and carotid-to-femoral pulse wave velocity (P=0.03). Mean nocturnal SpO_2 was correlated with baroreflex sensitivity (BRS) (ρ=0.28; P=0.0008), thus potentially influencing BP values and arterial stiffness. In multivariate stepwise regression analysis, diastolic BP was the only significant factor for aortic root size (P=0.0003). In OSA patients, nocturnal hypoxemia decreased BRS and increased diastolic BP, which was the main factor influencing aortic root size.[14]

Tachikawa *et al.*[15] retrospectively reviewed 427 patients aged >45 years who underwent polysomnography and abdominal computed tomography. Adjusted (by age, body surface area, smoking, and hypertension) diameter was not significantly different among OSA severity categories (58 patients with non-OSA [AHI<10, 63.1±9.4 years], 167 patients with mild-to-moderate OSA [AHI 10-30, 63.5±9.4 years], and 202 patients with severe OSA [AHI[SE]≥30, 63.1±9.6 years]) at the upper (21.0±0.25 [SE], 21.3±0.15 [SE], and 21.4±0.13 [SE] mm, respectively) and infra-renal aorta (19.5±0.35 [SE], 20.2±0.20 [SE], and 19.9±0.19 [SE] mm, respectively) but was significantly different at the lower abdominal aorta (17.3±0.25 [SE], 18.2±0.14 [SE], and 18.2±0.13 [SE] mm, respectively, P=0.006) with larger diameters in patients with OSA. Multivariate linear regression analyses revealed that risk profiles for aortic dilatation varied according to the location and gender and that OSA (AHI≥10 events/hour) was an independent risk factor for infra-renal and lower abdominal aortic dilatation only in men (standardized partial regression coefficient = 0.10 and 0.18, P=0.049 and 0.001, respectively). It is suggested that OSA may enhance dilatation of the distal abdominal aorta in men. Limitations discussed by the authors were: 1) the cross-sectional nature of the study precluding any conclusions regarding the causal relation between OSA and abdominal aortic diameters; 2) the lack of a dose-response relation between OSA and aortic diameters most likely implying the presence of other confounders related to aortic dilatation; 3) the study population of Japanese participants with suspected sleep-disordered breathing (potential selection bias); and 4) data not including a family history of AAA, which did not allow the authors to evaluate possible genetic predispositions.[15]

Marfan syndrome and OSA

Kohler *et al.*[16] performed a sleep study in 61 patients with Ghent criteria positive Marfan syndrome (38.3±12.9 years) and in 26 control subjects matched for age, gender, height, and weight (37.2±9.8 years). More patients with Marfan syndrome than controls had

OSA with AHI>5 (32.8% compared with 11.5%; MD 21.3%; 95% CI: 4.2 to 38.3%; P=0.04) and AHI>15 (18.0% compared with 0%; MD 18.0%, 95% CI: 8.4 to 27.7%; P=0.02). Mean aortic root diameter was significantly greater in patients with OSA (4.5±0.6 cm) compared with those without OSA (3.7±0.6 cm; MD 0.8 cm; 95% CI: 0.4 to 1.2 cm; P<0.0001), and AHI was correlated with aortic root diameter (ρ=0.50; 95% CI: 0.26 to 0.69; P=0.0003). The prevalence of OSA is considerably higher in patients with Marfan syndrome than matched control subjects, and OSA may be a risk factor for aortic root dilatation in Marfan syndrome.[16]

Kohler *et al.*[17] studied the effect of OSA on aortic events in Marfan syndrome. Of 44 patients (mean age 37.4 years), 15 patients (34.1%) had OSA defined as AHI of >5 events/hour. Five patients had an aortic event within the median 29-month follow-up, and median event-free survival was 51.6 months. Event-free survival was significantly shorter in patients with OSA compared to patients without OSA (P=0.012). In univariate analysis, AHI was associated with aortic events (hazard ratio [HR] 1.09; 95% CI: 1.01 to 1.18, P=0.023). Taking the interaction between BMI and AHI into account increased the HR for AHI (HR 1.75; 95% CI: 1.003 to 3.048, P=0.049). This association was, however, no longer significant (P=0.246) when other covariates were forced into the multivariate analysis. These data suggest that aortic event-free survival may be shorter in patients with Marfan syndrome and OSA compared to patients without OSA. Limitations discussed by the authors were: 1) not using full polysomnography and 2) the relatively small number of patients with Marfan syndrome without previous aortic root replacement.[17]

Discussion

Wang *et al.*[3] recently conducted a meta-analysis including 12 prospective cohort studies involving a total of 25,760 participants. The overall combined relative risks (RRs) for individuals with severe OSA compared with individuals with an AHI of <5 events/hour were 1.79 (95% CI: 1.47 to 2.18; P<0.001) for CVD, 1.21 (95% CI: 0.75 to 1.96; P=0.432) for incident fatal and non-fatal coronary heart disease, 2.15 (95% CI: 1.42 to 3.24; P<0.001) for incident fatal and non-fatal stroke, and 1.92 (95% CI: 1.38 to 2.69; P<0.001) for deaths from all-causes. A positive association with cardiovascular disease (CVD) was observed for moderate OSA (RR 1.15; 95% CI: 1.01 to 1.32; P=0.036) but not for mild OSA (RR 0.98; 95% CI: 0.87 to 1.11; P=0.748). The results of the dose–response relationship indicated that per 10-unit increase in the AHI was associated with a 17% greater risk of CVD in the general population (RR 1.17; 95% CI: 1.07 to 1.29; P=0.001). Severe OSA significantly increases CVD risk, stroke, and all-cause mortality and that moderate but not mild OSA is positively associated with CVD.[3] Furthermore, another recent meta-analysis [5] including a total of 4620 patients from 11 reports suggests that CPAP therapy can effectively reduce the incidence of cardiovascular death and non-fatal cardiovascular events in patients with OSA, particularly in patients with moderate-to-severe OSA. Although the underlying mechanisms by which OSA increases the risk of CVD are uncertain, several different pathways are likely involved.[3] During non-rapid-eye movement sleep, metabolic rate, sympathetic nervous activity, blood pressure, and heart rate all decrease, whereas cardiac vagal tone increases from wakefulness, and OSA interrupts this cardiovascular quiescence by triggering a cascade of acute hemodynamic, autonomic, chemical, inflammatory, and metabolic effects, with chronic after-effects capable of initiating or exacerbating CVD.[18]

Pathophysiology mechanisms of the association of aortic disease with OSA could be explicated by the following findings. First, the repeated hypopneas and apneas in OSA occur from repetitive partial or complete closure of the upper airway despite ongoing respiratory efforts, and each respiratory event is associated with increased inspiratory effort resulting in swings in intrathoracic pressure occasionally even to the extremes of -80 cm of water during inspiration.[19] Repeated changes in intra-thoracic pressure, regarded as intimately related to factors of fluctuations of dp/dt_{max}, have significant effects on AD pathogenesis.[11] Further, the pressure difference between the intra-aortic and intra-thoracic space results in an increase in trans-mural pressure gradient, which may contribute to an increase in aortic wall stress/tension.[19] If the excessive shear stresses imposed by concomitant hypertension persist, the inner wall's transformation and damage to the aorta will be accelerated.[11]

Second, intermittent hypoxia in OSA activates the renin–angiotensin system and increases the levels of endothelin-1.[19] The subcutaneous infusion of angiotensin II has been shown to induce AAA in Apo56 knockout

mice, which suggests that renin–angiotensin system may act as a molecular and therapeutic target for treating AAA.[20] Endothelin-1 also plays a role in progression of atherosclerosis and AAA formation by decreasing high-density lipoprotein, and increasing oxidative stress, inflammatory cell infiltration, and matrix metalloproteinase-2 in perivascular fat, vascular wall, and atherosclerotic lesions.[21]

Third, OSA appears to result in oxidative stress (as evidenced by elevated levels of xanthine oxidoreductase, lipid peroxidation, and the presence of reactive oxygen species) and there may be a decrease in antioxidant capacity in OSA patients.[19] As AAA size increases, plasma levels of antioxidants (vitamins C and E, β-carotene, ubiquinone) decrease and specific markers of lipid peroxidation (Cu/Zn ratio and isoprostanes) increase, which suggests the potential role of the oxidative stress in AAA.[22]

Fourth, endothelial dysfunction appears to be prevalent in those with OSA.[19] Endothelium dependent vasodilation has a linear and negative correlation with the AAA diameter, and the positive correlation between the flow-mediated dilation of the brachial artery and C-reactive protein supports the hypothesis that inflammation and endothelial dysfunction are processes associated with the physiopathology of AAA and vary with their growth.[23]

Fifth, various studies support the notion that OSA is a state of systemic inflammation and therefore predisposes atherosclerosis.[19] Although the initial trigger is unknown, many believe that hypoxia secondary to repeated upper airway closure might be the initial insult. Levels of C-reactive protein, interleukin (IL)-6, nuclear factor-kappa B (NF-κB), tumor necrosis factor-alpha (TNF-α), intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1, and E-selectin elevate in OSA patients, which could suggest that OSA is a predisposing factor for atherogenesis.[19] In a meta-analysis [24] of 13 studies enrolling 1029 cases and 924 controls, circulating IL-6 levels are greater in patients with AAA than those in subjects without AAA, which suggest that greater circulating IL-6 levels are associated with AAA presence. Endothelial NF-κB activation up-regulates adhesion molecule expression, which may trigger macrophage infiltration and inflammation in the adventitia and media; and thus the endothelium plays important roles in vascular remodeling and aneurysm formation through its intracellular NF-κB signaling.[25] Further, TNF-α is the most consistently upregulates cytokines in large AAA.[26] Patients with AAA and aortic occlusive disease display a significant upregulation of the expression of ICAM-1, suggesting a role for this protein in the initiation or maintenance of degenerative aortic diseases.[27] Different forms of ICAM-1 (ICAM-1 and soluble ICAM-1), present on or released by the activated aortic endothelium, may be involved in leucocyte adhesion to and migration into the vessel wall.[28] Levels of VCAM-1 are increased in the circulation but not in aortic tissue of people with AAA.[29] In apolipoprotein E-deficient mice, angiotensin II infusion results in an increased expression of E-selectin as well as TNF-α and IL-6.[30] In summary, through the nocturnal perturbations of intermittent hypoxia, intrathoracic pressure swings, and increased sympathetic neural activation, OSA patients appear to be at increased risk for vascular changes related to oxidative stress, inflammation, and endothelial dysfunction,[19] which may present as risks for aortic diseases.

Notwithstanding the probable association of aortic disease and OSA, there has been no evidence that CPAP therapy for OSA can reduce the incidence of aortic diseases. However, CPAP is suggested to reduce the incidence of cardiovascular events in patients with OSA. Wang *et al.*[5] recently performed a meta-analysis including a total of 4620 patients from 11 reports to investigate the effects of CPAP therapy on the incidence of cardiovascular death and non-fatal cardiovascular events in patients with OSA, particularly in patients with moderate-to-severe OSA (AHI≥20). The meta-analysis showed that, compared with patients without CPAP therapy, the risk of cardiovascular death was reduced by 68% in patients undergoing CPAP therapy (OR 0.32; 95% CI: 0.24 to 0.41, P<0.0001). Additionally, the risk of non-fatal cardiovascular events was reduced by 43% in patients undergoing CPAP therapy compared with patients without CPAP therapy (OR 0.57; 95% CI: 0.43 to 0.75; P<0.0001). Subgroup analysis on patients with moderate-to-severe OSA revealed that CPAP therapy reduced the risk of cardiovascular death by 71% compared with patients without CPAP (OR 0.29; 95% CI: 0.18 to 0.47, P<0.0001).[5] Amplifying these findings, CPAP therapy for OSA may reduce the incidence of aortic diseases.

A high prevalence of OSA exists in patients with Marfan syndrome. The potential reasons are craniofacial abnormalities and lax upper airway muscles, which lead to high nasal airway resistance and upper airway collapse.[31]

Moreover, OSA mechanically may deteriorate aortic dilatation and accelerate progression of aortic aneurysm.

Despite the above-mentioned findings, it remains unclear whether common etiology leads to both OSA and aortic diseases or whether OSA itself causes aortic diseases. The following type of studies with long-term follow-up would be required: 1) a prospective cohort study comparing the incidence of aortic diseases in OSA patients with that in non-OSA subjects, and 2) a randomized controlled trial determining whether CPAP therapy for OSA reduces the incidence of aortic diseases.

Conclusions

In conclusion, OSA is highly prevalent in patients with aortic diseases and associated with aortic expansion. To establish causal relationship between aortic diseases and OSA, a prospective cohort study or randomized controlled trial would be required.

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