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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

The impact of continuous positive airway pressure therapy on cardiovascular events in patients with obstructive sleep apnoea: an updated systematic review and meta-analysis

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Abstract

Objective Obstructive sleep apnoea (OSA) is positively associated with cardiovascular diseases, and continuous positive airway pressure (CPAP) is a common treatment for such patients. This study aimed to explore the impact of CPAP on cardiovascular outcomes and prognosis in patients with OSA.

Methods A search was conducted in the PubMed, Embase and CENTRAL databases for relevant studies published up to March 2024. Two independent reviewers screened the studies based on inclusion and exclusion criteria, and data were synthesised using RevMan 5.3 software. Heterogeneity was assessed using the Cochran Q test and the I^2 statistic.

Results A total of 10 randomised controlled trials and 3 observational studies, comprising 13,832 patients, were included. Compared with standard treatment, the use of CPAP did not significantly reduce the risk of major adverse cardiovascular events (MACE) (risk ratio [RR]: 0.73, 95% confidence interval [CI]: 0.52–1.03; $p=0.07$; $I^2=66\%$), all-cause mortality (RR: 0.92, 95% CI: 0.72–1.16; $p=0.48$; $I^2=0\%$), cardiovascular mortality (RR: 0.63, 95% CI: 0.33–1.19; $p=0.15$; $I^2=70\%$) or non-cardiovascular mortality (RR: 0.81, 95% CI: 0.57–1.15; $p=0.23$; $I^2=0\%$). Similarly, there were no significant differences in the incidence of myocardial infarction, stroke, hospitalisation due to unstable angina or heart failure or atrial fibrillation among those using CPAP. However, when CPAP adherence was ≥ 4 h, CPAP significantly reduced the risk of MACE and cardiovascular mortality.

Conclusion Although CPAP's cardiovascular benefits in patients with OSA are not confirmed, it may be that bias risks, CPAP adherence and characteristics of the study population may attenuate the perceived benefits of CPAP. Further research is needed to optimise CPAP therapy.

Keywords Continuous positive airway pressure · Obstructive sleep apnoea · Cardiovascular · Meta-analysis

Introduction

Obstructive sleep apnoea (OSA) is a common sleep breathing disorder characterised by recurrent partial or complete obstruction of the upper airway during sleep, leading to pauses in breathing or reduced airflow, resulting in oxygen desaturation and decreased sleep quality [1]. Obstructive sleep apnoea is often accompanied by symptoms such as frequent nocturnal awakenings, snoring, breathing pauses and excessive daytime sleepiness, significantly affecting patients' quality of life [2]. Previous studies have confirmed a close association between OSA and cardiovascular diseases. Patients with OSA often have an increased risk of developing hypertension, coronary artery disease and cardiac arrhythmias. Frequent nocturnal hypoxaemia and sympathetic nervous system activation during sleep may lead to abnormal cardiovascular responses, including elevated blood pressure and impaired endothelial function, thereby promoting the occurrence and progression of cardiovascular diseases [3]. Therefore, gaining a deeper understanding of the pathogenesis of cardiovascular diseases in patients with OSA and exploring effective treatment methods are crucial for improving patient outcomes.

Continuous positive airway pressure (CPAP) therapy is a commonly used and effective treatment for OSA [4]. This treatment method involves providing CPAP during sleep to prevent the upper airway from collapsing during exhalation, thereby maintaining airway patency and reducing the occurrence of breathing pauses. Continuous positive airway pressure

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is typically administered through a nasal or face mask connected to a ventilator, delivering positive pressure airflow to the patient's airway to keep it open [5]. Past studies have shown that CPAP therapy can effectively alleviate symptoms in patients with OSA, including reducing nocturnal awakenings, improving sleep quality and decreasing excessive daytime sleepiness [6]. Additionally, some studies have found a slight reduction in blood pressure in some patients receiving CPAP therapy [7]. However, there is considerable controversy regarding the effects of CPAP therapy on cardiovascular diseases [8]. Although several meta-analyses have been conducted to evaluate the impact of CPAP therapy on cardiovascular diseases, inconsistencies in conclusions exist due to differences in study methods and included studies [9]. Furthermore, with the emergence of new research and evolving definitions of cardiovascular diseases and implementation methods of CPAP therapy, assessing its impact on cardiovascular diseases becomes increasingly complex.

Therefore, this updated meta-analysis aims to comprehensively assess the impact of CPAP therapy on the incidence and outcomes of cardiovascular diseases in patients with OSA. By including the latest studies and integrating different research findings, we aim to provide more reliable evidence for clinical practice and further clarify the role of CPAP therapy in improving cardiovascular health in patients.

Methods

Search strategy and literature selection

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines recommended by the Cochrane Collaboration were adopted in the execution of this study [10]. Three major electronic databases, namely PubMed, Embase and the Cochrane Library, were primarily searched between the inception of the database and 5 March 2024, with no language restrictions. A comprehensive search strategy combining 'Medical Subject Headings' and 'Embase Subject Headings' terms with free text terms was employed, covering topics such as OSA syndrome, CPAP therapy and randomised controlled trials (RCTs). Additionally, manual screening of potentially relevant references from related studies, reviews or meta-analyses was attempted. After the database search, retrieved records were imported into the Endnote reference management software for automatic and manual deduplication. Two independent reviewers initially screened potentially relevant records based on titles and abstracts, and full-text articles were then assessed to confirm study inclusion. Any discrepancies between the two reviewers were resolved by a third experienced researcher (Table 1).

Inclusion and exclusion criteria

The inclusion criteria for this study were established based on five elements: participants, intervention, comparison, outcome and study design. The inclusion criteria were as follows: 1) adult patients diagnosed with OSA; 2) intervention group receiving CPAP therapy; 3) control group receiving sham CPAP or standard treatment; 4) outcome measures including cardiovascular event incidence or prognosis; and 5) RCTs or observational studies. The exclusion criteria were as follows: 1) duplicate studies; 2) studies with intervention duration < 12 weeks or incorrect intervention methods; 3) studies with incomplete data or unreported predefined outcomes; and 4) irrelevant literature types, such as literature reviews and conference abstracts.

Table 1 Search strategy for electronic databases

Databases	Search terms
PubMed ($n=1527$)	("Sleep Apnea Syndromes"[MeSH Terms] OR "sleep apnea"[Title/Abstract] OR "sleep hypopnea"[Title/Abstract] OR (("sleep"[MeSH Terms] OR "sleep"[All Fields] OR "sleeping"[All Fields] OR "sleeps"[All Fields] OR "sleep s"[All Fields]) AND "cessation"[Title/Abstract]) OR "OSAS"[Title/Abstract] OR "OSA"[Title/Abstract] OR "SAHS"[Title/Abstract] OR "SAS"[Title/Abstract] OR "snoring"[Title/Abstract]) AND ("Continuous Positive Airway Pressure"[MeSH Terms] OR "CPAP"[Title/Abstract] OR "Continuous Positive Airway Pressure"[Title/Abstract]) AND ("randomized controlled trials"[Title/Abstract] OR "RCT"[Title/Abstract] OR "controlled clinical trial"[Title/Abstract] OR "randomized"[Title/Abstract] OR "Randomized Controlled Trial"[Publication Type])
Embase ($n=2854$)	('Sleep Apnea Syndromes'/exp OR 'sleep apnea':ab,ti OR 'sleep hypopnea':ab,ti OR (('sleep'/exp OR 'sleep' OR 'sleeping' OR 'sleeps' OR 'sleep s') AND 'cessation':ab,ti) OR 'OSAS':ab,ti OR 'OSA':ab,ti OR 'SAHS':ab,ti OR 'SAS':ab,ti OR 'snoring':ab,ti) AND ('Continuous Positive Airway Pressure'/exp OR 'CPAP':ab,ti OR 'Continuous Positive Airway Pressure':ab,ti) AND ('randomized controlled trials':ab,ti OR 'RCT':ab,ti OR 'controlled clinical trial':ab,ti OR 'randomized':ab,ti)
Cochrane Library ($n=623$)	((MeSH descriptor: [Sleep Apnea Syndromes] explode all trees) OR (sleep apnea OR sleep hyponea OR sleep cessation OR OSA OR OSAS OR SAHS OR SAS OR snoring):ti,ab,kw) AND ((MeSH descriptor: [Continuous Positive Airway Pressure] explode all trees) OR (CPAP OR Continuous Positive Airway Pressure):ti,ab,kw) AND ((MeSH descriptor: [Randomized Controlled Trial] explode all trees) OR (randomized controlled trials OR RCT OR controlled clinical trial OR randomized):ti,ab,kw)

Data extraction and risk of bias assessment

After finalising the list of included studies, two independent reviewers extracted characteristics and data from them by reading full-text articles, including study details (e.g. first author, publication date, follow-up period, sample size, blinding method), baseline characteristics of participants, intervention methods, control settings and study outcomes. For RCTs, bias risk assessment was conducted by two independent reviewers according to the Cochrane Handbook for Systematic Reviews of Interventions 5.1 version, which mainly includes assessment of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective reporting. The Newcastle–Ottawa Scale (NOS) was used to assess the methodological quality of observational studies. The NOS is a commonly used tool for assessing the methodological quality of observational studies, including three major domains: selection, comparability and outcome.

Statistical analysis

This meta-analysis was performed using RevMan 5.3 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark) software. For dichotomous variables, the risk ratio (RR) and its corresponding 95% confidence interval (CI) were used as the statistical analysis indicators for effect size. The primary predefined study outcomes included cardiovascular prognosis, such as major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular mortality and non-cardiovascular mortality and cardiovascular outcomes, such as myocardial infarction, stroke, hospitalisation due to unstable angina or heart failure and atrial fibrillation. The Cochran Q test combined with the I^2 statistic was used to assess the degree of heterogeneity among the included study results. When the statistical heterogeneity among the included study results was low ($p > 0.1$ or $I^2 < 50\%$), the analysis was performed using a fixed-effect model; when there was statistical heterogeneity among the included study results ($p < 0.1$ or $I^2 \geq 50\%$), a random-effects model for meta-analysis was used. The significance level of the meta-analysis was set at $\alpha = 0.05$. Publication bias was assessed by plotting a funnel plot. Sensitivity analysis was performed to evaluate the influence of individual studies on the overall effect by observing changes in effect size after excluding individual studies. In addition, subgroup analyses were conducted to examine the effect of CPAP on the occurrence of cardiovascular diseases or prognosis in patients with OSA under different conditions (study design, CPAP adherence and duration of follow-up).

Results

According to the search strategy, a total of 5,004 electronic records were retrieved, with 1,527 from PubMed, 2,854 from Embase, 623 from the Cochrane Library and 1 manually extracted from other sources. After removing 1,135 duplicate records, an initial screening of titles and abstracts resulted in the exclusion of 3,840 irrelevant articles. Following full-text assessment, 16 articles were further excluded for not meeting the inclusion criteria, leaving a final inclusion of 13 articles [11–23] for meta-analysis. The literature selection process is illustrated in Fig. 1.

Characteristics of included studies

The basic characteristics of the 13 included studies are summarised in Table 2. Among them, the majority of studies (61.5%) were conducted in Europe, comprising 10 RCTs and 3 observational studies, and the majority (69.2%) were multicentre studies. The total sample size of patients receiving CPAP intervention was 6,864, while the control group comprised 6,968 patients. Only RCTs reported daily CPAP usage duration, ranging from a mean or median of 1.4 to 6.6 h/day. Regarding the diagnosis of sleep apnoea, seven studies used cardiorespiratory or respiratory polygraphy, whereas four studies used polysomnography. In the process of including patients with OSA, eight studies used the apnoea–hypopnoea index for discrimination. The median follow-up period ranged from 6 to 90 months.

The characteristics of the included patients are presented in Table 3. The mean age ranged from 51.5 to 71.1 years, with a male proportion ranging from 64 to 97%, body mass index (BMI) ranging from 27 to 33.8 kg/m^2, current smoking status ranging from 5 to 58%, type 2 diabetes prevalence ranging from 16.1% to 37.8%, apnoea–hypopnoea index ranging from 23 to 40.1 events/h and the Epworth Sleepiness Scale score ranging from 5.3 to 11.6. Adherence to CPAP was set at 4 h in five studies.

Risk of bias assessment

Detailed information regarding the risk of bias for RCTs is shown in Fig. 2. Due to the open-label design, all studies may have a high risk of performance bias. Additionally, two studies had unclear risks due to factors such as allocation concealment and outcome assessment blinding. None of the RCTs had evidence of incomplete outcome data, selective reporting or other biases. For observational studies, detailed information on the risk of bias is provided in Table S1. Two studies scored 8 points, while one study scored 7 points.

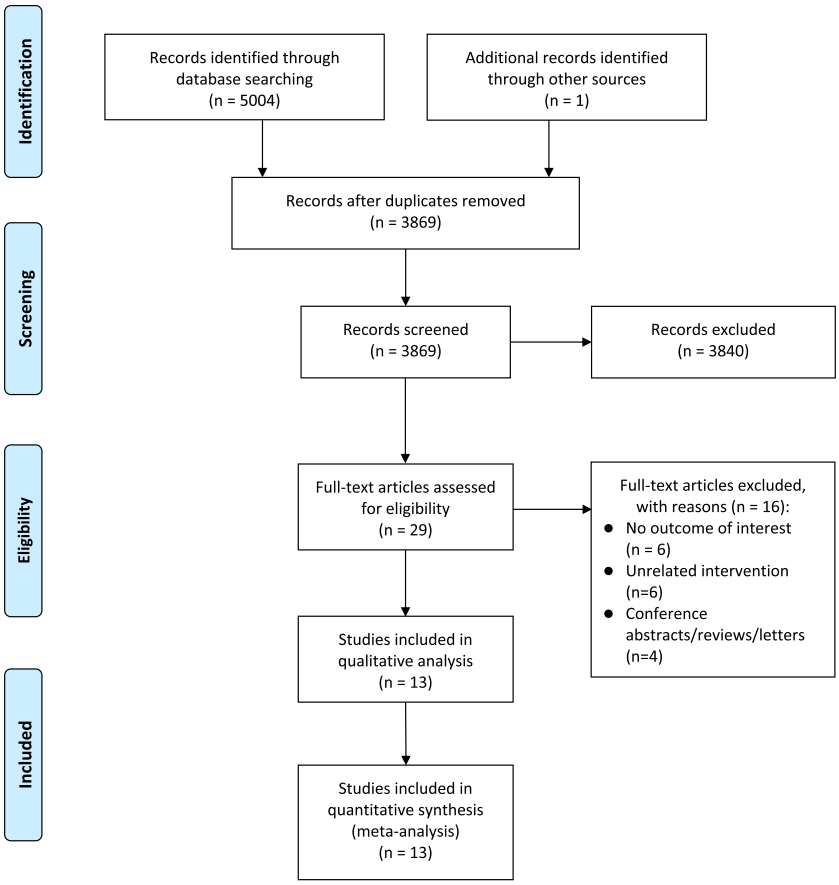

Fig. 1 Study flow diagram of screening and selection

Meta-analysis

In assessing the relationship between CPAP and cardiovascular prognosis, after synthesising the data, it was found that CPAP use did not significantly reduce the risk of MACE, all-cause mortality, cardiovascular mortality or non-cardiovascular mortality compared with conventional treatment. The pooled RR values were 0.73 (95% CI: 0.52–1.03; $p = 0.07$; $I^2 = 66\%$), 0.92 (95% CI: 0.72–1.16; $p = 0.48$; $I^2 = 0\%$), 0.63 (95% CI: 0.33–1.19; $p = 0.15$; $I^2 = 70\%$) and 0.81 (95% CI: 0.57–1.15; $p = 0.23$; $I^2 = 0\%$), respectively (Fig. 3).

Moreover, similar results were obtained for the relationship between CPAP and cardiovascular outcomes. Relative to conventional treatment, there was no significant difference in the likelihood of myocardial infarction, stroke, hospitalisation due to unstable angina or heart failure or atrial fibrillation in the CPAP group. The pooled RR values were 0.94 (95% CI: 0.74–1.20; $p = 0.42$; $I^2 = 2\%$), 0.88 (95% CI: 0.70–1.10; $p = 0.60$; $I^2 = 0\%$), 1.12 (95% CI: 0.90–1.40; $p = 0.49$; $I^2 = 0\%$), 0.92 (95% CI: 0.69–1.24; $p = 0.92$; $I^2 = 0\%$) and 1.01 (95% CI: 0.96–1.07; $p = 0.12$; $I^2 = 45\%$), respectively (Fig. 4).

Subgroup analysis

Subgroup analyses were conducted for study design, CPAP adherence and follow-up duration to evaluate the effect of CPAP on cardiovascular diseases. The results showed that CPAP contributed to a reduction in MACE and cardiovascular mortality in the combined observational studies but not in RCTs (Fig. 3). For other outcomes, no significant differences were observed between CPAP and conventional control groups in both study types (Fig. 4). As shown in Table 4, studies with CPAP adherence ≥ 4 h demonstrated a significant reduction in the risk of MACE and cardiovascular mortality, while non-significant effects were mainly observed in studies with CPAP adherence < 4 h. However, no effect of different follow-up durations on CPAP efficacy was observed, as CPAP did not reduce cardiovascular events in studies with median follow-up durations greater or less than 48 months.

Publication bias and sensitivity analysis

Funnel plot analysis for cardiovascular prognosis and outcomes revealed a symmetric distribution in most studies, except for MACE and hospitalisation due to heart failure,

Table 2 Main characteristics of included studies

First author, year	Country	Design	Sample size (CPAP vs. control)	CPAP, hours/day	Sleep apnea diagnosis	Inclusion criteria	Follow-up, median, months
Randomized controlled trials							
Barbé, 2012 [11]	Spain	Multi-center	357 vs. 366	5.0 (2.18–6.25)	PSG or PG	AHI ≥ 20/h, ESS ≤ 10	48
Bradley, 2005 [12]	Canada	Multi-center	128 vs. 130	median, 3.6	PSG	AHI ≥ 15/h, central apnea and hypopnea ≥ 50%	24
Craig, 2012 [13]	UK and Canada	Multi-center	196 vs. 195	median, 2.4	PG	ODI ≥ 7.5/h	6
Huang, 2015 [14]	China	Single-center	36 vs. 37	4.5 ± 1.1	PSG	CVD, AHI ≥ 15/h	36
Kushida, 2012 [15]	USA	Multi-center	556 vs. 542	mean, 3.8	PSG	AHI ≥ 10/h	6
McEvoy, 2016 [16]	Asia, Australia, Europe, North and South America	Multi-center	1346 vs. 1341	3.3 ± 2.3	PG	CVD, 4% ODI ≥ 12/h	44
McMillan, 2014 [17]	UK	Multi-center	140 vs. 138	median, 1.4	PG	New OSA	12
Parra, 2014 [18]	Spain	Multi-center	57 vs. 69	5.3 ± 1.9	PG	CVD	68
Peker, 2016 [19]	Sweden	Single-center	122 vs. 122	6.6 ± 1.3	PG	CVD, AHI ≥ 15/h	57
Sánchez-de-la-Torre, 2019 [20]	Spain	Multi-center	629 vs. 626	2.78 ± 2.73	PG	AHI ≥ 15/h, ACS	84
Observational studies							
Capodanno, 2014 [21]	Italy	Single-center	17 vs. 122	104 (101–137) months	PSG	AHI ≥ 15/h	34
Gill, 2022 [22]	USA	Multi-center	2250 vs. 2250	NR	NR	NR	NR
Myllylä, 2019 [23]	Finland	Single-center	1030 vs. 1030	NR	PG	AHI ≥ 15/h	90 (48–132)

CPAP continuous positive airway pressure, P*SG* polysomnography, *PG* cardiorespiratory or respiratory polygraphy, *AHI* apnea–hypopnea index, *ESS* Epworth Sleepiness Scale score, *UK* the United Kingdom, *ODI* oxygen desaturation index, *USA* the United States, *CVD* cardiovascular disease, *OSA* obstructive sleep apnea, *AHI* apnea–hypopnea index, *ACS* acute coronary syndrome, *NR* not reported

suggesting no significant publication bias (Figures S1 and S2). Additionally, no substantial changes in the summary results were observed after excluding any single study, indicating a limited influence of individual studies on the overall results.

Discussion

In this meta-analysis, we assessed the impact of CPAP therapy on the incidence and outcomes of cardiovascular diseases in patients with OSA. The main findings of this study are as follows: 1) Compared with the control group, patients with OSA receiving CPAP did not show a significant difference in the incidence of MACE, all-cause mortality, cardiovascular mortality or non-cardiovascular mortality events; 2) CPAP use did not reduce the likelihood of myocardial infarction, stroke, hospitalisation due to unstable angina or heart failure or atrial fibrillation in OSA populations; 3) CPAP adherence ≥ 4 h may be a key factor for CPAP to achieve cardiovascular benefits, significantly reducing the risk of MACE and cardiovascular mortality. This study is expected to provide the latest evidence-based medicine evidence for the use of CPAP in preventing future cardiovascular diseases in patients with OSA and provide a reference for subsequent related research.

Existing studies have shown that patients with OSA are more prone to cardiovascular diseases, such as hypertension, diabetes and dyslipidaemia. This connection may be due to the repeated hypoxaemia and sympathetic

Table 3 Clinical characteristics of included population

First author, year	Age, years	Men, %	BMI, kg/m^2	Current smoker, %	T2DM, %	AHI, events/h	ESS, points	Adherence, hours
Randomized controlled trials								
Barbé, 2012 [11]	51.9 ± 11.0	85	31.2 ± 4.9	29	NR	median, 38.5	6.5 ± 2.26	4
Bradley, 2005 [12]	63.4 ± 9.5	97	29.1 ± 6.0	NR	NR	40.0 ± 16.0	NR	NR
Craig, 2012 [13]	57.7 ± 7.4	78	32.4 ± 5.6	12	16.1	NR	7.95 ± 4.31	2.39
Huang, 2015 [14]	62.4 ± 6.8	72	27.7 ± 3.1	51	35.6	28.5 ± 12.7	8.8 ± 3.25	7
Kushida, 2012 [15]	51.5 ± 12.2	65	32.3 ± 7.2	NR	NR	40.1 ± 25.3	NR	4
McEvoy, 2016 [16]	61.3 ± 7.8	64	29.4 ± 4.3	15	29.8	29.3 ± 16.2	7.4 ± 3.6	3.3
McMillan, 2014 [17]	71.1 ± 4.7	82	33.8 ± 6.1	5	29.9	28.7	11.6 ± 3.65	6
Parra, 2014 [18]	64.7 ± 9.1	64	29.4 ± 4.3	34	36.5	38.4 ± 13.7	7.8 ± 3.68	4
Peker, 2016 [19]	66.0 ± 8.4	84	28.5 ± 3.7	16	24.2	28.8 ± 13.4	5.5 ± 2.3	4
Sánchez-de-la-Torre, 2019 [20]	60.3 ± 10.0	84	29.5 ± 4.5	47	26.2	36.0 ± 18.5	5.3 ± 2.5	2.78
Observational studies								
Capodanno, 2014 [21]	68 (58–74)	81	27 (24–34)	58	36.4	23 (18–30)	7 (5–9)	NR
Gill, 2022 [22]	NR	NR	NR	NR	NR	NR	NR	NR
Myllylä, 2019 [23]	56 ± 10.4	76	32.1 (28–36)	25	37.8	27.5 (12–42)	8.9 ± 4.7	4

Values are expressed as mean ± standard deviation or median (25th quartile-75th quartile)

BMI: body mass index; *T2DM*: type 2 diabetes mellitus; *AHI*: apnea–hypopnea index; *ESS*: Epworth Sleepiness Scale score; *NR*: not reported

activation caused by OSA, leading to abnormal reactions in the cardiovascular system, thereby promoting the occurrence and development of cardiovascular diseases [24, 25]. However, previous studies and meta-analyses have not supported the cardiovascular benefits of CPAP therapy for patients with OSA [4, 9, 26, 27]. In our study, CPAP treatment consistently did not significantly reduce the incidence or mortality of cardiovascular diseases in patients with OSA. However, this result needs to be interpreted with caution and further explored. First, we focused on CPAP treatment compliance. Our subgroup analysis found that in studies with compliance > 4 h, the summary results showed that CPAP significantly reduced the risk of MACE and cardiovascular mortality in patients with OSA, while this effect was not observed in studies with compliance < 4 h. A recent meta-analysis of three large RCTs also supported this finding, suggesting that patients with good CPAP treatment compliance have a lower risk of MACE, indicating that CPAP may play a crucial role in preventing OSA-related cardiovascular events [9]. Second, we considered the impact of follow-up duration. Unfortunately, our subgroup analysis did not find a significant effect of follow-up duration on the results, which may be due to insufficient sample size or too short a follow-up duration. More studies are needed to explore this issue further to clarify the impact of follow-up duration on the efficacy of CPAP treatment. Finally, we need to investigate how to improve CPAP treatment compliance. Various strategies can be adopted to address this issue, including improving the comfort and portability of CPAP devices, providing positive feedback, remote monitoring, strengthening patient education and psychological support and developing personalised treatment plans [28, 29]. These measures are expected to increase patient acceptance and compliance with CPAP treatment, thereby more effectively preventing OSA-related cardiovascular events.

This meta-analysis has several notable strengths. First, the number of studies included in our analysis is the most comprehensive among all existing meta-analyses, including not only RCTs but also additional observational studies. This approach makes our analysis more comprehensive, integrating the results of different types of studies, thereby improving the representativeness and credibility of the study. In the subgroup analysis, although the quality of observational studies was lower, the combined data suggested that CPAP could effectively reduce the risk of MACE and cardiovascular mortality in patients with OSA. However, this effect was not observed in RCTs, which may be due to biases in observational studies and small sample sizes. Therefore, we are more cautious in our neutral judgment of the overall results, emphasising the need for further research. Additionally, we specifically included the latest large RCT ISAACC [20], which makes our study more comprehensive compared with other meta-analyses, avoiding the possibility of missing important studies. Meanwhile, considering previous studies suggesting that CPAP may reduce incident atrial fibrillation, we also explored the effect of CPAP on atrial fibrillation outcomes. Although the number of studies reporting this

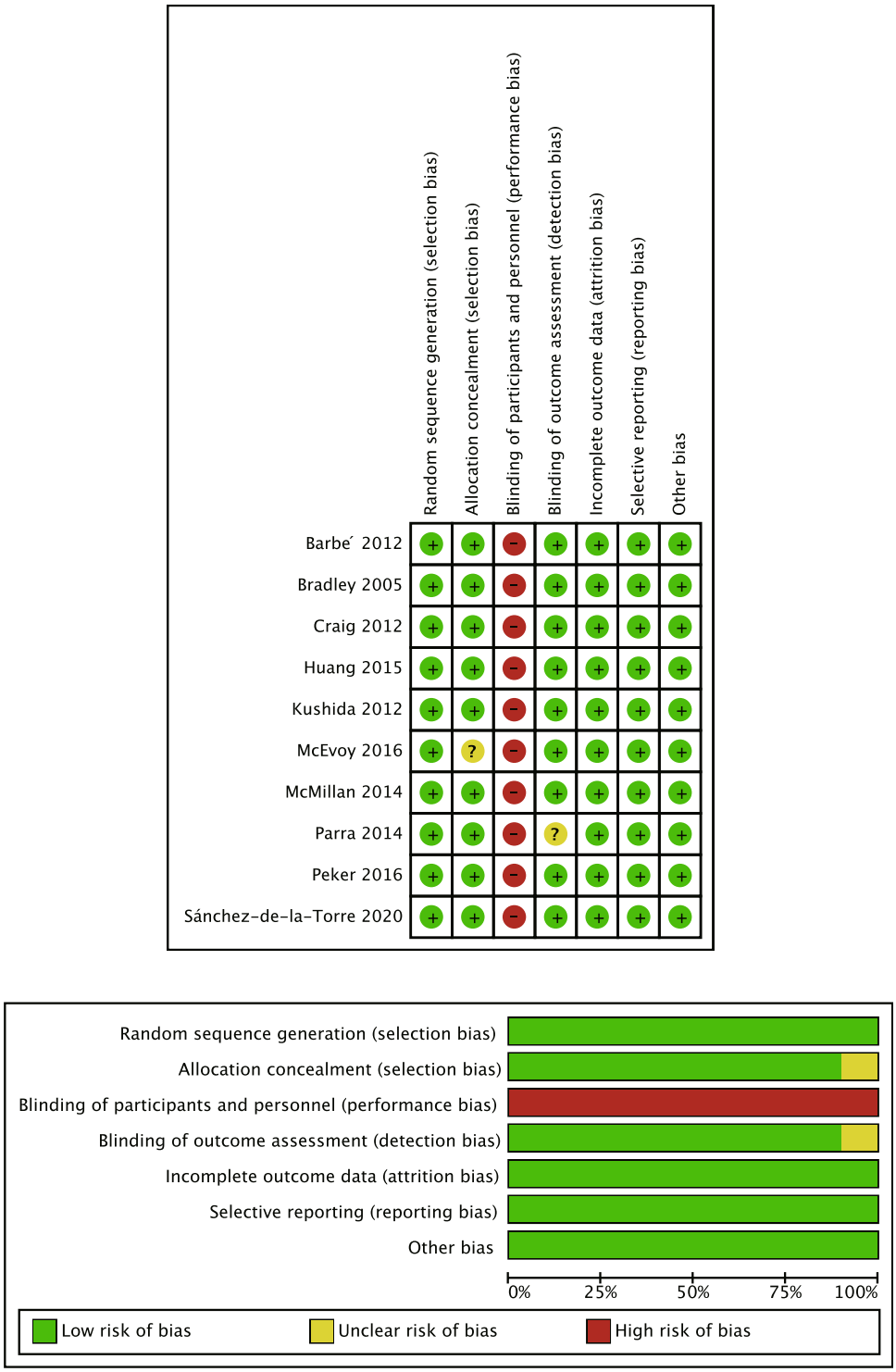

Fig. 2 Methodological quality of the randomized controlled trials

outcome was small, our analysis provided a new perspective. Despite not finding a significant effect of CPAP on the risk of atrial fibrillation in patients with OSA, the importance of this disease outcome cannot be ignored as the population ages, warranting further investigation in the future.

However, this study also has some limitations to note. First, although we included a comprehensive range of studies, we relied on published study results and thus could not access individual patient data (IPD), which prevented us from conducting more detailed analyses. Obtaining IPD would allow us to explore potential factors underlying the lack of significant effects of CPAP treatment, such as baseline characteristics of participants, treatment compliance and airway pressure during treatment, thus finding new ways to improve future treatments.

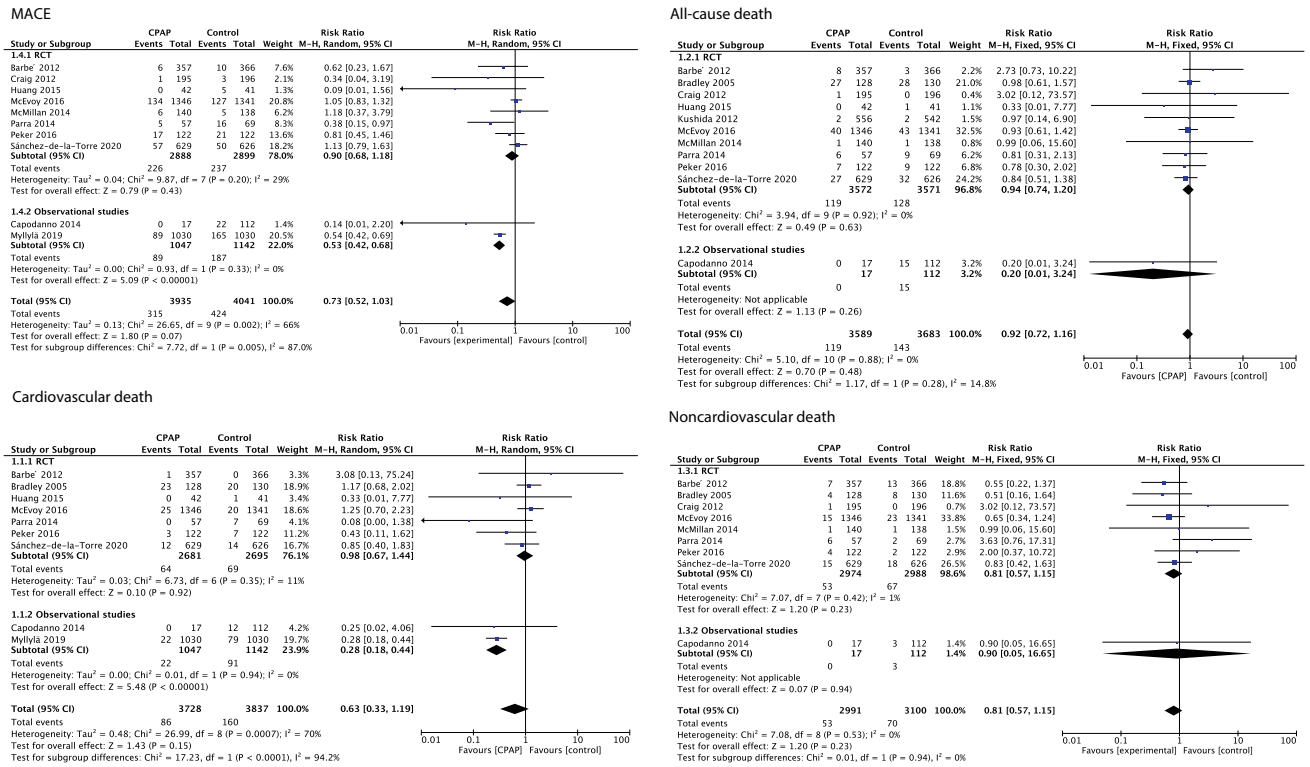

Fig. 3 Forest plot of association between CPAP and cardiovascular events. CPAP: continuous positive airway pressure

Second, the proportion of women included in the studies was low, which may limit the generalisability of our findings regarding the efficacy and safety of CPAP treatment. Due to the lower proportion of women among patients with OSA, we were unable to fully assess the effects and safety of CPAP treatment in female patients. Therefore, future studies need to pay special attention to female patients and conduct gender-specific analyses. Another limitation of our study is that most included studies set CPAP adherence at 4 h per day, which may not capture the full potential benefits of longer adherence durations. While our results suggest benefits at this threshold, it remains unclear if adherence of ≥ 8 h could yield different outcomes. Future research should explore the impact of longer CPAP usage durations to provide more comprehensive insights. Additionally, this study may suffer from some biases. Lack of blinding of the intervention process may affect the participants and thus affect the reliability of the study results. Therefore, future studies should adopt more rigorous study designs, including blinding of the intervention process, to reduce the impact of bias on study results. Most importantly, our analysis did not observe a potential correlation between BMI and the risk of major adverse cardiovascular events. Recent studies suggest that BMI, more so than the severity of OSA, may be a better marker for evaluating major cardiovascular risks in these patients [30, 31]. This is an important bias that should be considered. Carratù et al. [32] found that cardiovascular risk was more strongly related to obesity than to the apnoea–hypopnoea index in a population of southern Italy. Therefore, future research should investigate the role of BMI in assessing cardiovascular risk in patients with OSA. Another important aspect not examined in this paper is the concomitant presence of OSA and hypertension, which together have an additive role in the progression of carotid atherosclerosis and in increasing blood levels of inflammatory markers for atherosclerosis, such as interleukin-6 and pentraxin-3 [33]. Damiani et al. [34] highlight that the coexistence of OSA and hypertension significantly increases carotid intima-media thickness and levels of these inflammatory markers, suggesting a higher cardiovascular risk. Future research should address the combined impact of OSA and hypertension to better understand their effects on cardiovascular outcomes.

Conclusion

Although there is currently no clear evidence supporting CPAP as a treatment to prevent cardiovascular events in patients with OSA, factors such as study design, methodological quality, CPAP compliance and the characteristics of the study population may affect the evidence of CPAP cardiovascular benefits. Further exploration of factors affecting CPAP efficacy is needed to enhance its evidence for patients with OSA.

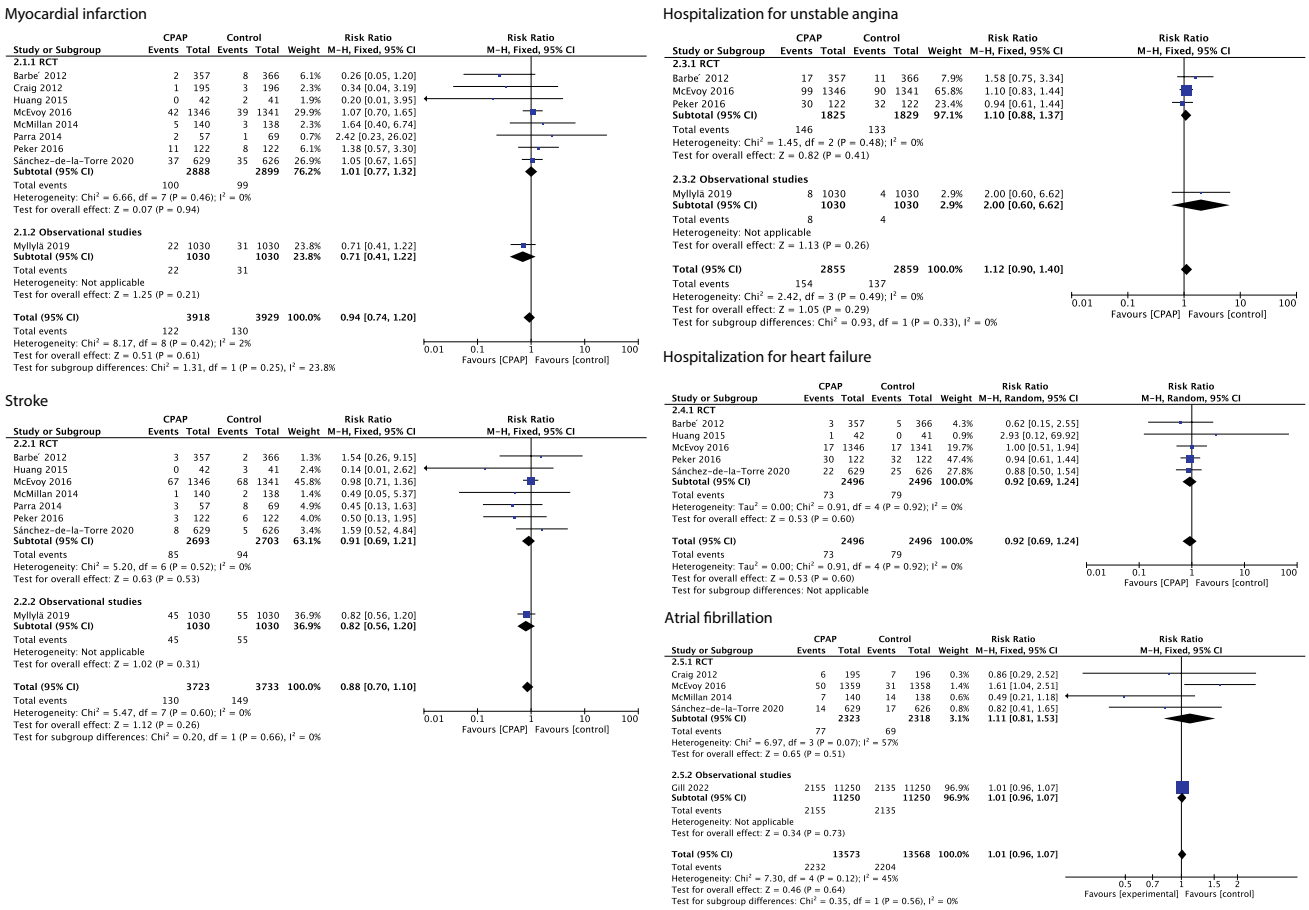

Fig. 4 Forest plot of association between CPAP and cardiovascular outcomes. CPAP: continuous positive airway pressure

Table 4 Subgroup analysis of the association between CPAP and cardiovascular events

Subgroup	No. of studies	Risk ratio (95% CI)	Heterogeneity
MACE			
Adherence ≥ 4 h	6	0.58 (0.46–0.69)	P = 0.36, I^2 = 9%
Adherence < 4 h	3	1.06 (0.88–1.29)	P = 0.57, I^2 = 0%
Median of follow-up > 48 months	4	0.70 (0.44–1.12)	P = 0.005, I^2 = 77%
Median of follow-up ≤ 48 months	6	0.94 (0.76–1.17)	P = 0.22, I^2 = 28%
Cardiovascular death			
Adherence ≥ 4 h	5	0.29 (0.19–0.44)	P = 0.52, I^2 = 0%
Adherence < 4 h	2	1.08 (0.68–1.72)	P = 0.44, I^2 = 0%
Median of follow-up > 48 months	4	0.40 (0.19–0.87)	P = 0.06, I^2 = 59%
Median of follow-up ≤ 48 months	5	1.13 (0.76–1.66)	P = 0.70, I^2 = 0%
All-cause death			
Adherence ≥ 4 h	6	1.02 (0.59–1.75)	P = 0.67, I^2 = 0%
Adherence < 4 h	3	0.90 (0.66–1.25)	P = 0.73, I^2 = 0%
Median of follow-up > 48 months	3	0.82 (0.55–1.23)	P = 0.99, I^2 = 0%
Median of follow-up ≤ 48 months	8	0.98 (0.73–1.31)	P = 0.71, I^2 = 0%
Noncardiovascular death			
Adherence ≥ 4 h	5	1.11 (0.60–2.07)	P = 0.25, I^2 = 25%
Adherence < 4 h	2	0.73 (0.46–1.16)	P = 0.61, I^2 = 0%
Median of follow-up > 48 months	3	1.17 (0.67–2.05)	P = 0.18, I^2 = 41%
Median of follow-up ≤ 48 months	6	0.64 (0.40–1.01)	P = 0.93, I^2 = 0%

CI confidence interval

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Data availability The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of Jinhua Central Hospital.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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