International Journal of Cardiology 191 (2015) 128–131

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Continuous positive airway pressure treatment reduces cardiovascular death and non-fatal cardiovascular events in patients with obstructive sleep apnea: A meta-analysis of 11 studies

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ARTICLE INFO

Article history:
Received 15 April 2015
Accepted 2 May 2015
Available online 5 May 2015

Keywords:
Obstructive sleep apnea
Cardiovascular death
Non-fatal cardiovascular events
Obstructive sleep apnea

The prevalence of obstructive sleep apnea (OSA) is 3% to 7% in the general population [1]. OSA has been found to be associated with cardiovascular disease, leading to high rates of morbidity and mortality [2]. Dong et al. reported that moderate to severe OSA significantly increased cardiovascular risk, particularly the risk of stroke [3]. Continuous positive airway pressure (CPAP) therapy can correct airway obstruction so to improve the quality of nighttime sleep in patients with OSA [1]. It is considered as the first-line therapy for severe OSA [4]. However, the cardiovascular outcomes in patients undergoing CPAP therapy remain unclear. The purpose of this meta-analysis is 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 (apnea–hypopnea index, AHI ≥ 20).

Reports investigating the effects of CPAP therapy on cardiovascular outcomes were searched in the literature databases PubMed, Ovid Medline, and EMBASE by 2 investigators independently. The following search terms were used: "obstructive sleep apnea", "continuous positive airway pressure", and "cardiovascular outcomes". The latest search was performed on March 31, 2015. Duplicated reports, abstracts, reviews, comments, or editorial, and publications including less than 30 participants were excluded. The quality of each included study was estimated by Downs and Black score. A score ≥ 20 was considered good quality and <20 was considered poor quality. The definition for mild OSA and moderate to severe OSA was 10 ≤ AHI ≤ 20 and AHI ≥ 20, respectively. The primary endpoint was the incidence rates of cardiovascular death and non-fatal cardiovascular events. Non-fatal cardiovascular events included non-fatal myocardial infarction, non-fatal stroke, coronary artery bypass surgery, and percutaneous transluminal coronary angiography. Odds ratio (OR) with 95% confidence interval (95% CI) was calculated. The study heterogeneity was assessed by calculating the I^2 index with $I^2 > 50\%$ indicating a statistically significant heterogeneity. Sensitivity analysis was conducted to evaluate the effects of each individual report on the overall results. Publication bias was estimated by funnel plot and Egger's weighted regression test. All the analyses were performed using the STATA statistical analysis software. *P* value was 2 sided and $P < 0.05$ was considered statistically significant.

A total of 4620 patients from 11 reports were included in the meta-analysis (Table 1). The quality of the 11 reports was satisfactory because Downs and Black scores of the reports were from 20 to 25 (Table 1) [1, 4–13]. The overall results were not sensitive to each individual study (Fig. 1). Total study heterogeneity ($I^2 = 19.9\%$, $P = 0.254$) and the study heterogeneity ($I^2 = 0.0\%$, $P = 0.730$) of the subgroup analysis of patients with moderate to severe OSA (AHI ≥ 20) were low. Thus, a fixed-effects model was used for the meta-analysis. 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 = 0.24–0.41, Z = 8.51, $P < 0.0001$, Fig. 2). 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 = 0.18–0.47, Z = 4.97, $P < 0.0001$, Fig. 3). In addition, 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 = 0.43–0.75, Z = 3.96, $P < 0.0001$, Fig. 4) without significant heterogeneity ($I^2 = 42.4\%$, $P = 0.123$). Funnel plot (Fig. 5) and Egger's weighted regression test found no significant publication bias ($P = 0.542$).

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http://dx.doi.org/10.1016/j.ijcard.2015.05.003

Table 1
Characteristics of included studies (n = 11).

Author	Year	Patient with CPAP	Patient without CPAP	Patient selection	Downs and Black score
Marin	2005	372	638	Unselected	24
Doherty	2005	107	61	Unselected OSA	21
Cassar	2007	131	127	Moderate to severe OSA	24
Campos-Rodriguez	2009	28	68	Moderate to severe OSA	22
Barbe	2012	357	366	Unselected OSA	24
Campos-Rodriguz	2012	576	262	Unselected OSA	21
Martinez-Garcia	2012	503	281	Unselected OSA	20
Martinez-Garcia (b)	2012	28	70	Moderate–severe OSA	21
Anandam	2013	177	212	Moderate–severe OSA	22
Parra	2015	57	69	Moderate–severe OSA	21
Nishihata	2015	64	66	Unselected OSA	20

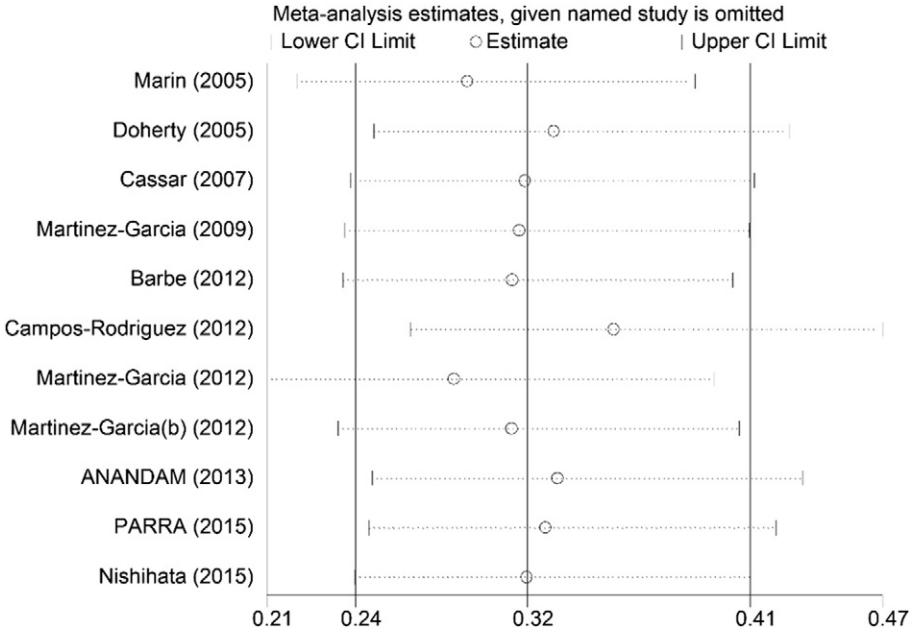

Fig. 1. Sensitivity analysis of the included studies.

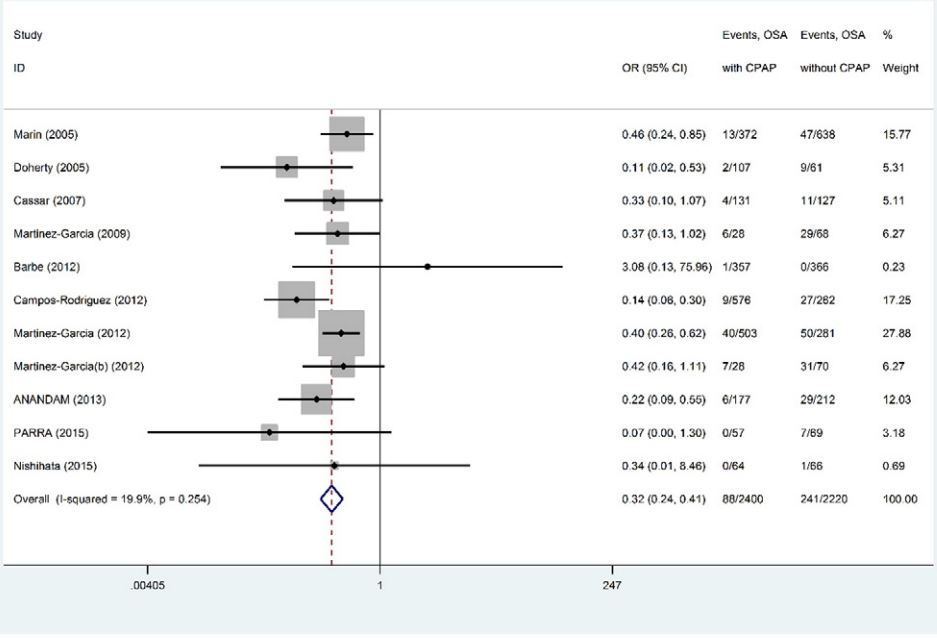

Fig. 2. Forest plot of the effect of CPAP on the incidence of cardiovascular death in patients with OSA.