

A Systematic Review and Meta-Analysis of Prevalence of Obstructive Sleep Apnea in Iranian Patients with Cardiovascular Disease: Perspective of Prevention, Care and Treatment

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Background: Obstructive sleep apnea (OSA) is a chronic breathing disorder during sleep. It is prevalent among patients with cardiovascular disease (CVD) and can increase its severity and mortality. Various studies have reported different results in Iran. This systematic review and meta-analysis aimed to determine the prevalence of OSA in Iranian patients with CVD.

Materials and Methods: In this study, eight papers published in Persian and English languages were reviewed. The articles were searched using the following keywords and all their possible combinations: "obstructive sleep apnea", "sleep-disordered breathing", "sleep apnea", "OSA", "cardiovascular disease", "hypertension", and "Iran". Scientific databases, including the Scientific Information Database (SID), Magiran, Web of Science, PubMed, and Scopus, were searched with no time limitations. Data were analyzed using a meta-analysis and a random effects model. Besides, heterogeneity was assessed using the I² statistic. Data analysis was performed in Stata version 11.

Results: The review of eight studies, with a total sample size of 1646 patients, showed that the prevalence of OSA was 59.21% (95% CI: 53.11-65.32) among CVD patients. Also, the prevalence of OSA was higher in men (60.12%; 95% CI: 60.12-82.54) than in women (41.01%; 95% CI: 16.08-65.94). Besides, it was estimated to be higher based on the STOP and STOP-BANG questionnaires (63%; 95% CI: 52.89-73.10) as compared to the Berlin questionnaire (56.63%; 95% CI: 49.20-64.06).

Conclusion: More than half of Iranian CVD patients have OSA. Therefore, identifying high-risk patients to reduce the adverse effects of sleep apnea seems necessary.

Key words: Cardiovascular disease; Obstructive sleep apnea; Systematic review

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of mortality worldwide (1). Approximately 16.7 million people die from CVD (especially heart attack and stroke) each year. The mortality rate was predicted to reach 24

million by 2020 (2). Although cardiovascular mortality has declined in industrialized countries, in developing countries, such as Iran, mortality from CVD has increased, which can be attributed to urbanization, weight gain, reduced physical activity, and increased blood lipids (3).

Various studies have shown that one-third and one-quarter of Iranians suffer from metabolic syndrome and hypertension, respectively (4, 5). High blood pressure, cigarette smoking, abdominal obesity, abnormal lipids, diabetes, stress, low consumption of fruits and vegetables, and lack of regular physical activity are the major modifiable risk factors for CVD (6, 7). In recent decades, although therapies and preventive strategies have been used to control CVD worldwide, they appear to be ineffective. One possible reason for the failure of current strategies to control CVD may be the lack of identification of some important risk factors (8).

Obstructive sleep apnea (OSA) is one of the risk factors associated with CVD, which is often undiagnosed. OSA is a common sleep disorder, characterized by repetitive upper airway collapse during sleep, causing nocturnal arousals and sleep fragmentation (9). The prevalence of OSA in the general population varies between 9% and 38% (10). Patients may complain of fatigue, excessive daytime sleepiness, poor performance, and morning headaches; however, many of these patients are asymptomatic (11). OSA, by activating the sympathoadrenal system, oxidative stress, systemic inflammation, and alteration of adipokines, can increase the risk of CVD, hypertension, and metabolic syndrome (12).

Although the gold standard for the diagnosis of OSA is polysomnography (PSG), because of the high prevalence of OSA and the lack of access to sleep laboratories, screening tests, such as STOP, STOP-BANG, and Berlin questionnaires are often used to identify patients (13). OSA is a risk factor for CVD, which is often neglected. It is necessary to identify people at risk to reduce the risk of developing or exacerbating the disease. The first step to implement any health plan is to identify the current condition (prevalence of OSA). Therefore, this study aimed to estimate the prevalence of OSA in Iranian patients with CVD.

MATERIALS AND METHODS

Search strategy

In this study, the prevalence of OSA was evaluated among Iranian patients with CVD, according to the

Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement (14). To find relevant articles, national databases, including the Scientific Information Database (SID) and Magiran, as well as international databases of Web of Science, Scopus, and PubMed, were searched without any time limitation. The keywords included “obstructive sleep apnea”, “sleep disordered breathing”, “sleep apnea”, “OSA”, “cardiovascular disease”, “hypertension”, and “Iran”. Since the Iranian databases were not sensitive to Boolean operations, the search was performed as single words. A reference list of eligible articles was also reviewed to access more articles.

Study selection and data extraction

First, all articles examining the prevalence of OSA among Iranian patients with CVD were retrieved by two independent researchers. Full-text observational studies, published in Persian or English language, were included in the analysis. Irrelevant studies, gray literature, interventional studies, review articles, and duplicates were excluded. Two reviewers independently reviewed the titles and abstracts of the retrieved studies and reviewed the full-text of selected studies, according to the eligibility criteria. Any disagreements were resolved by further discussion. The reviewers independently recorded the required information, such as the first author's name, year of study publication, location of the study, sample size, mean age of the samples, body mass index (BMI), and prevalence of OSA in the data extraction sheet. The methodological quality of the articles was examined, based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (15).

Statistical analysis

In this systematic review and meta-analysis, the point estimate and 95% confidence interval for OSA were calculated based on the binomial distribution. Heterogeneity between studies was evaluated by Cochran Q (P-value <0.10 was considered significant) and I² statistic. Based on the I² statistic, heterogeneity was classified into <25% (low heterogeneity), 25-75% (moderate

heterogeneity), and >75% (high heterogeneity) (16). Regarding the heterogeneity of selected studies, the pooled prevalence was estimated using a random effects model (17). A univariate meta-regression analysis was also performed to examine the association between OSA and the publication year, mean age of the samples, sample size, and BMI.

Besides, using a subgroup analysis, the pooled prevalence was determined by the type of screening tool. To ensure the stability of the results, a sensitivity analysis was carried out. Therefore, studies were removed from the analysis one by one to examine their effect on the overall prevalence of OSA. To ensure that all published articles were included in the study, an Egger's weighted regression analysis was performed (18). Data analysis was performed in Stata version 11.

RESULTS

In this study, all articles on OSA among Iranian CVD patients were systematically evaluated without any time limitation. The initial search yielded 132 articles. Of retrieved articles, 119 were not related to the objectives of this review, and five studies were omitted due to lack of information; finally, eight studies were included in the meta-analysis. The screening and selection processes are presented in Figure 1.

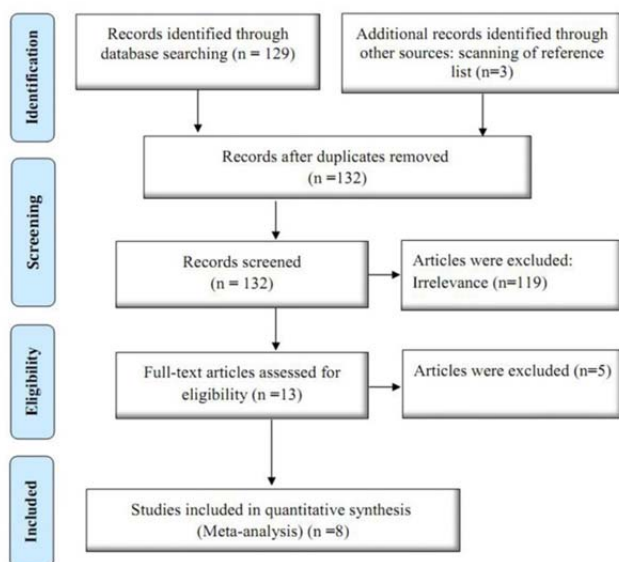


Figure 1. Flowchart of the process of screening and selection of articles

The sample size varied from 61 to 406 patients. In three studies, STOP-BANG and STOP tools were used, and in the rest of studies, Berlin instrument was used. Details of the selected studies are presented in Table 1.

The results showed that publication bias was not significant ($P=0.787$) (Figure 2). Based on the sensitivity analysis, it was found that the exclusion of each study alone did not affect the overall prevalence of OSA.

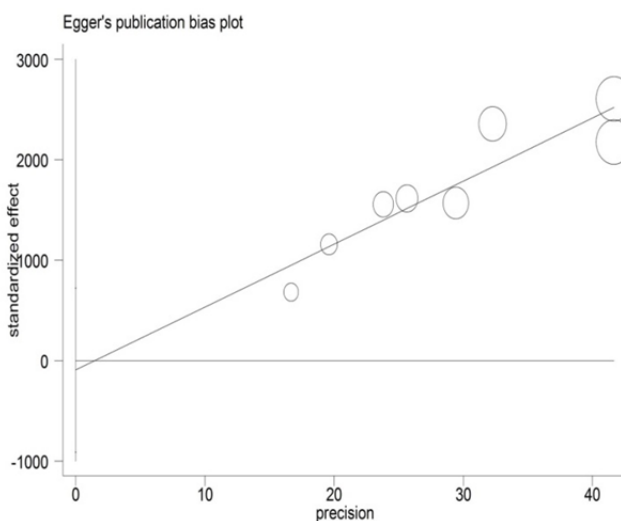


Figure 2. Publication bias. The size of the circles represents the sample size of the studies

According to Figure 3, the pooled prevalence of OSA was 59.21% (95% CI: 53.11-65.32) in Iranian patients with CVD. Also, the prevalence of OSA was higher in men (60.12%; 95% CI: 60.12-82.54) than in women (41.01%; 95% CI: 16.08-65.94). The results of the subgroup analysis revealed that the prevalence of OSA was 63% (95% CI: 52.89-73.10), based on the STOP and STOP-BANG questionnaires and 56.63% (95% CI: 49.20-64.06), based on Berlin instrument.

As shown in Figure 4, the meta-regression analysis showed no significant relationship between the overall prevalence of sleep apnea and variables of publication year, mean age of the patients, BMI, and sample size.

Table 1. Characteristics of the selected articles

First Author	Year	Age	BMI	City	Sample size		Prevalence	Screening Tool
					Total	M/F		
Setareh et al.(19)	2018	63±11.53	-	Sari	400	216/184	62.5	STOP-BANG
Ghanei Gheshlagh et al. (20)	2016	70.7	28.9	Saghez	200	92/118	73	STOP
Khajeh-Mehrizi et al. (21)	2016	59±12.3	26.7±4	Tehran	210	62/148	53.3	STOP-BANG
Ghazal et al.(22)	2015	59±9	26.67±4.59	Isfahan	127	74/53	65.4	BQ
Mozafari et al.(23)	2015	-	-	Ghom	92	-	59	BQ
Amra et al.(24)	2014	58.6±11.1	27.3±4.1	Isfahan	61	48/13	40.9	BQ
Javadi et al. (25)	2014	61.83±10.5	26.7 ± 3.6	Qazvin	406	235/171	52.2	BQ
Rezaei et al.(26)	2013	64.46±13.5	-	Saghez	150	69/81	63	BQ

BQ: Berlin Questionnaire

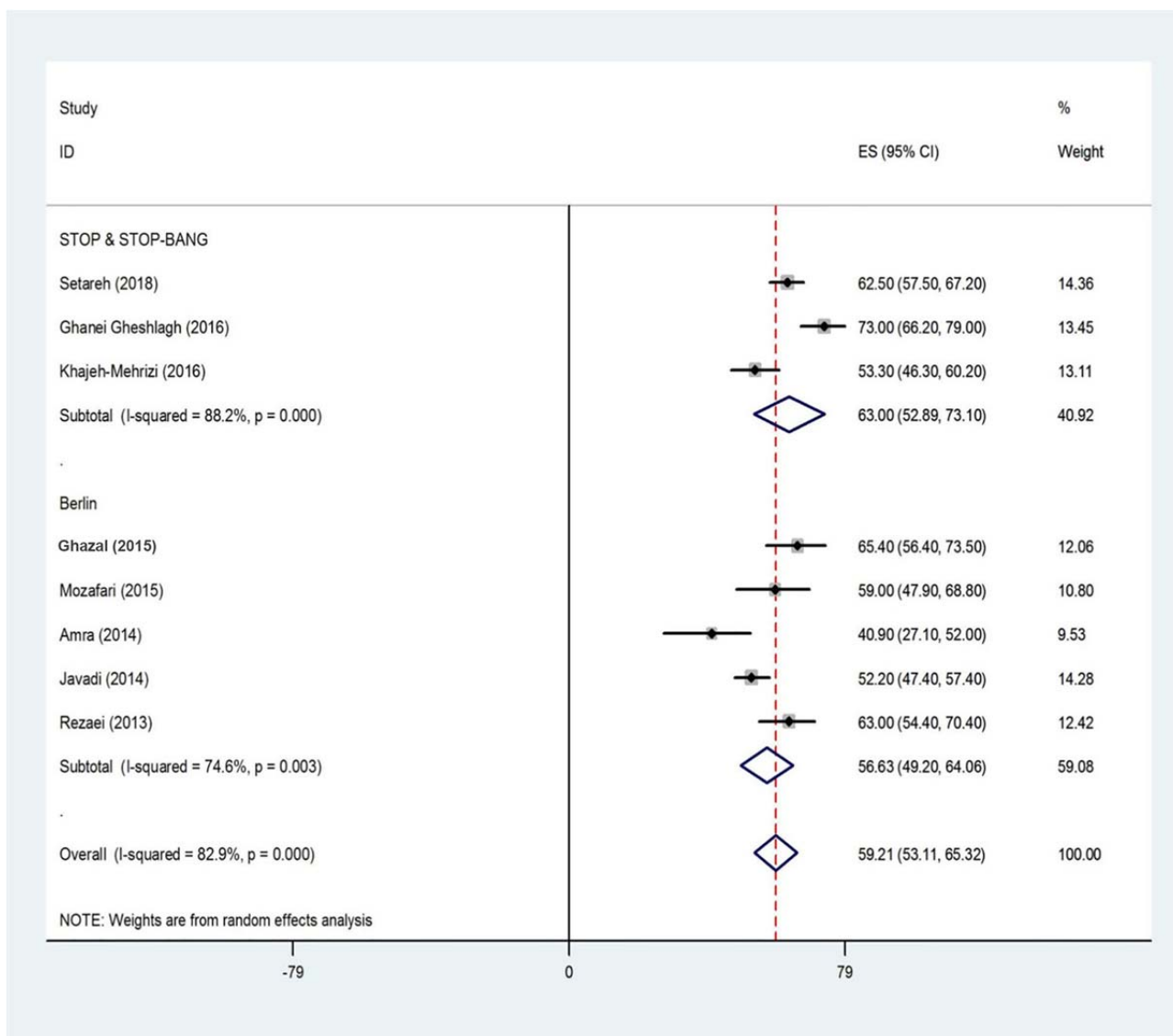


Figure 3 OSA prevalence and its 95% confidence interval in Iranian cardiovascular patients based on the screening tools according to the random effects model. The point in the middle of each line segment shows the prevalence of OSA in each study, whereas the rhombus shape demonstrates the prevalence of OSA for all studies

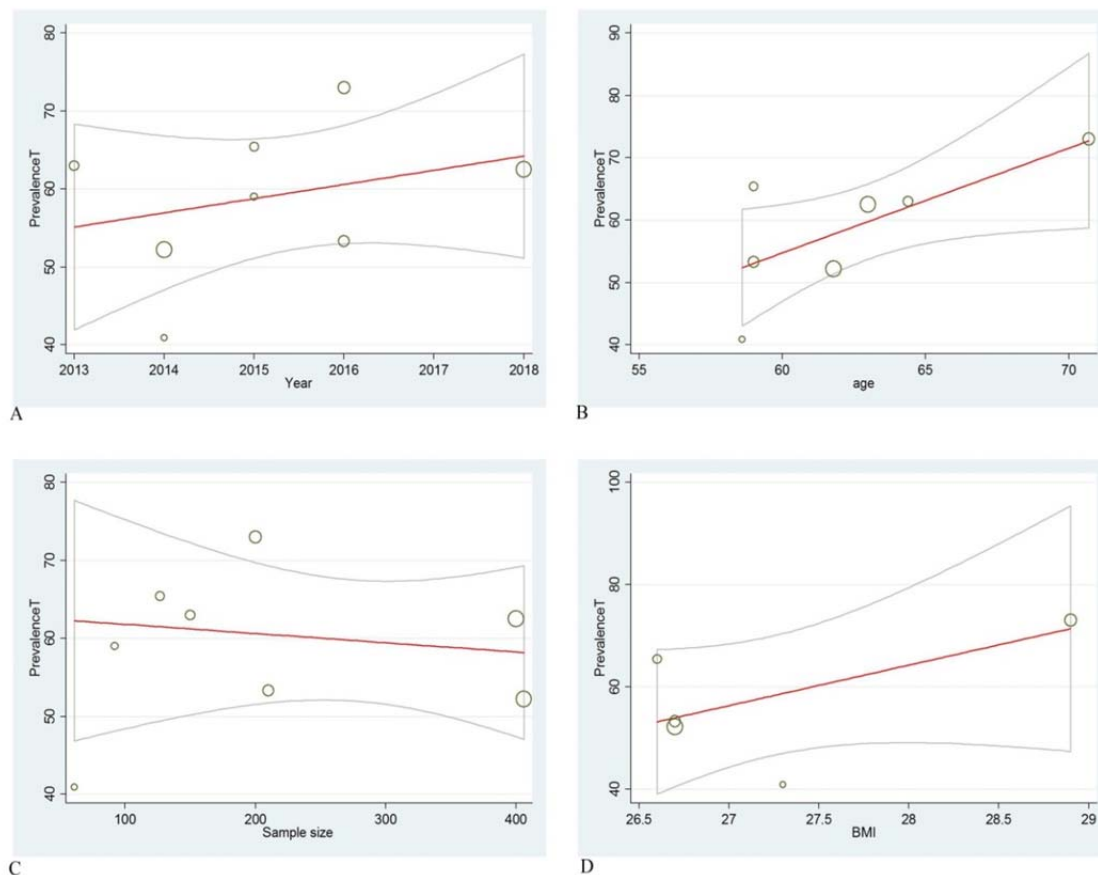


Figure 4. Meta-regression results. Relationship between OSA and the articles' publication year (A), age (B), sample size (C) and BMI (D)

DISCUSSION

This systematic review and meta-analysis was conducted to estimate the pooled prevalence of OSA among Iranian patients with CVD. The findings showed that the prevalence of OSA was 59.21% in these patients; in other words, more than half of patients with CVD suffered from OSA. In a study by Cho et al., the prevalence of OSA was 69.2% in patients with acute coronary syndrome (27). In two other studies, the prevalence of OSA in men and women with coronary artery disease was 37% and 30%, respectively (28, 29).

A recent meta-analysis that combined the results of five observational studies reported that the prevalence of OSA was 54.5% in Iranian patients with type 2 diabetes (12). OSA causes endothelial damage and dysfunction; therefore, it may lead to generalized atherosclerosis (30).

The results of various studies have shown that the prevalence of OSA in patients with hypertension (31), chronic heart failure (32), ischemic heart disease (33), and stroke (34) is higher than the general population. Moreover, the results of a study on 218 patients with heart failure showed that the prevalence of OSA was 26% in these patients, and older age, male sex, and higher BMI were predictors of OSA (35).

Moreover, in a study by Porthan et al., the prevalence of OSA in patients with atrial fibrillation was estimated at 32% (36). OSA leads to arrhythmias with autonomic nervous system activation, hypoxia, and elevated catecholamines (26). The present results revealed that OSA was present in 82% of patients with resistant hypertension (37). Although the exact mechanism is unclear,

hypertension is thought to be due to activation of the sympathetic system, resulting in hypoxia (38).

The subgroup analysis showed that the prevalence of OSA in men was higher than in women (60.12% vs. 41.01%), which is consistent with the results of previous studies (39, 40). Other studies have shown that in both the general population and patients with CVD, OSA is two to three times more common in men than in women; it is also more common in the elderly than in the youth (31, 35, 41). Simpson et al. reported that fat deposition can be the reason for the observed difference among men and women. The results of their study revealed that fat percentage in the neck region and BMI together explained 33% and 37% of total variance in the apnea-hypopnea index in women and men, respectively (42). Considering the higher prevalence of OSA in men than in women, some researchers consider OSA as a condition with male dominance (20, 43).

The results of our meta-regression analysis showed no significant relationship between the overall prevalence of OSA and the patient's age. This finding is consistent with the results of previous cohort studies (44, 45). Some studies have also identified aging as a risk factor for OSA (46, 47). Bixler et al. reported that the prevalence of OSA in men and women over 65 years was twice as high as middle-aged individuals (48). On the other hand, in a study by Ciavarella et al., there was no significant association between OSA and BMI, which is consistent with the results of our study (49). In the study by Wall et al., the likelihood of OSA in people with BMI above 30 kg/m² was 6.5 times higher than those with a normal BMI (50). So far, various studies have reported inconsistent results; therefore, further research is needed in this field. It should be noted that due to the low number of selected studies, we could not report the prevalence of OSA by disease type.

One of the limitations of this study is the lack of analysis of the gray literature (conferences, abstracts, and dissertations). The main strength of this study is its novelty, because it is the first report on the prevalence of OSA in patients with heart disease in Iran.

The findings of this study, examining the prevalence of OSA in patients with CVD for the first time, showed that 60% of these patients suffered from OSA. The presence of OSA can cause or aggravate heart disease; therefore, identifying and treating patients at risk of OSA is necessary.

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