Effects of obstructive sleep apnea and its treatment on cardiovascular risk in CAD patients

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Summary
This study, in optimally treated CAD patients with newly diagnosed OSA, focused on (1) The relationships between OSA and serum biomarkers of four potential pathways of cardiovascular injury in OSA: high-sensitivity C-reactive protein (hs-CRP), endothelin-1 (ET-1), N terminal pro B type natriuretic peptide (NT-proBNP) and fibrinogen; and (2) The effect of continuous positive airway pressure (CPAP) therapy on these markers.

151 Chinese patients with proven CAD and standard medication were enrolled. After polysomnography, patients were classified into four groups according to apnea–hypopnea index (AHI): no OSA (n = 25); mild OSA (n = 50); moderate OSA (n = 43); severe OSA (n = 33). Morning levels of hs-CRP, ET-1, NT-proBNP and fibrinogen were assayed and repeated in severe OSA patients after 3-months CPAP treatment.

Hs-CRP was greater in patients with severe OSA than those with no OSA or mild OSA (P < 0.001, P < 0.003; respectively). After adjustment for confounders, the hs-CRP levels correlated most strongly with AHI and oxygen desaturation index (ODI) (r = 0.439, P < 0.001; r = 0.445, P < 0.001; respectively). In stepwise multiple linear regressions, the strongest predictor of hs-CRP levels was ODI (P < 0.001). After 3 months of CPAP treatment, the hs-CRP levels deceased (P = 0.005) in CAD patients with severe OSA.

In CAD patients on current optimal medications, hs-CRP is significantly correlated with the severity of OSA, and the elevated hs-CRP levels can be decreased by CPAP. This suggests that OSA could activate vascular inflammation in CAD patients despite current best practice medications.

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Introduction

Obstructive sleep apnea (OSA) is a major public health hazard affecting 3–5% of the adult population. Increasing evidence is emerging that OSA is a risk factor for coronary artery disease (CAD)\(^1\,^2\). Middle-aged patients with untreated OSA are at high risk of developing coronary artery disease. Patients with established coronary artery disease have a high prevalence of sleep disordered breathing\(^3\,^4\) and the long-term prognosis is poor in patients with both CAD and untreated OSA\(^3\,^5\). New cardiovascular events reduced in CAD patients who had co-existing OSA and accepted sleep apnea treatment versus those who refused treatment\(^6\).

While definitive proof of a causal link between OSA and CAD awaits the results of well-designed randomized controlled trials of OSA treatment, there is considerable uncertainty about which patho-physiological mechanisms in OSA might mediate vascular injury and CAD progression\(^7\). A number of neural and humoral abnormalities including sympathetic activation, vascular endothelial dysfunction, inflammation, abnormal coagulation and metabolic dysregulation\(^8\,^9\), have been reported in patients with OSA which may be implicated in the initiation and progression of cardiovascular diseases. However, whether continuous positive airway pressure (CPAP) treatment for OSA could inhibit the putative pathways of vascular injury remains controversial.

The present study, to our knowledge, is the first study to assess the relationship of OSA with various biomarkers of cardiovascular risk in Chinese subjects with optimally treated CAD. In this way we sought to determine which pathways were most strongly associated with OSA and might therefore warrant further evaluation for CAD secondary prevention in the future. In the first part, we conducted a cross-sectional analysis examining the relationship between OSA severity and four key biomarkers: (1) endothelin-1 (ET-1), a marker of endothelium dysfunction, (2) high-sensitivity C-reactive protein (hs-CRP), a marker of inflammation, (3) N terminal pro B type natriuretic peptide (NT-proBNP), a marker of ventricular strain, and (4) fibrinogen, a marker of hyper-coagulation. We next evaluated the effect of CPAP treatment on these biomarkers in CAD patients with severe OSA.

Methods

Patient selection

The study was approved by the Human Ethics committee of Fuwai Hospital and all patients gave their written informed consent. Consecutive CAD patients were recruited from the fifth inpatient department of the Fuwai Hospital, from March 2008 to June 2010.

Inclusion criteria

(1) Men and women aged between 25 and 80 years; (2) CAD verified by coronary angiography (either ≥70% stenosis in one major coronary artery or ≥50% stenoses in two or more major coronary arteries); (3) On appropriate medications for at least 3 months for CAD risk reduction as per AHA/ACC guidelines\(^8\); (4) Normal routine laboratory screening results including white cell count, serum electrolytes, glucose, thyroid-stimulating hormone (TSH) and urinary albumin.

Exclusion criteria

(1) predominantly central sleep apnea; (2) heart failure with New York Heart Association Functional Classification III–IV; (3) pulmonary diseases causing dyspnea at rest or on minimal exertion; (4) plasma alanine aminotransferase (ALAT) > 200 U/L; (5) chronic inflammatory disorders such as rheumatoid arthritis or inflammatory bowel disease; (6) plasma creatinine >200μmol/L; (7) acute cerebrovascular insult within 3 months; (8) history of drug abuse; (9) pregnancy; (10) history of blood donation less than 1 month before entry into the study; or (11) previous treatment with CPAP. If patients had suffered from an acute systemic inflammatory process such as infection, trauma, or infarction, blood sampling was delayed until the patient had made a full recovery.

Sleep studies

All patients underwent overnight Type 3 polysomnography (PSG) in the Sleep Center of Fuwai Hospital using an Embletta recording device (Embletta 9, Medcare Flaga, Reykjavik, Iceland) which recorded nasal airflow (with an oro-nasal thermistor), finger pulse oximetry, thoracic and abdominal movement, body position and snoring. The PSG device was programmed to begin recording at the patient’s usual bedtime and was turned off at the time of the patient’s final morning awakening. All polysomnography data were manually scored using standard criteria\(^9\) by a sleep technician, who was blinded to the clinical characteristics of the patients. Hypopnea was defined as more than 50% reduction in nasal airflow for ≥10 s which was accompanied by a ≥4% fall in artery oxygen saturation (SaO\(_2\)). Apnea was defined as a cessation in airflow for ≥10 s.

The apnea-hypopnea index (AHI) was calculated as the total number of respiratory events (apneas plus hypopneas) per hour of overnight recording. Patients were divided into one of four groups depending on their AHI: no OSA (AHI <5 events per hour), mild OSA (AHI 5 to <15), moderate OSA (AHI 15 to <30), and severe OSA (AHI≥30). Other PSG variables included oxygen desaturation index (ODI), mean SaO\(_2\), minimal SaO\(_2\), and percentage of time with SaO\(_2\)<90%. The Epworth Sleepiness Scale (ESS) was used to measure changes in subjective daytime sleepiness.

Blood samples

In the morning (between 6:00 AM and 6:30 AM), fasting blood samples were drawn from an antecubital vein and collected in appropriate tubes for different measurements. Samples were placed immediately on crushed ice, and centrifuged within 10 min of collection. The supernatant plasma or serum was drawn off and kept in a refrigerator at –80° Celsius for assay. Plasma ET-1 was measured using a commercial, highly sensitive and specific sandwich-enzyme immunoassay (Biomedica, Wien, Austria). Serum hs-CRP was measured using particle enhanced immunonephelometry (Dade Behring, nc. Deerfield, Illinois). Plasma
NT-proBNP levels were measured using an enzyme immunoassay kit (BIOMEDICA, GmbH, Germany). Fibrinogen and other biochemical factors were measured by routine enzymatic method. All samples were processed by technicians blinded to the clinical condition of the patients.

**CPAP treatment**

CAD patients with severe OSA were offered treatment with CPAP. They were prescribed fixed-level CPAP which corresponded to the 95th centile pressure recorded during a single night of in-laboratory pressure titration using an automated pressure setting device (S7 Autoset-T, ResMed, Sydney, Australia), and patients were supplied with a CPAP generator (S6, ResMed, Sydney, Australia) for home use. All the patients were followed-up at three months at which CPAP adherence and AHI were recorded from the machine microprocessor, and repeat fasting blood samples were obtained and processed using the same method at the baseline for the investigational biomarkers as well as serum lipids and fasting blood glucose.

**Statistical analysis**

Statistical analyses were performed on SPSS for Windows, version 16 (SPSS Inc, Chicago, IL). Quantitative variables were expressed as mean ± standard deviation (SD) after checking normality with the Kolmogorov–Smirnov test. The chi-square test was used to compare categorical data. The significance of differences between 2 groups was analyzed with Student’s t test. Differences in variables among the 4 groups were evaluated by analysis of variance (ANOVA) and a Boneronnio correction was applied for multiple comparisons. Relationships between the level of NT-proBNP, fibrinogen, hs-CRP, ET-1 and baseline characteristics were assessed using Pearson correlation coefficient for continuous variables and Spearman correlation coefficient for categorical variables. Both unadjusted and adjusted (for conventional risk factors, such as sex, age, BMI, smoking and drinking status, diabetes mellitus, hypertension, lipid profiles, fasting blood glucose, and medication) associations were calculated to identify variables that were independently associated with the four biomarkers. Multivariate linear regression analysis using a stepwise selection of the explicative variables was undertaken. A value of $p < 0.05$ was considered statistically significant.

**Results**

**Characteristics of the study population**

Of 178 consecutive patients who met the selection criteria for CAD and underwent PSG in the sleep lab, 27 were subsequently excluded because of the following conditions: previous stroke, liver damage, or renal dysfunction (12); recent surgery (1); prior CPAP therapy for sleep disordered breathing (1); failure to comply with recommended statin and anti-platelet medicine (aspirin) (13). This left 151 subjects who were considered suitable for blood biomarker measurements.

Table 1 shows the anthropomorphic data, PSG results, and clinical characteristics of the study population divided into the four OSA severity groups. Twenty-five patients were found to have no OSA, 50 had mild OSA, 43 had moderate OSA, and 33 had severe OSA. Thus of the 151 CAD patients, 83% had OSA and 50% had moderate to severe OSA. There was a marked male predominance of patients in all four categories. As expected, average BMI was significantly higher in the more severe OSA groups.

Levels of hs-CRP were significantly higher in patients with severe OSA (4.29 ± 3.49 mg/L) than patients with no OSA (1.95 ± 1.16 mg/L, $P = 0.003$) or in patients with mild OSA (2.07 ± 1.91 mg/dL, $P = 0.001$; Table 2, Fig. 1). There were no between group difference in the levels of the other biomarkers of cardiovascular risk.

**Correlation between OSA severity and biomarkers of cardiovascular risk**

Pearson correlation coefficients of PSG variables with clinical parameters and investigational biomarkers are given in Table 3. The hs-CRP correlated most strongly with AHI, ODI, minimal SaO2 and percentage of time with SaO2 <90% ($r = 0.439$, $P < 0.001$, Fig. 2; $r = 0.444$, $P < 0.001$; $r = -0.250$, $P = 0.001$; $r = 0.177$, $P = 0.03$; respectively). These correlations remained essentially unchanged after adjustment for confounders. Adjusted correlations between hs-CRP and AHI, ODI, and minimal SaO2 were: $r = 0.439$, $P < 0.001$; $r = 0.445$, $P < 0.001$; $r = -0.249$, $P = 0.003$, respectively.

Stepwise multiple linear regression was used to evaluate the relative strength of association, between hs-CRP and OSA severity (AHI, ODI) as well as the other possible confounders. The strongest predictor of serum hs-CRP levels was ODI ($P < 0.001$), followed by age ($P = 0.005$) and sex ($P = 0.018$). Indices that reflect the intermittent nature of the breathing and gas exchange disturbance (e.g. AHI) appeared to be more strongly associated with increased hs-CRP than parameters of SaO2 (e.g. time with SaO2 <90%).

None of the PSG variables correlated with the levels of NT-proBNP, ET-1 or fibrinogen in univariate analyses. NT-proBNP was, however, strongly correlated with age ($r = 0.193$, $P = 0.009$) although this association was weaker ($r = 0.147$, $P = 0.05$) after adjustment for confounders. In multiple linear regression, only age was found to be was significantly correlated with the NT-proBNP levels ($R = 0.193$, $P = 0.018$). In univariate analyses, clinical parameters that significantly correlated to ET-1 were age ($P = 0.015$). However, in both Pearson’s correlation and stepwise multivariate analysis, there was no reliable predictor for the ET-1 levels. The levels of fibrinogen had no significant relationship with all these related clinical factors.

**Effects of CPAP on biomarkers of cardiovascular risk in patients with severe OSA**

Thirty three consecutively recruited CAD patients with severe OSA were offered CPAP treatment. Four patients declined CPAP treatment after titration and two patients had very poor compliance (i.e. less than 1 h per day). The
27 patients who completed 3 months CPAP treatment had a mean compliance of 4.9 ± 1.2 h per day. CPAP treatment decreased the AHI (47.81 ± 11.30 to 3.49 ± 1.28 events/hr, P < 0.0001) and ESS value (10.67 ± 2.81 to 6.00 ± 2.68, P < 0.001). There was no change in the BMI (27.51 ± 3.08 to 27.25 ± 3.07, P = 0.792) and no new cardiovascular diseases or infectious diseases were detected during the follow-up period.

CPAP significantly decreased hs-CRP (4.18 ± 3.26 to 2.27 ± 2.42 mg/L, P = 0.005; Fig. 3). Changes in AHI after treatment with CPAP were positively correlated with changes in levels of hs-CRP (r = 0.546, P < 0.01) and ESS (r = 0.652, P < 0.01). However, none of the other biomarkers, lipid profiles or glucose changed after 3 months of CPAP treatment.

Discussion

The current study suggested that in Chinese patients with CAD on current optimal medications, the levels of hs-CRP were significantly and independently correlated with the severity of OSA, and the elevated hs-CRP levels can be decreased by CPAP treatment supporting an independent, causal relationship between OSA and systemic inflammation.

These results are consistent with a several previous reports. The observed correlation between AHI and hs-CRP levels was also found by Boudjeltia et al demonstrating that AHI is an independent predictor of hs-CRP elevation. However, they did not take ODI as a confounding factor. A recent study showed significant decreases in the levels of hs-CRP in OSA patients after 6-months CPAP treatment.

Table 1 Baseline Characteristics of CAD Patients in the four OSA groups.

<table>
<thead>
<tr>
<th></th>
<th>No OSA</th>
<th>Mild OSA</th>
<th>Moderate OSA</th>
<th>Severe OSA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>25</td>
<td>50</td>
<td>43</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Sex, Male/Female</td>
<td>20/5</td>
<td>45/5</td>
<td>38/5</td>
<td>27/6</td>
<td>0.515</td>
</tr>
<tr>
<td>Age, years</td>
<td>56.1 ± 9.3</td>
<td>57.7 ± 11.1</td>
<td>57.6 ± 10.5</td>
<td>63.2 ± 12.3</td>
<td>0.053</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.5 ± 2.3</td>
<td>26.2 ± 2.5</td>
<td>27.3 ± 3.3</td>
<td>28.2 ± 2.8</td>
<td>0.001</td>
</tr>
<tr>
<td>AHI, events/h</td>
<td>2.7 ± 1.5</td>
<td>9.5 ± 3.0</td>
<td>20.6 ± 4.2</td>
<td>47.3 ± 15.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ODI (4%), events/h</td>
<td>3.5 ± 2.0</td>
<td>9.7 ± 3.4</td>
<td>21.0 ± 5.4</td>
<td>46.4 ± 16.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean SaO₂, %</td>
<td>93.5 ± 1.7</td>
<td>90.0 ± 7.8</td>
<td>92.8 ± 1.8</td>
<td>90.2 ± 5.5</td>
<td>0.384</td>
</tr>
<tr>
<td>Minimum SaO₂, %</td>
<td>87.7 ± 3.0</td>
<td>80.4 ± 7.2</td>
<td>80.8 ± 5.5</td>
<td>71.2 ± 12.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SaO₂&lt;90% (%TST)</td>
<td>2.9 ± 6.0</td>
<td>5.6 ± 11.2</td>
<td>9.4 ± 13.5</td>
<td>27.0 ± 29.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2 Biochemical factors in CAD patients divided into four categories of OSA severity.

<table>
<thead>
<tr>
<th></th>
<th>No OSA</th>
<th>Mild OSA</th>
<th>Moderate OSA</th>
<th>Severe OSA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>hs-CRP, mg/L</td>
<td>1.95 ± 1.6</td>
<td>2.07 ± 1.9</td>
<td>2.95 ± 2.61</td>
<td>4.29 ± 3.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Endothelin-1, fmol/mL</td>
<td>0.61 ± 0.16</td>
<td>0.78 ± 0.92</td>
<td>0.71 ± 0.33</td>
<td>0.67 ± 0.24</td>
<td>0.664</td>
</tr>
<tr>
<td>NT-proBNP, fmol/mL</td>
<td>816.7 ± 492.3</td>
<td>751.3 ± 433.0</td>
<td>857.4 ± 431.1</td>
<td>940.2 ± 657.4</td>
<td>0.530</td>
</tr>
<tr>
<td>Fibrinogen, g/L</td>
<td>4.09 ± 0.87</td>
<td>3.79 ± 0.79</td>
<td>3.91 ± 0.73</td>
<td>4.33 ± 0.74</td>
<td>0.058</td>
</tr>
<tr>
<td>Triglyceride, mmol/L</td>
<td>1.83 ± 0.88</td>
<td>2.08 ± 1.39</td>
<td>1.90 ± 1.17</td>
<td>1.73 ± 0.83</td>
<td>0.564</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>4.53 ± 1.19</td>
<td>4.34 ± 1.05</td>
<td>4.19 ± 1.09</td>
<td>4.11 ± 1.03</td>
<td>0.446</td>
</tr>
<tr>
<td>HDLC, mmol/L</td>
<td>1.11 ± 0.32</td>
<td>1.13 ± 0.38</td>
<td>1.10 ± 0.31</td>
<td>1.05 ± 0.23</td>
<td>0.711</td>
</tr>
<tr>
<td>LDLC, mmol/L</td>
<td>2.52 ± 1.05</td>
<td>2.21 ± 0.84</td>
<td>2.23 ± 0.83</td>
<td>2.21 ± 0.88</td>
<td>0.484</td>
</tr>
<tr>
<td>Fasting glucose, mmol/L</td>
<td>5.41 ± 1.17</td>
<td>6.19 ± 1.92</td>
<td>5.64 ± 1.38</td>
<td>6.30 ± 1.88</td>
<td>0.110</td>
</tr>
</tbody>
</table>

Abbreviations: ACE inhibitors, angiotensin-converting enzyme inhibitors; AHI, apnoea-hypopnea index; ALAT, alanine aminotransferase; BMI, body mass index; CCB, calcium channel blockers; ODI, oxygen desaturation index; SaO₂, artery oxygen saturation.

Abbreviations: HDLC, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; LDLC, low-density lipoprotein cholesterol; NT-proBNP, N terminal pro B type natriuretic peptide; TC, Total cholesterol.

Values are expressed as mean ± s.d. or n (%).
treatment with good compliance, compared with poor compliance group and those who refused CPAP treatment. On the other hand, not all previous reports have reported such a relationship or shown changes with CPAP. Dorkova et al. failed to find significant changes in hs-CRP levels after 8 weeks of CPAP therapy, whereas reduction in tumor necrosis factor-α which is also a marker of inflammation were observed.

In contrast to previous studies, we could find no association between the other biomarkers of ET-1, NT-proBNP or fibrinogen. One important explanation might be that previous studies focused on OSA patients who were free of other diseases and were taking no medications. The medications for CAD are known to effect the expression of these biomarkers. The current study suggest that these medications might suppress or reverse any tendency for OSA to induce endothelial dysfunction, left ventricular strain or hyper-coagulopathy, but apparently not OSA-induced systemic inflammation. There may be other reasons why levels of ET-1, NT-proBNP, and fibrinogen were not significantly correlated with PSG variables in our study. Gjørup et al. found that the mean nocturnal level of ET correlated significantly to the apnea–hypopnea index (AHI). The biased results of ET-1 with the previous studies might due to the short half-life of endothelin-1 whose activity is difficult to measure in vivo. Previous study reported elevated levels of NT-proBNP in school-aged children with OSA, however, most studies failed to identify such an association. The role it played between OSA and CAD needed to be further assessed.

Hs-CRP is a biomarker of inflammation. To date no better marker has been found to replace hs-CRP as a marker of inflammation and atherosclerosis. Statin therapy is an important medication for CAD patients, and has the dual effect of both regulating blood lipids and reducing levels of hs-CRP. Fifty-four prospective cohort studies have shown

![Figure 1](image_url)  
Figure 1  Serum levels of hs-CRP in control subjects (n = 25), patients with mild OSA (n = 50), patients with moderate OSA (n = 43), and patients with severe OSA (n = 33).

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Pearson’s correlation of PSG variables with clinical measurements and investigational biomarkers.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AH1 correlations (P value)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.234 (&lt;0.004)</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.308 (&lt;0.001)</td>
</tr>
<tr>
<td>hs-CRP</td>
<td>0.439 (&lt;0.001)</td>
</tr>
<tr>
<td>Endothelin-1</td>
<td>0.044 (&lt;0.59)</td>
</tr>
<tr>
<td>NP-proBNP</td>
<td>0.105 (&lt;0.197)</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0.114 (&lt;0.198)</td>
</tr>
</tbody>
</table>

For definition of abbreviations, see footnote to Tables 1 and 2.
that hs-CRP is a strong independent predictor of risk of future myocardial infarction, stroke, and vascular death, regardless of the LDL cholesterol level. The JUPITER study was the largest one to evaluate the role of hs-CRP. In apparently healthy persons without hyperlipidemia but with elevated hs-CRP levels, statin treatment significantly reduced the incidence of major cardiovascular events. It also suggested that elevated hs-CRP levels rather than elevated LDL cholesterol levels had greater effects on the prognostic prediction. Therefore, for patients who have

Figure 2  Correlation between serum levels of hs-CRP and AHI.

Figure 3  Effect of CPAP on serum levels of hs-CRP in patients with severe OSA (n = 27). Patients with severe OSA were treated with CPAP for 3 month. Changes in levels of hs-CRP before and after treatment with CPAP were demonstrated.
already suffered from cardiovascular disease, especially CAD, the percent fall in hs-CRP level may be a very useful marker of how successful the secondary prevention for CAD is likely to be.

In this study, with moderate dose statin therapy the levels of lipids were not related to the severity of OSA, however hs-CRP levels were still significantly correlated with OSA severity. One conclusion that might be drawn is that standard doses of statin cannot satisfactorily control the levels of hs-CRP in CAD patients with OSA, especially those with severe OSA. Thus OSA may induce further cardiovascular events through activating vascular inflammation in CAD patients, even in those who are optimally treated with standard medications. CPAP treatment in patients with CAD and severe OSA may therefore be good secondary prevention treatment.

There are some limitations in the current study. Firstly, we did not use a randomized placebo-controlled trial design to test the effects of CPAP. Regression to the mean or a sustained drug effect might theoretically therefore account for the findings. The other limitation of the current study is that different kinds of statins were used in the CAD patients. Focusing on one statin might result in more convincing data. However, these statins in the present study are all used in moderate doses, which remains the question whether the relationship between OSA and hs-CRP still exist with statins in intensive doses. Future large-scale, randomized placebo-controlled OSA treatment studies are needed to assess the roles of OSA and inflammation play in the progression of CAD. Future studies evaluating the effects of statin on hs-CRP should take account of OSA as a potential confounding factor.

In conclusion, our study shows that hs-CRP is positively correlated with the severity of OSA in CAD patients who are taking standard medications for secondary cardiovascular risk reduction. It also suggests that elevated hs-CRP levels can be decreased by CPAP. It will be important in future studies to determine whether elevated hs-CRP levels in CAD patients suffering from OSA are indicative of increased risk of future adverse cardiovascular events, and whether CPAP or other therapies specifically targeting the inflammatory pathways implicated in atherogenesis can reduce that risk.

Conflict of interest statement

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled, "Effects of obstructive sleep apnea and its treatment on cardiovascular risk in CAD patients”.

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References


