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Review

Effect of continuous positive airway pressure on lipid profile in patients with obstructive sleep apnea syndrome: A meta-analysis of randomized controlled trials

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ABSTRACT

Background: Obstructive sleep apnea syndrome (OSAS) is an independent risk factor for development of dyslipidemia. Continuous positive airway pressure (CPAP) is the first-line treatment for OSAS. However, it is unclear whether CPAP improves lipid metabolism.
Objectives: To review the effect of CPAP on lipid profile of patients with OSAS.
Methods: We searched PubMed, Embase, and the Cochrane Library to identify eligible articles published prior to October 30, 2013. Six randomized controlled trials (RCTs) were subjected to meta-analysis using Comprehensive Meta-Analysis software.
Results: Six RCTs meeting the inclusion criteria were enrolled. The total numbers of measurements of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol, in CPAP intervention patients and sham/control groups, were 370 and 371, 330 and 328, 276 and 274, and 269 and 266 respectively. The pooled estimate of the difference in the mean TC level between the CPAP and sham CPAP/control groups was significantly different (−0.15 [95% confidence interval, −0.27 to −0.03]; $p = 0.01$). Subgroup analysis revealed that OSAS patients of younger age, who were more obese, and who had been treated via CPAP for a longer duration, showed a significant decrease in TC levels (the differences in the means were −0.27, −0.24, and −0.20; and the p values 0.001, 0.01, and 0.04, respectively).
Conclusion: We confirmed that CPAP decreases the TC level, especially in OSAS patients who are younger, more obese, and who use CPAP for a longer period. CPAP did not alter TG, LDL, or HDL levels, suggesting that CPAP may have no clinically important effect on lipid metabolism.

Contents

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1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder, affecting about 24% of middle-aged males and 9% of middle-aged females [1]. OSAS is characterized by repetitive episodes of partial or complete upper airway obstruction during sleep, causing intermittent hypoxia, in turn triggering oxidative stress or inflammation [2]. An increasing body of research shows that OSAS is an independent risk factor for development of cardiovascular events and morbidity, including dyslipidemia [3–5].

Continuous positive airway pressure (CPAP) therapy is the first-line treatment for OSAS [6]. The benefits of CPAP include elimination of upper airway collapse, micro-arousals, and oxidative stress during sleep; and improvement in clinical symptoms, including snoring and excessive daytime sleepiness [7,8]. Previous studies have shown that CPAP exerts a positive effect on metabolic syndrome [9]. In particular, the influence of CPAP on the levels of total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride (TG), were investigated [10–15].

Several articles exploring the beneficial effects of CPAP treatment on blood lipid levels have been published in the past few years [10–16]. These include randomized controlled trials (RCTs), original studies, and a review. However, few definite conclusions can be drawn. Recently, three new RCTs exploring the effects of CPAP on the blood lipid profile have been conducted [12–14]. These RCTs enrolled more OSAS subjects than did all prior studies combined. It was thus necessary to systematically review and meta-analyze all relevant RCTs to explore the effects of CPAP therapy on lipid profile.

2. Materials and methods

We strictly followed the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) [17]. Our registration number is CRD42013005732.

2.1. Search strategy and selection of trails

We systematically searched PubMed, Embase, and the Cochrane library. All pre-September 2013 literature examining the effects of CPAP on blood lipid profiles was included. No language or other restriction was imposed. The search terms used were: (Continuous positive airway pressure or CPAP) and (obstructive sleep apnea or OSA) combined with (lipids or lipid profile or metabolic profile or dyslipidemia or cholesterol or TC or triglycerides or TG or HDL or LDL). In addition, we manually searched for relevant published studies and review articles.

We selected RCTs that met the following inclusion criteria: (1) only adults (aged $\geq$ 18 years) with newly diagnosed OSAS were studied; (2) CPAP was applied; (3) the duration of CPAP therapy was $\geq$2 weeks; and, (4) the level of at least one of TC, TG, LDL, or HDL was measured both before and after application of CPAP. Reviews, abstracts, case reports, letters, and non-human studies were excluded. Other exclusion criteria were: (1) treatment of adolescents (age $<$ 18 years); (2) diagnosis of OSAS in a manner other than by determination of the AHI (AHI $\geq$ 5) or the oxygen desaturation index (ODI) (ODI $\geq$ 7.5); (3) failure to record lipid levels both before and after CPAP therapy, or the inadequacy of supplied information in terms of allowing such values to be estimated; and/or, (4) a duration of therapy of less than 2 weeks. Two investigators (Drs. Xu and Guan) screened all relevant published material using the abovementioned criteria. If disagreement arose, a third reviewer (Prof. Yin) participated in resolution of the issue by discussion.

2.2. Quality assessment

We evaluated the quality of each study with the Jadad score. The Jadad score represents the quality of randomization, blinding, withdrawal reporting, generation of random numbers, and allocation concealment. One point was allotted to each of these features, and the score thus varied from 0 to 5 (the highest quality level). Quality assessment was subjected to sensitivity analysis, because low-quality trials may influence outcome measures. Quality was independently assessed by two investigators (Drs. Xu and Guan).

2.3. Data extraction

Data were extracted from RCTs meeting the inclusion criteria. These data were the first author; year of publication; the country in which the work was performed; study design; number of subjects; sex, age, body mass index (BMI), and AHI or ODI values of the participants; the duration of CPAP intervention; the extent of adherence to CPAP; post-intervention TC, TG, LDL, HDL, weight, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting glucose, and/or homeostasis model assessment of insulin resistance (HOMA-IR) data from both the CPAP and the sham CPAP/control groups; and the mean differences in the levels of TC, TG, LDL, HDL, and weight, BMI, SBP, DBP, fasting glucose, HOMA-IR between the test and control groups. Our final analysis featured examination of these differences and the associated confidence interval (CI). The differences were calculated if not directly provided.

2.4. Quantitative data synthesis

Data on differences in TC, TG, LDL, HDL levels, and weight, BMI, SBP, DBP, fasting glucose, and HOMA-IR between the two groups were analyzed using pooled estimates of the differences in means, and the associated CIs were calculated. Funnel plots of standard errors and differences in means were used to assess publication bias. We also used Begg's test and the Mazumdar rank correlation approach to this end [18]. Heterogeneity was assessed with the aid of the I-squared index. If a p value was $<$0.10, the existence of statistical heterogeneity was suggested and the data were analyzed using a random-effects model. Otherwise, the data were considered to be homogeneous and a fixed model was employed. Comprehensive Meta Analysis software, version 2.2.064, was used to analyze all data.

3. Results

3.1. Search results

One hundred and forty-two articles were initially identified by electronic and manual searching. After review of the titles and abstracts, 104 studies were excluded whereas 38 were considered to be potentially relevant. Of these, 29 articles not met the requirements were next excluded. A total of nine RCTs were considered worthy of additional analysis. Of these, one was subsequently excluded because it dealt with postprandial lipidemia [19]; another was excluded because randomization was used only to assign patients to early or late initiation of CPAP therapy, and no control/sham group was included [20]; and a third study lacked sufficient information on lipid levels [21]. The detailed steps of our literature search are shown in Fig. 1. Finally, six studies meeting the inclusion criteria were included in the meta-analysis [10–15]. The total numbers of measurements of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol made in CPAP intervention patients and sham/control groups were 370 and 371, 330 and 328, 276 and 274, and 269 and 266, respectively.

3.2. Characteristics of the studies

All eligible studies were published between 1991 and 2013. Three studies were conducted in the United Kingdom [10,12,15], one in Canada [11], one in Switzerland [13], and one in India [14]. Of the six studies, three featured a crossover design [10,11,14] and the other three a parallel design [12,13,15]. All participants were at least 30 years of age and had BMIs of 31 kg/m^2 or more. The duration of effective CPAP treatment was 2–24 weeks. Four studies defined OSAS as an AHI of ≥5 events per hour and all subjects had severe OSAS [10,11,13,14]. The other two studies defined OSAS as an ODI ≥ 7.5 or 10 instances of oxygen desaturation of 4% or more per hour, respectively [12,15]. CPAP nightly usage varied from 2.39 to 6.2 ± 1.1 h. Five studies had Jadad scores ≥3 [10,12–15], and one study scored only 1 [11]. Relevant features of all studies are shown in Table 1.

3.3. Pooled lipid profile analysis

The pooled estimates of differences in mean TC, TG, LDL, and HDL levels between the CPAP and the sham CPAP/control groups were −0.15 [95% CI, −0.27 to −0.03; $p = 0.01$]; 0.00 [95% CI, −0.11 to 0.11; $p = 0.96$]; −0.04 [95% CI, −0.17 to 0.10; $p = 0.58$] and −0.02 [95% CI, −0.07 to 0.02; $p = 0.26$], respectively, indicating that CPAP therapy lowered only the TC level (Fig. 2). The mean and standard deviation data for TC, TG, LDL, and HDL are recalculated and summarized in Table 2.

3.4. Pooled analysis on other metabolic syndrome components and the anthropometric variables

Only two studies have reported weight and BMI data before and after CPAP treatment [12,14]. Craig et al. found that the mean difference in BMI between CPAP and sham CPAP/control groups increased (0.40 [95% CI, −0.10 to −0.70]; $p = 0.02$) [12]. However, Sharma et al. found that the difference in mean weight and BMI between CPAP and sham CPAP/control groups decreased significantly (−0.70 [95% CI, −1.40 to −0.03]; $p = 0.03$); (−0.29 [95% CI, −0.51 to −0.06]; $p < 0.01$) [14]. No significant difference was observed in the pooled estimate of the difference in the mean BMI between the CPAP and sham CPAP/control groups (0.096 [95% CI, −0.11 to −0.30]; $p = 0.35$).

Components of metabolic syndrome, including SBP [10,11,13,14], DBP [10–14], fasting glucose [10–14], and HOMA-IR [10–14] were pooled in this meta-analysis. We found that CPAP had a positive

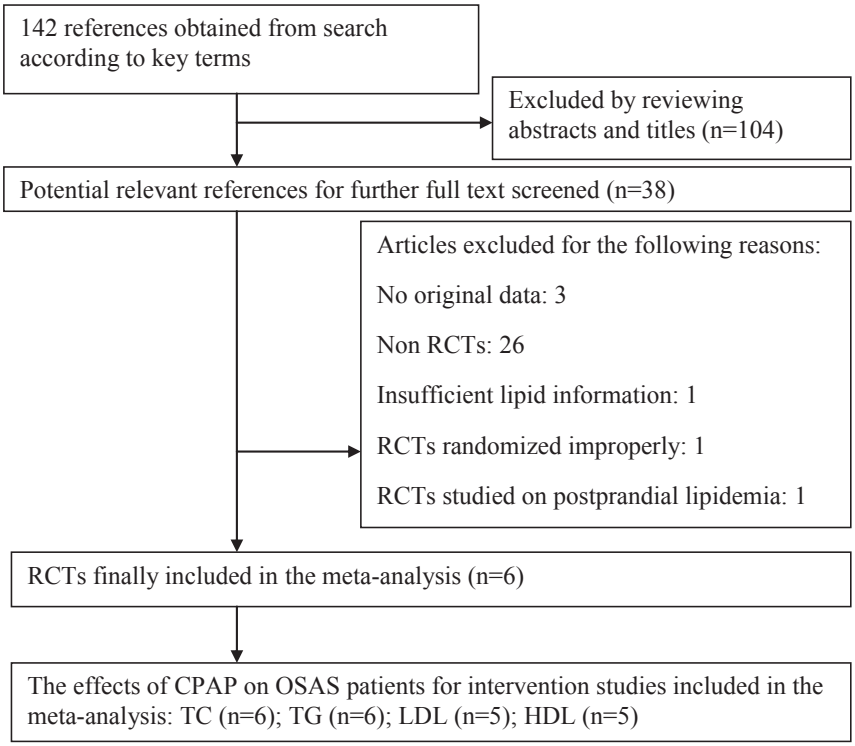


Fig. 1. Flow diagram of study selection process. 6, 6, 5 and 5 studies referring CPAP therapy on TC, TG, LDL, and HDL were eligibly included in the meta-analysis, the combined samples for TC, TG, LDL, and HDL in CPAP intervention groups and sham/control groups were 370, 330, 276, 269 and 371, 328, 274, 266, respectively.

Table 1
Characteristics of the enrolled studies in the meta-analysis.

First author/year	Country	Study design	No.	Males (%)	Age(yr)	BMI (Kg/m^2)	AHI or ODI(events per hr)	Duration of trails (weeks)	CPAP adherence (hr)	Jadad score	Outcome measures
Coughlin 2007 [10]	UK	crossover	34	100	49.0 ± 8.3	36.1 ± 7.6	39.7 ± 13.8*	6W	3.9 ± 0.74	5	TC,TG,LDL,HDL
Comondore 2009 [11]	UK	crossover	13	69	55.5 ± 7.1	31.1	27.9*	4W	5.53	1	TC,TG,LDL,HDL
Craig 2012 [12]	UK	parallel	195	78.5	57.9 ± 7.2	32.2 ± 5.6	10.2※	24W	2.39	3	TC,TG,LDL,HDL
Kohler 2011 [13]	Switzerland	parallel	20	95	63.6 ± 5.1	32.9 ± 6.5	36.0 ± 17.3*	2W	6.2 ± 1.1	5	TC,TG,LDL,HDL
Sharma 2011 [14]	India	crossover	43	†Seq 1(84)	45 ± 8	33.8 ± 4.7	47.9 ± 19.6*	12W	5.1 ± 1.0	5	TC,TG,LDL,HDL
			43	‡Seq2(95)	45 ± 8	31.8 ± 5.2	47.8 ± 17.3*	12W	5.2 ± 1.1		TC,TG,LDL,HDL
Robinson 2004 [15]	UK	parallel	108	100	49.7 ± 10.3	35.6 ± 7.6	38.9 #	4W	5.0 ± 1.9	4	TC,TG

Abbreviation: AHI = apnea hypopnea index; ODI = oxygen desaturation index; BMI = body mass index; CPAP = continuous positive airway pressure; TC = total cholesterol; TG = total triglyceride; LDL = low-density lipoprotein; HDL = high-density lipoprotein. Note: †Seq1 indicates the group that was treated with CPAP first in the crossover study, ‡Seq2 indicates the group that was treated with sham CPAP first in the crossover study, *OSAS defined as AHI >5 events per hour ※OSAS defined as ODI >7.5 events per hour with oxygen desaturation of >4%. # OSAS defined as more than 10 dips of 4% oxygen desaturation per hour.

effect on the pooled SBP estimate, and that the difference in means between the CPAP and sham CPAP/control groups was −2.236 (95% CI: −3.314 to −1.158, $p < 0.001$). CPAP also improved DBP, and the difference in means between the CPAP and sham CPAP/control groups was −1.640 (95% CI: −2.342 to −0.938, $p < 0.001$). However, CPAP had no effect on fasting glucose (difference in means: −0.004, 95% CI: −0.050 to 0.042, $p = 0.857$) or HOMA-IR (difference in means: 0.056, 95% CI: −0.125 to 0.238, $p = 0.543$).

3.5. Subgroup lipid profile analysis

Subgroup analysis of the TC data was performed after segregation by age (<50 years and ≥50 years); severity of obesity (BMI <35 kg/m^2 and ≥35 kg/m^2); duration of intervention (<12 weeks and ≥12 weeks); and nightly CPAP duration (<5 h and ≥5 h) (Table 3). In younger (<50 years) patients, the pooled estimates of the difference in the mean TC value significantly decreased (−0.27; 95% CI, −0.42 to −0.11; $p = 0.001$); however, this was not evident in older (≥50 years) patients (0.02; 95% CI, −0.16 to 0.20; $p = 0.84$). In severely obese subjects, TC levels fell upon application of CPAP (−0.24; 95% CI, −0.41 to −0.06; $p = 0.01$) but this was not the case in obese subjects (−0.08; 95% CI, −0.28 to 0.08; $p = 0.31$). A longer duration of CPAP application (≥12 weeks) caused a significant reduction in TC level (−0.20, 95% CI, −0.40 to −0.01; $p = 0.04$) but this was not the case when the duration of CPAP application was shorter (−0.12; 95% CI, −0.27 to 0.03; $p = 0.11$). The extent of adherence to the CPAP protocol did not affect TC levels (−0.18; 95% CI, −0.39 to 0.02; $p = 0.08$) and (−0.14; 95% CI −0.28 to 0.01; $p = 0.07$), respectively (Table 2). Sensitivity analysis revealed that if data from the lower quality study (Jadad score ≤3) were excluded, the positive effect of CPAP intervention on TC levels remained (−0.22; 95% CI, −0.37 to 0.08; $p = 0.00$). Subgroup analysis of TG, LDL, and HDL data yielded no finding of interest (Table 3).

3.6. Heterogeneity and publication bias

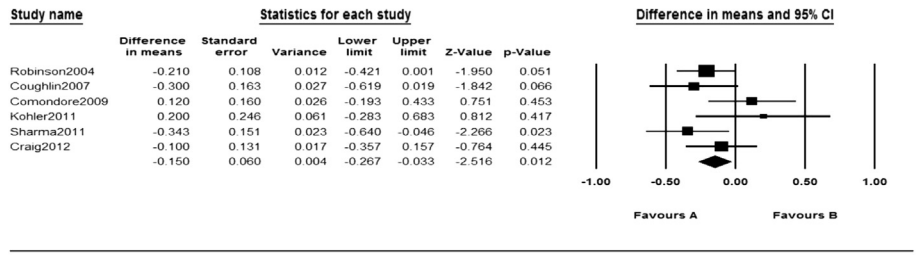
We used the I-squared index to explore variability in effect-size estimates among studies. The index values for the differences in mean TC, LDL, and HDL values between tests and controls were 35.93, 0.00, and 0.00, respectively ($p = 0.17$; $p = 0.45$; and $p = 0.66$), indicating that the studies were homogeneous in nature. However, significant heterogeneity in TG data was evident (65.016; $p = 0.014$). We excluded data from a report that used CPAP for only 2 weeks [13], and the I^2 index of TG changed to 0.00 ($p = 0.852$). Funnel plots were not obviously asymmetric (picture not shown). The Begg's and Mazumdar rank correlation test did not suggest the presence of publication bias (Table 4).

4. Discussion

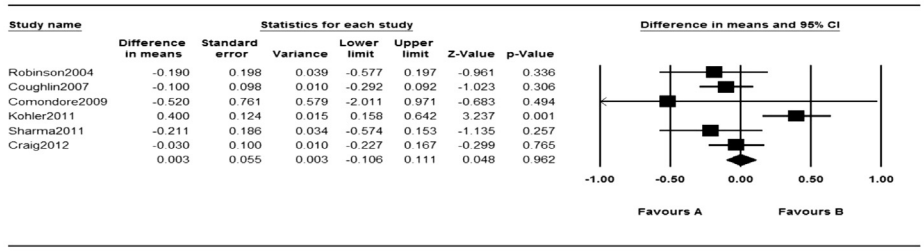
We found that CPAP treatment of patients with OSAS lowered metabolic dyslipidemia, as evidenced by the difference in mean TC levels between the test and control groups; however, TG, LDL, and HDL levels did not decrease. CPAP was more effective in younger (<50 years) severely obese (BMI ≥ 35 kg/m^2) patients when applied for ≥12 weeks (Table 3). Our findings show that CPAP did not alter TG, LDL, or HDL levels, suggesting that CPAP may have no clinically important effect on lipid metabolism. CPAP lowered the SBP and DBP of patients with OSAS. However, CPAP had no effect on BMI, fasting glucose, or HOMA-IR.

Studies of the association between OSAS status and lipid profile have yielded conflicting results [16]. Some authors found that OSAS was independently associated with abnormalities in lipid levels [22–25], while others suggested that dyslipidemia was linked to obesity and not to OSAS per se [26,27]. However, the cited studies

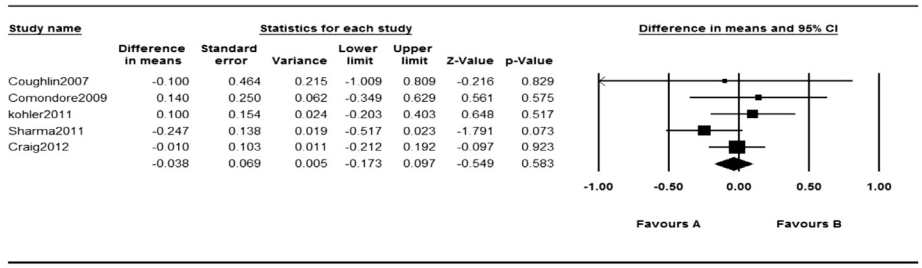
2.1. Forest plot for differences in means and 95%CIs in assessment of TC.



2.2. Forest plot for differences in means and 95%CIs in assessment of TG.



2.3. Forest plot for differences in means and 95%CIs in assessment of LDL.



2.4. Forest plot for differences in means and 95%CIs in assessment of HDL.

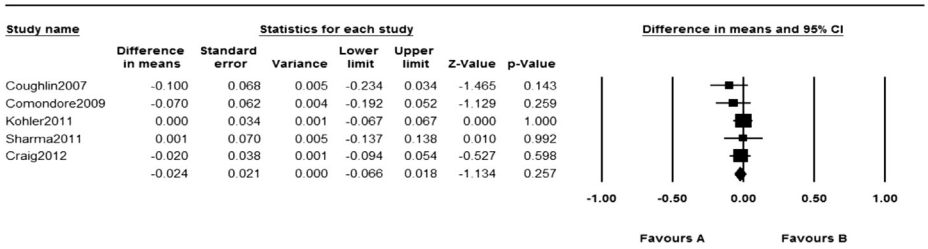


Fig. 2. Forest plots for differences in means and corresponding 95% confidence intervals (CIs) in assessment of lipid profile. The pooled estimate of the difference in means in TC, TG, LDL, and HDL between the CPAP and the sham CPAP/control groups were (−0.15[95%CI, −0.27 to −0.03]; $p = 0.01$); (0.00[95%CI, −0.11 to 0.11]; $p = 0.96$); (−0.04[95%CI, −0.17 to 0.10]; $p = 0.58$) and (−0.02[95%CI, −0.07 to 0.02]; $p = 0.26$) respectively. In Figure 2.1, 2.2, 2.3 and 2.4, A means CPAP intervention group; B means sham/control group.

had small sample sizes and did not control for confounding factors. Thus, the works did not directly explore the relationship between OSAS and dyslipidemia. Interventional studies may potentially reveal any causal relationship between OSAS and an abnormal lipid profile. CPAP is the first accepted treatment for OSAS. Many non-controlled trials claimed that CPAP treatment was of benefit to those with metabolic disorders [28–30]. However, other non-controlled studies came to the opposite conclusion [31–33]. Thus, the precise mechanism by which CPAP treatment affects the lipid profile remains incompletely understood. The RCT is the gold standard for clinical trials. However, only a few relevant RCTs have been conducted, and the results differed [10–15]. Thus, a meta-analysis is required to explore the possible relationship between CPAP therapy and lipid profiles in patients with OSAS.

We found that only the TC level decreased in patients with OSAS. Establishment of dyslipidemia in patients with OSAS is a long process that is affected by several factors, including the OSAS severity, nocturnal hypoxia, obesity, sympathetic activity, diet, and exercise [15,22,23,34]. Thus, OSAS is just one of several risk factors triggering dyslipidemia, and it is not surprising that not all lipid levels were affected. TC is one of the first components to respond to the reduction in oxidative stress associated with OSAS treatment

Table 2
Outcome of lipid variables in individual studies included in the meta-analysis.

First author, year	TC				TG			
	Comp*		CPAP*		Comp*		CPAP*	
	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up
Coughlin, 2007	NR	NR	5.7 ± 0.1	5.5 ± 0.1	NR	NR	1.9 ± 0.2	1.8 ± 0.2
Comondore, 2009*	4.78 ± 1.44	4.80 ± 1.28	4.80 ± 2.29	4.94 ± 2.10	1.53 ± 1.9	1.90 ± 2.17	1.83 ± 2.5	1.68 ± 1.78
Craig, 2012	5.2 ± 1.1	5.1 ± 1.2	5.3 ± 1.2	5.1 ± 1.1	1.69 ± 0.9	1.71 ± 0.9	1.68 ± 1.00	1.67 ± 0.88
Kohler, 2011	5.1 ± 1.44	4.9 ± 1.28	4.8 ± 2.29	4.8 ± 2.10	1.7 ± 1.06	1.5 ± 1.39	1.2 ± 0.55	1.4 ± 0.78
Sharma, 2011	4.94 ± 1.02	5.04 ± 0.89	5.47 ± 0.93	5.23 ± 0.94	1.76 ± 0.70	1.76 ± 0.87	2.23 ± 1.05	2.02 ± 0.95
Robinson, 2004	5.7 ± 1.1	5.63 ± 1.13	5.6 ± 1.3	5.32 ± 1.01	2.6 ± 1.9	2.55 ± 2.17	3.3 ± 2.5	3.06 ± 1.78
First author, year	LDL				HDL			
	Comp*		CPAP*		Comp*		CPAP*	
	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up	Baseline	Follow up
Coughlin, 2007	NR	NR	3.7 ± 0.1	3.6 ± 0.1	NR	NR	1.1 ± 0.1	1.1 ± 0.1
Comondore, 2009*	2.91 ± 1.44	2.85 ± 1.25	2.84 ± 1.32	2.92 ± 1.00	1.10 ± 0.38	1.14 ± 0.34	1.15 ± 0.44	1.12 ± 0.40
Craig, 2012	3.09 ± 1.0	2.99 ± 1.1	3.18 ± 0.99	3.07 ± 0.97	1.28 ± 0.32	1.26 ± 0.33	1.32 ± 0.39	1.28 ± 0.35
Kohler, 2011	3.2 ± 1.44	3.0 ± 1.25	3.1 ± 1.32	3.0 ± 1.00	1.1 ± 0.38	1.1 ± 0.34	1.3 ± 0.44	1.3 ± 0.40
Sharma, 2011	3.03 ± 0.80	3.13 ± 0.71	3.32 ± 0.76	3.17 ± 0.73	1.08 ± 0.17	1.08 ± 0.28	1.14 ± 0.15	1.14 ± 0.29
Robinson, 2004	NR	NR	NR	NR	NR	NR	NR	NR

Abbreviation: TC = total cholesterol; TG = total triglyceride; LDL = low-density lipoprotein; HDL = high-density lipoprotein; CPAP = continuous positive airway pressure; Comp = comparator; NR = not reported. Note: *no reported SD of weight change so assumed as SD of highest of rest of group.

[15]. Patients treated with CPAP altered their diets and increased their levels of physical activity, eventually leading to a fall in TC levels [15]. The fact that CPAP therapy enhances the sympathetic response to hypoxic chemoreflex stimulation may also contribute to the lowered serum TC level noted in OSAS patients [34,35].

Changes in weight affect blood pressure and glucose and lipid metabolism. Improvements in blood pressure, glucose metabolism, hypertriglyceridemia, and low HDL-C levels are observed after weight loss [36]. Our findings show that CPAP decreased TC level, SBP, and DBP of patients with OSAS but had no effect on BMI, HOMA-IR, or metabolism of TG, LDL, HDL, or serum glucose. BMI as well as metabolic syndrome components—such as fasting glucose and HOMA-IR—are confounding factors in the correlation between OSAS and serum lipids [37]. All studies included in our meta-analysis were RCTs, which should consider matching confounding factors. Because our meta-analysis focused on the effect of CPAP on lipids, only RCTs that included this subject were enrolled, and so the pooled population was different from those in previous meta-analyses designed specifically for the aforementioned factors. Thus, the results of our meta-analysis may show little difference from those of previous meta-analyses [38–40].

We performed subgroup analysis to identify the principal factors influencing lipid profiles. No changes in TG, LDL, or HDL levels were evident in OSAS patients subdivided by age, BMI, nightly duration of CPAP application, or overall duration of CPAP therapy. However, the TC levels fell significantly in younger, more obese patients treated with CPAP for longer periods. Particularly, CPAP therapy sharply decreased the TC level in younger patients (<50 years). We speculate that dyslipidemia in younger patients is mild and reversible, but severe and irreversible in older patients. CPAP

Table 3
Results of subgroup and sensitivity analyses for evaluating the effect of CPAP usage on lipid profile.

Variables	TC	TG	LDL	HDL
	Mean difference (mmol/L) with 95% confidence intervals and *P* value			
Age				
<50 years old	−0.265(−0.416–0.113)	−0.135(−0.290–0.021)	−0.235(−0.494–0.024)	−0.051(−0.147–0.045)
	P = 0.001	*P* = 0.089	*P* = 0.075	*P* = 0.297
>50 years old	0.020(−0.164–0.203)	0.134(−0.018–0.286)	0.036(−0.123–0.195)	−0.018(−0.064–0.028)
	P = 0.835	*P* = 0.084	*P* = 0.656	*P* = 0.449
Weight of subjects				
Obesity(BMI<35 kg/m^2)	−0.081(−0.237–0.075)	0.083(−0.057–0.223)	−0.037(−0.173–0.100)	−0.016(−0.060–0.028)
	P = 0.310	*P* = 0.247	*P* = 0.601	*P* = 0.475
Severe obesity(BMI > 35 kg/m^2)	−0.237(−0.413–0.061)	−0.118(−0.289–0.054)	−0.100(−1.009–0.809)	−0.100(−0.234–0.034)
	P = 0.008	*P* = 0.179	*P* = 0.829	*P* = 0.143
Interventional duration				
<12W	−0.119(−0.266–0.027)	0.050(−0.089–0.190)	0.095(−0.152–0.343)	−0.030(−0.084–0.024)
	P = 0.110	*P* = 0.478	*P* = 0.450	*P* = 0.275
>12W	−0.203(−0.398–0.009)	−0.071(−0.224–0.102)	−0.095(−0.256–0.067)	−0.015(−0.081–0.050)
	P = 0.040	*P* = 0.422	*P* = 0.250	*P* = 0.646
CPAP adherence				
<5 h	−0.178(−0.387–0.022)	−0.066(−0.203–0.071)	−0.014(−0.211–0.183)	−0.039(−0.104–0.026)
	P = 0.081	*P* = 0.346	*P* = 0.887	*P* = 0.241
>5 h	−0.135(−0.279–0.009)	0.118(−0.060–0.295)	−0.059(−0.246–0.127)	−0.014(−0.068–0.040)
	P = 0.066	*P* = 0.194	*P* = 0.534	*P* = 0.618
Sensitivity analyses				
Excluding low quality studies (Jadad ≤3)	−0.223(−0.368–0.079)	0.021(−0.110–0.152)	−0.093(−0.290–0.103)	−0.017(−0.072–0.038)
	P = 0.002	*P* = 0.751	*P* = 0.353	*P* = 0.549

Abbreviation: AHI = apnea hypopnea index; BMI = body mass index; CPAP = continuous positive airway pressure; TC = total cholesterol; TG = total triglyceride; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

Table 4
Kendall's tau b (corrected for ties, if any) with one-tailed or two-tailed *P* value (based on continuity-corrected normal approximation).

	TC	TG	LDL	HDL
Kendall's tau b	0.13	0.13	0.00	−0.30
Kendall's tau b with a one-tailed *P* value	0.35	0.35	0.50	0.73
Kendall's tau b with a two-tailed *P* value	0.71	0.71	1.00	0.46

therapy had a more obvious effect on the TC level of severely obese patients (BMI > 35 kg/m^2) compared to obese subjects (BMI 30–35 kg/m^2). OSAS is always associated with obesity, and adiposity is a confounding risk factor for metabolic dyslipidemia [41]. Inflammatory marker levels in OSAS patients rise as obesity becomes more pronounced [42,43]. Meta-analysis revealed that CPAP therapy could partially suppress systemic inflammation in OSAS patients [44]. CPAP application may also directly reduce fat levels [14]. This may explain why the TC level decreased significantly in severely obese patients. CPAP therapy had a more obvious effect on TC level when such therapy was of long duration. This may be because an elevated blood lipid level in OSAS patients is a chronic condition. The total number of patients in our meta-analysis was small (230–250 per group), and smaller when we performed the subgroup analysis. Thus, the lack of statistical significance in TG, LDL, and HDL levels in the subgroup analysis may be due to the small group sizes.

To our knowledge, this is the first meta-analysis to investigate the effects of CPAP treatment, administered in the course of RCTs, on lipid profile, and our work has some advantages. First, pooling of information from all eligible RCTs yielded results that these were more precise and reliable than the results of individual studies. Second, no significant heterogeneity was evident among the included studies. Third, the funnel plots did not reveal any publication bias. Finally, patient age, BMI, duration of CPAP intervention, and extent of nightly CPAP usage were comparable among the studies.

Our study had some limitations. First, few RCTs have addressed the topic of interest, and the total sample size was relatively small. Additional large-scale well- designed RCTs featuring good adherence to therapy and long-term follow-up are required. Second, negative results may not have been published, creating publication bias. Third, the duration of CPAP therapy (2–24 weeks) was relatively short, and may have been inadequate to change lipid profiles. Fourth, physical activity and consumption of a high-fat diet can affect serum lipid levels independently of OSAS [45]. Finally, RCTs evaluating long-term CPAP intervention face an ethical problem, because long-time sham CPAP treatment may have serious consequences for OSAS patients [46]. Thus, future RCTs with larger patient samples and longer follow-up durations remain challenging.

In conclusion, we found that application of CPAP significantly reduced the TC level, especially in younger, more obese patients, and was associated with longer duration of CPAP application. This was not true of the levels of TG, LDL, or HDL.

Conflict of interest statement

The authors comment no conflicts.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.atherosclerosis.2014.03.034.

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