Satu Sarin

Sleep Apnea Prevalence and Severity after Coronary Revascularization versus no Intervention: A Systematic Review & Meta-analysis

UNIVERSITY OF TURKU

Faculty of Medicine

Autumn semester 2024

Supervisor: Jenni Toivonen MD, PhD

Satu Sarin

Uniapnean esiintyvyys ja vaikeusaste akuutin vaiheen sepelvaltimotoimenpiteen jälkeen: systemaattinen kirjallisuuskatsaus & meta-analyysi

Turun yliopisto

Lääketieteellinen tiedekunta

Syyslukukausi 2024

Ohjaaja: dos Jenni Toivonen

TURUN YLIOPISTO

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SARIN, SATU: Uniapnean esiintyvyys ja vaikeusaste akuutin vaiheen sepelvaltimotoimenpiteen jälkeen: systemaattinen kirjallisuuskatsaus & meta-analyysi

Syventävät opinnot, 35 sivua

Anestesiologia, tehohoito, ensihoito ja kivunhoito

Syyslukukausi 2024

Obstruktiivinen uniapnea on yleinen sairaus sepelvaltimotautipotilaiden keskuudessa ja sen vaikeusaste vaihtelee merkittävästi näiden potilaiden välillä. Tässä systemaattisessa katsauksessa ja meta-analyysissä verrataan uniapnean esiintyvyyttä ja vaikeusastetta niillä epävakaata sepelvaltimotautia sairastavilla potilailla, joille tehtiin revaskularisaatio toimenpide vs. joille ei tehty revaskularisaatiota.

Katsaukseen sisällytettiin ne tutkimukset, joissa aikuisille potilaille tehtiin joko sepelvaltimoiden ohitusleikkaus (CABG), perkutaaninen sepelvaltimotoimenpide (PCI) tai ei mitään revaskularisaatio interventiota epävakaan sepelvaltimotaudin vuoksi. Lisäkriteerinä tutkimuksissa piti olla suoritettuna intervention jälkeen luotettava unitutkimus. Haku suoritettiin 27.1.2023 neljästä eri tietokannasta (Pubmed, Google Scholar, ScienceDirect and Cochrane).

Kahdeksasta mukana olleesta tutkimuksesta viisi oli suorittanut unitutkimuksen PCI:n jälkeen, kaksi sen jälkeen, kun revakularisaatiota ei tehty, ja vain yksi tutkimus oli tutkinut uniapneaa CABG:n jälkeen. Keskimääräinen AHI (apnea-hypopnea-indeksi) uniapneapotilailla PCI:n jälkeen oli 34,9 /h (95 % CI 25,9 - 43,8; SD 4,6) vs. 24,1 /h (15,6 - 32,6; SD 4,3) ei revaskularisaation jälkeen. Keskimääräinen alhaisin happisaturaatiotaso (SpO_2) uniapneapotilailla PCI:n jälkeen oli 82,6 % (81,5-83,8; SD 0,3) vs. 83,3 % (80,7-85,6; SD 1,8) ei intervention jälkeen.

CABG:n jälkeen uniapneapotilaiden keskimääräinen AHI oli 32,3/h (SD 16,3) ja alin SpO_2 79,3 % (SD 9,1).

Tässä katsauksessa havaitsimme, että uniapnea oli vakavampi niillä potilailla, joille tehtiin revaskularisaatio epävakaan sepelvaltimotaudin vuoksi, kuin potilailla, joille ei tehty mitään sepelvaltimointerventiota.

Avainsanat: sepelvaltimotauti, uniapnea-oireyhtymät, obstruktiivinen uniapnea, perkutaaninen sepelvaltimotoimenpide, sepelvaltimoiden ohitusleikkaus

Lisäselvitys allekirjoittaneen osuudesta kirjallisuuskatsauksen teossa

Artikkeli kirjoitettiin yhteistyössä el Marjo Ajosenpään kanssa, osana hänen väitöskirjatutkimustaan. Marjo suoritti kirjallisuuskatsauksen haun, yhdessä ennalta sovittujen hakutermien perusteella. Hakutulokset tallennettiin paitsi Zoteroon myös Google Sheets -alustalle, josta molemmat (MA ja SS) pystyivät ajantasaisesti käymään läpi hakutuloksia otsikoiden perusteella (yhteensä 551 artikkelia). Ensimmäisessä läpikäynnissä poistettiin paitsi kaksoiskappaleet, myös samanaikaisesti ne artikkelit, joiden otsikot sisälsivät ennalta sovittuja poissulkukriteerejä. Lopulta näistä jäljellä olevista artikkeleista (yht. 188) jaettiin kaikki tasan molempien kesken, itsenäiseen tiivistelmien läpikäymiseen. Mukaan valittiin ne artikkelit, jotka sisälsivät ennalta sovitut sisäänottokriteerit ja eivät sisältäneet ennalta sovittuja poissulkukriteerejä. Tiivistelmien perusteella valikoituneet artikkelit käytiin läpi molempien (MA ja SS) toimesta, lukemalla ne kokonaan itsenäisti läpi (yhteensä 54). Lopullinen päätös artikkelien valinnasta mukaan systemaattiseen katsaukseen tehtiin yhdessä. Lopulta kirjallisuuskatsaukseen valikoitui mukaan 8 artikkelia ja näistä 7 meta-analyysiin.

Artikkelin kirjoitusprosessissa Marjo Ajosenpää vastasi lähinnä statistiikasta sekä meta-analyysistä, joiden tulokset Marjo myös kirjoitti artikkeliin auki. Allekirjoittaneen vastuulla oli puolestaan kirjoittaa artikkelin esittely ja katsauksen suorittamisen menetelmä -kappaleet. Lopulta tiivistelmä ja pohdinta -kappaleet kirjoitettiin yhdessä tulosten perusteella. Kirjoitustyö oli jatkuvaa yhteistyötä, jossa molemmat avustivat toinen toistaan.

Kirjoitusprosessin lisäksi allekirjoittanut on osallistunut UNI-CABG-tutkimuksen suorittamiseen mm. rekrytoimalla potilaita mukaan tutkimukseen ja keräämällä dataa, tekemällä unipolygrafia-laitteiden kiinnitystä sekä tutkimusyön valvontaa Turun yliopiston Unitutkimuskeskuksessa. Syventävien opintojen kirjallinen työ on mahdollistanut laajan tutustumisen kliinisen tutkimuksen suorittamiseen sekä tieteellisen artikkelin kirjoittamiseen.

Sleep Apnea Prevalence and Severity after Coronary Revascularization versus no Intervention: A Systematic Review & Meta-analysis

Ajosenpää Marjo[1,2,3], Sarin Satu[1], Vahlberg Tero[4], Yüksel Peker[6,7,8,9], Kalleinen Nea[1,5], Toivonen Jenni[1,2,3]

[1]Department of Pulmonary Diseases and Clinical Allergology, Sleep Research Center, University of Turku, Turku, Finland,

[2]Department of Anesthesiology and Intensive Care, University of Turku, Turku, Finland, [3]Division of Perioperative Services, Intensive Care and Pain Medicine, Turku University Hospital, Turku, Finland, [4]Department of Biostatistics, University of Turku and Turku University Hospital, Turku, Finland, [5]Heart Center, Turku University Hospital, University of Turku, Turku, Finland, [6]Department of Pulmonary Medicine, Koc University School of Medicine, TR 34010 Istanbul, Turkey, [7] Department of Molecular and Clinical Medicine, Sahlgrenska Academy, University of Gothenburg, SE 40530 Gothenburg, Sweden[8]Department of Clinical Sciences, Respiratory Medicine and Allergology, Faculty of Medicine, Lund University, SE 22185 Lund, Sweden, [9]Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA

Abstract

Study Objectives : Obstructive sleep apnea (OSA) is a common disease in patients with coronary artery disease (CAD). The manifestation of OSA can vary significantly in different types of CAD patients. This systematic review and meta-analysis compares the prevalence and severity of OSA in acute coronary syndrome (ACS) patients with or without coronary intervention.

Methods : The studies in which either coronary artery bypass grafting surgery (CABG), percutaneous coronary intervention (PCI) or no coronary intervention was done on adult patients with ACS were included. As an additional criterion, the study had to include a reliable sleep study after the intervention. The search was conducted 27.1.2023 and all suitable articles after 1.1.2010 were included from four different valid databases. This systematic review followed the PRISMA guidelines.

Results: Of the eight included studies, five had performed a sleep study after PCI, two after no coronary intervention and only one study had studied OSA after CABG. Mean AHI in no-OSA group after PCI was 9.6 /h (95% CI 3.6-15.6) and in no intervention group 6.4 /h (95% CI 3.5-9.4). In OSA patients, mean AHI after PCI was 34.9 /h (95% CI 25.9-43.8) vs 24.1 /h without intervention (95% CI 15.6-32.6).

Conclusions : Sleep apnea is very common among ACS patients and it is important to take account after intervention. Moreover, we found that OSA is more severe in patients who underwent PCI for ACS than in patients who did not undergo any coronary intervention.

Keywords: CAD, coronary artery disease; OSA, obstructive sleep apnea; AHI; PCI; CABG

Statement of Significance

This systematic review and meta-analysis synthesize that OSA should also be suspected in patients with ACS. This patient group may benefit from a sleep study 6 months after acute phase.

Introduction

Untreated obstructive sleep apnea (OSA) is known to cause various pathophysiological changes in the human body and increase both morbidity and mortality.[1–3] The worldwide prevalence of OSA is alarmingly high and it is estimated that at least 936 million men and women between the ages 30 and 69 have mild to severe OSA (apnea-hypopnea index, AHI; measured as events/hour, ≥ 5).[4] The prevalence of sleep apnea has increased over time.[5] Up to 17% of men and 9% of women with 50-70 years of age suffer from moderate to severe sleep apnea (AHI ≥ 15/h), either unaware or aware of their diagnosis.[5] This is the clinically important OSA population (AHI ≥ 15/h) as they are the ones whose treatment would be recommended even in the absence of associated symptoms or disorders.[6] Symptomatic sleep apnea with AHI ≥ 5/h and excessive daytime sleepiness is referred as OSA syndrome and its prevalence has been estimated to be 6% of all men and 4% of all women.[7]

OSA has been shown to be an independent risk factor for development of coronary artery disease (CAD), especially in middle-aged people.[8,9] Despite this knowledge, studies have discovered that up to 37-64% of coronary artery bypass grafting (CABG) surgery patients suffer unknowingly at least of a moderate state of OSA.[10–14] Acute coronary syndrome (ACS) patients undergoing less invasive percutaneous coronary intervention (PCI) also suffer from OSA with estimated prevalence of 35-62%.[15] The rate of underdiagnosis in these CAD patients with OSA is concerning as several studies have linked OSA to significant postoperative complications after revascularization.[16–24] However, it has not been

investigated whether the revascularization technique or the procedure itself affects the severity or prevalence of OSA.

The aim of this systematic review is to expose what is known about OSA in ACS patients, as well as determine the differences between the prevalence and severity of OSA in different intervention groups; those undergoing PCI or CABG and those without coronary intervention.

Methods

This systematic review and meta-analysis followed the accepted guidelines for reporting of systematic reviews and meta-analysis (PRISMA). Ethical approval was not required as the systematic review was based on secondary data. The systematic review's protocol was registered in the PROSPERO database (registration number: CRD42023418669).

Search strategy

The search was completed on January 27, 2023 and was carried out using four different reliable databases (Pubmed, Google Scholar, ScienceDirect and Cochrane). The strategy of the search and the search terms were created with a committed research librarian and an experienced colleague. In the search, the limits set for the year of publication were between 1.1.2010 and 1.12.2023. Additional search was performed September 7, 2023 and on May 26, 2024 was verified that no new articles to this topic had been published. The records were limited to include the form of either clinical trial or randomized controlled trial. The search terms used in different databases were coronary artery disease, percutaneous coronary intervention, coronary artery bypass grafting surgery, obstructive sleep apnea and different versions of these terms (Appendix A). All the results were uploaded and saved on the Zotero platform. For screening all titles, abstracts, and full texts by two reviewers (MA and SS) the search results were also stored in Google Forms Sheets platform.

Inclusion and exclusion criteria

The inclusion of selected records was limited by pre-selected inclusion and exclusion criteria. Inclusion criteria were: 1) studies where was either CABG surgery, PCI or no coronary intervention done for the adult patients suffering ACS, 2) revascularization was done because of the CAD, 3) studies including reliable sleep research for example polysomnography (PSG) or reliable sleep monitoring at home after the revascularization.

Exclusion criteria were: 1) study population under the age of 18 years old, 2) published in another language than English, 3) revascularization was done for the peripheral arteriosclerosis, 4) pathophysiological studies, 5) drug trials and 6) animal studies. For more detailed additional exclusion criteria see **Figure 1** and Appendix B.

Screening

In the first removal, all duplicates were removed. Simultaneously records with titles directly containing any exclusion criteria were also excluded. From these remaining records, the material was distributed equally to two reviewers (MA and SS) for independent screening. Any potential ambiguities regarding the inclusion were reviewed and discussed with the second author, and disagreements were presented to a third reviewer (TJ). After selection, both reviewers screened the remaining full-text records.

At this stage, records were excluded if reliable sleep study was performed but not reported or stated whether it was done before or after intervention. Records were also excluded if they did not report which intervention was performed, both PCI and CABG were performed, the type of intervention could not be extracted from the data or the missing data was not obtained

from the first author. More detailed list of excluded articles that might appear to meet the inclusion criteria are in Appendix B.

The subjects were divided into OSA or no-OSA groups based on their AHI scores. American Academy of Sleep Medicine (AASM) has published the International Classification of Sleep Disorders (3th Edition) where the cutoffs for mild, moderate and severe OSA presents AHI being 5.0 and 14.9 /h; AHI 15.0-29.9 /h, and AHI ≥ 30 /h.[25] Most of the included studies classified OSA-patients having AHI ≥ 15 /h ja no-OSA < 15 /h. Except in the study of Lee[16] the cutoff in AHI was ≥ 30 /h and in a study made by Schiza[26] AHI ≥ 10 /h.

Data extraction

All data was stored and sorted into an Excel file, where extraction and final inclusion was done. Two independent researchers (MA and SS) performed initial data collection on the outcomes of each article. These records were listed using a standardized chart to extract data and assess study quality. Extracted information included publication title, first author, publication year, study design, study population, age and gender distribution, PCI/CABG/no (coronary) intervention, PSG findings (AHI and lowest oxygen saturation level (SpO_2) value during night), observation time, outcomes and possible confounding factors and factors reducing the quality of the research. Any missing data was requested from the first author of the studies. Additional data was received from M.D. PhD Y. Peker of the CABG population.

Quality assessment

The records and their quality were evaluated based on the principles and procedural guidelines of systematic reviews presented by Egger.[27] The Newcastle-Ottawa scale was used to assess the methodological quality of the selected studies. Both reviewers independently screened all included records using this 8-criteria checklist classifying the studies to low (7-9

points), moderate (4-6 p.) or high risk (0-3 p.) of bias. The strength of the epidemiologic evidence for the data in each record was rated as high, when p value was <0.001. The evidence was rated moderate when p value was <0.05 but >0.001, and weak with p value being >0.05. Reference lists of all included studies were manually checked, and the reliability was evaluated individually.

Statistical analysis

The data from all of the included records were separately evaluated. Study characteristics for continuous variables, which followed normal distribution were summarized with mean and standard deviation (SD) whereas non-normally distributed variables as median and interquartile range (IQR) or range. Categorical variables were summarized with counts (n) and percentages. The standard deviation (SD) and standard error (SE) were calculated with an established method from range or the interquartile range when they were not directly reported in the articles with the supposition the data follows normal distribution.[28]

Heterogeneity of the studies were estimated by the I^2-test, where I^2 >50% was considered as high heterogeneity. The Cochrain Q test was used to examine statistical heterogeneity between subgroups (significant at p <0.05). Assessment of publication bias was performed with visual evaluation of the funnel plots. A sensitivity analysis was conducted using a leave-one-out approach. All of the statistical analyses were performed using IBM SPSS Statistics (version 29.0.2.0, IBM Corp., Armonk, NY). Only reported data was analyzed and no data was imputed except from the timing of performing sleep monitoring after the revascularization. Studies that reported sleep monitoring timing to be “during the hospital stay” were assumed to be done approximately on the 7th day after the revascularization.[29,30]

Results

Search results

The flow chart of study selection is shown in **Figure 1**. Altogether 551 articles were identified using databases. In the end a total of 8 articles were included in the systematic review and 7 in the meta-analysis.

Study Characteristics

The characteristics of the included studies are presented in **Table 1.** Sleep monitoring was performed after PCI in 5 studies (with a total of 386 participants), in 2 after no coronary intervention (642 participants) and only in one after CABG (147 participants). In the CABG study,[31] participants had surgery for unstable CAD. ACS was defined as ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI) or unstable angina pectoris (UAP) following the current standard clinical guidelines.[32] Studies where there was no coronary intervention were either designed to compare prevalence of OSA after revascularization intervention and non-revascularization[30] or after acute myocardial infarction before revascularization.[26,33]

Overall studies contained 1 175 subjects with weighted average age of 57.7 years (SD 2.8) and weighted average of BMI 26.8 kg/m^2 (SD 0.75). The distribution of males was 961 (81.8%). 25 subjects were excluded from the review because their sleep monitoring findings were not reported. In the report of CABG participants (n = 23) with AHI between 5-15 /h were excluded from the study because there were OSA-patients with graded AHI being ≥ 15 /h and no-OSA with AHI < 5 /h.[31] Two of the participants (n = 2) were excluded from the no-OSA group in the study by Schiza.[33] In the end a total of 1 150 subjects were included in the review.

OSA after ACS

Selected studies contained altogether 610 (53.0%) participants who had OSA (OSA group) and 540 (47.0%) participants who didn't have OSA (no-OSA group). Mean AHI in no-OSA group after PCI was 9.6 /h (95% CI 3.6-15.6) and in no intervention group 6.4 /h (95% CI 3.5-9.4). Pooled effect size for AHI from all of the OSA groups was 31.7 /h (95% CI 24.2-39.3) and no-OSA groups 7.9 /h (95% CI 4.9-10.9). OSA prevalence after PCI was 48.7% and OSA patients' mean AHI was 34.9 /h (95% CI 25.9-43.8) in median 7 days (range 3.5-60). In no intervention group 49.2% had OSA and their mean AHI was 24.1 /h (95% CI 15.6-32.6) in median 5 days (range 3-7). Only one article performed sleep study after CABG, where 83% had OSA and the mean AHI of OSA patients was 32.3 /h, after an average of 73 days.

In the group of patients with sleep apnea, bypass surgery patients were older (mean age 65.3 years; SD 7.8) and had higher BMI (mean 28.5 kg/m^2; SD 3.9) than PCI and no coronary intervention. After PCI the mean age was 55.2 years (SD 1.8) and mean BMI 26.6 kg/m^2 (95% CI 25.0- 28.2). No intervention group mean age was 59 years (SD 0.3) and mean BMI 27.4 kg/m^2 (95% CI 23.2-31.6).

Lowest SpO2 value wasn't reported in Lee[16], Schiza[26,33] and Calcaianu[34] articles, but for those that did the mean lowest SpO_2 value in the OSA group was 82.3% (95% CI 80.5-84.1) and no-OSA group 87.0 % (95% CI 85.6-88.5). The variation of registered sleep registration timing after ACS was high (from a few days to 3 months). The mean lowest saturation level (SpO_2) in the OSA group after PCI was 82.6% (95% CI 81.8-83.4) after no coronary intervention median 83.2% (95% CI 80.7-85.6) after CABG was 79.3%. **Table 2** is comparing the sleep monitoring results between different intervention groups.

Meta-analysis

Funnel plots are shown in Appendix C and summary of Newcastle-Ottawa risk of bias scoring of each article in Appendix D. Publication bias was significant in both PCI and no coronary intervention based on funnel plots. The main reason was the difference of the AHI cutoff between the no-OSA and OSA. High heterogeneity between studies likely arrives from different performing dates of sleep study after ACS which varies from median 7 days (range 3.5 to 60 days) after PCI and median 5 days (range 3 to 7 days) after no coronary intervention.

Sufficient data for meta-analysis were reported for the lowest SpO_2 and AHI-levels in OSA patients after PCI and no intervention. CABG patients were not included in meta-analysis because there was only one study. Effect sizes for SpO_2 were after PCI 84.9 (SD 0.6) and no intervention 84.5 (SD 0.0).

Meta-analysis, AHI in OSA patients

Heterogeneity between patients with no intervention and patients who underwent PCI statistically insignificant p = 0.09). Meta-analysis of OSA patients reveals that after ACS AHI was lower in patients with no intervention than in patients who underwent PCI, 24.1/h (95% CI 15.6-32.6; I^2 =98.6%) vs 34.9 /h (95% CI 25.9-43.8; I^2=97.4%), (**Figure 2)**.

Meta-analysis, lowest SpO_2 in OSA patients

Among OSA patients, only five studies reported the lowest SpO_2 from performed sleep study. In OSA patients who underwent PCI, the lowest SpO_2 was 82.6% (95% CI 81.8-83.4 %; I^2= 0) vs median 83.2% (95% CI 80.8-85.6; I^2=90.7%) OSA patients with no coronary intervention. Heterogeneity between these subgroups was not significant (p = 0.71). **(Figure 3)**.

Discussion

This systematic review and meta-analysis show that approximately half of ACS patients have OSA and the severity of OSA varies between different intervention groups. OSA patients' that had no coronary intervention as a treatment for the ACS had lower AHI. The lowest saturation level in PCI groups was higher than in no intervention group PCI group than no coronary intervention, although the data was available only in three articles. Significance wasn't statistically relevant. Both groups are suffering low saturation level during nighttime.

Repetitive apneas, arousals from sleep and intermittent hypoxia are referred combined as sleep disordered breathing (SDB) which include obstructive sleep apnea and these patients are particularly vulnerable after acute myocardial infarction. The increased cardiac workload and endothelial dysfunction may ultimately lead SDB patients' oxygen supply to a mismatch between oxygen demand and supply after revascularization. Study done by Arzt[35] et al. showed that despite successful revascularization, patients with acute myocardial infarction and sleep-disordered breathing had predisposing factors for heart failure f. ex. prolonged myocardial ischemia compared with those without sleep-disordered breathing.[35]

OSA patients are more likely to prior CABG or PCI.[36] However, when AHI ≥ 30 /h and OSA is classified as severe, OSA participants have higher likelihood of prior CABG.[37] Patients with OSA had higher comorbidity and they had an increased risk of postoperative pneumonia and increased length of hospital stay.[36] CABG is usually done in the acute phase of unstable CAD and PSG is therefore difficult to schedule before the intervention. One study showed that easily done STOP-BANG questionnaire could predict pulmonary complications after CABG and it can reveal 36.1% of the risk patients.[38] STOP-BANG questionnaire have

five point questions about snoring, tiredness, other person observation about breathing problems during nighttime, high blood pressure level and BMI over 35 kg/m^2.

In the randomized controlled RICCADSA-trial, revascularized CAD cohort participants had more OSA than previously reported and majority of these didn't report daytime sleepiness. Worryingly, two-thirds of these patients had OSA, which was higher than other known risk indicators for CAD such as hypertension, diabetes, or current smoking in this cohort.[11] This reveals the importance of screening the OSA after revascularization and it should be considered as secondary prevention.

When comparing these three groups and specially PCI and no coronary intervention groups, it is impossible to say unequivocally whether OSA patients having revascularization are more multimorbid than patients who had no intervention, and that's why they have more severe apnea. It can be assumed that their disease pathophysiology differs in some way from the non-revascularization group. Patients with severe CAD are enrolled in the revascularization groups and PCI is the modality of choice for myocardial reperfusion.[39] CABG is usually offered to hospitalized patients with ACS and a higher comorbidity burden.[40] In the Zhang's[30] study revascularization was not considered in patients without significant coronary artery stenosis (≤ 70% diameter stenosis) but they highlighted that this did not mean the absence of lesions in coronary arteries. Their data showed that in the non-revascularization group OSA patients had significantly higher incidence of diseased coronary vessels and OSA was associated with higher risk of subsequent cardiovascular events in patients without revascularization. In this review OSA patients after PCI were younger and had lower BMI than those OSA patients that did not have revascularization but there was no significant difference between these characteristics. However, the finding suggests that the higher

incidence of OSA in these patients is not only related to traditional OSA risk factors (BMI and age), but also the severity and type of CAD. Further investigations about OSA patients having more apneic episodes during night after revascularization is needed.

The difficulty of diagnosing CAD patients with OSA is due to the fact that most of them suffer from non-sleepy type of apnea and thus, have the diagnosis unknowingly.[41] This is concerning because when OSA patients' AHI is over 30 the association to get cardiovascular disease or all cause mortality is 46% higher than the healthy ones.[42] In the meta-analysis done by Yu[43] results showed that even using a positive airway pressure (PAP) machine the occurrence of MACCE's (major adverse cardiac and/or cerebrovascular event) did not decrease later in life in OSA patients. Although there are other benefits of treatment with PAP for sleep apnea, their findings did not support treatment with PAP with a goal of prevention of cardiovascular outcomes or death.[43]

This review and meta-analysis displays the large degree of heterogeneity in currently published studies with varying criteria of timing to perform sleep monitoring and diagnosing OSA. In the selected studies all except one explored OSA less than two weeks after ACS. Schiza[26] showed in their study that there is a high prevalence of OSA in the acute phase of ACS but this did not persist and AHI was significantly lower 6 months later, indicating that OSA may be transient. They suspected that stunned myocardium and progressing heart failure after ACS could be causing tissue swelling in upper airways and worsen the obstruction. There is clearly a need for further well-designed prospective studies with a long-term follow-up after ACS to fully answer this question.

Many studies have shown how OSA is affecting the development of cardiovascular diseases, quality of life and mortality. Still, there are many open questions, such as, the causal relationships between OSA and CAD and the effect of coronary interventions on the prognosis of OSA patients in later life. For our knowledge there has been no previous systematic reviews investigating the prevalence and severity of OSA after ACS and its' differences between the intervention methods. More research is needed to reveal how ACS and its treatment is affecting patients' sleep disorders and apnea tendency later in life.

Strengths and limitations

The strength of our study is the accurate screening, as we only included articles that reported the results of reliable sleep monitoring after ACS. In the beginning of the search many articles were excluded because sleep monitoring was performed before ACS. However, it is possible that a few suitable articles were accidentally left out in the initial search. A significant limitation in our study is the small number of reliable studies found and the fact that only one study of the CABG patients fulfilled the search criteria. The main challenge of this meta-analysis arises from the significant amount of heterogeneity between the studies and not at least from the timing of sleep monitoring. For pure curiosity when removing one significantly longer follow-up[34] study from the meta-analysis the results didn't differ from the original analysis.

Conclusion

In summary, we state that 53% of ACS patients had OSA and mean AHI in all OSA groups was 31.9 /h which is indicated as severe sleep apnea. Sleep apnea should be considered in the CAD patient's treatment. It appears that the severity of OSA varies in different patient groups; especially many patients who have undergone PCI or CABG suffer from severe OSA.

Disclosure statement

None. The authors have no conflicts of interest to closure.

Supplementary material

Supplementary data to this article can be found online.

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Figures and tables

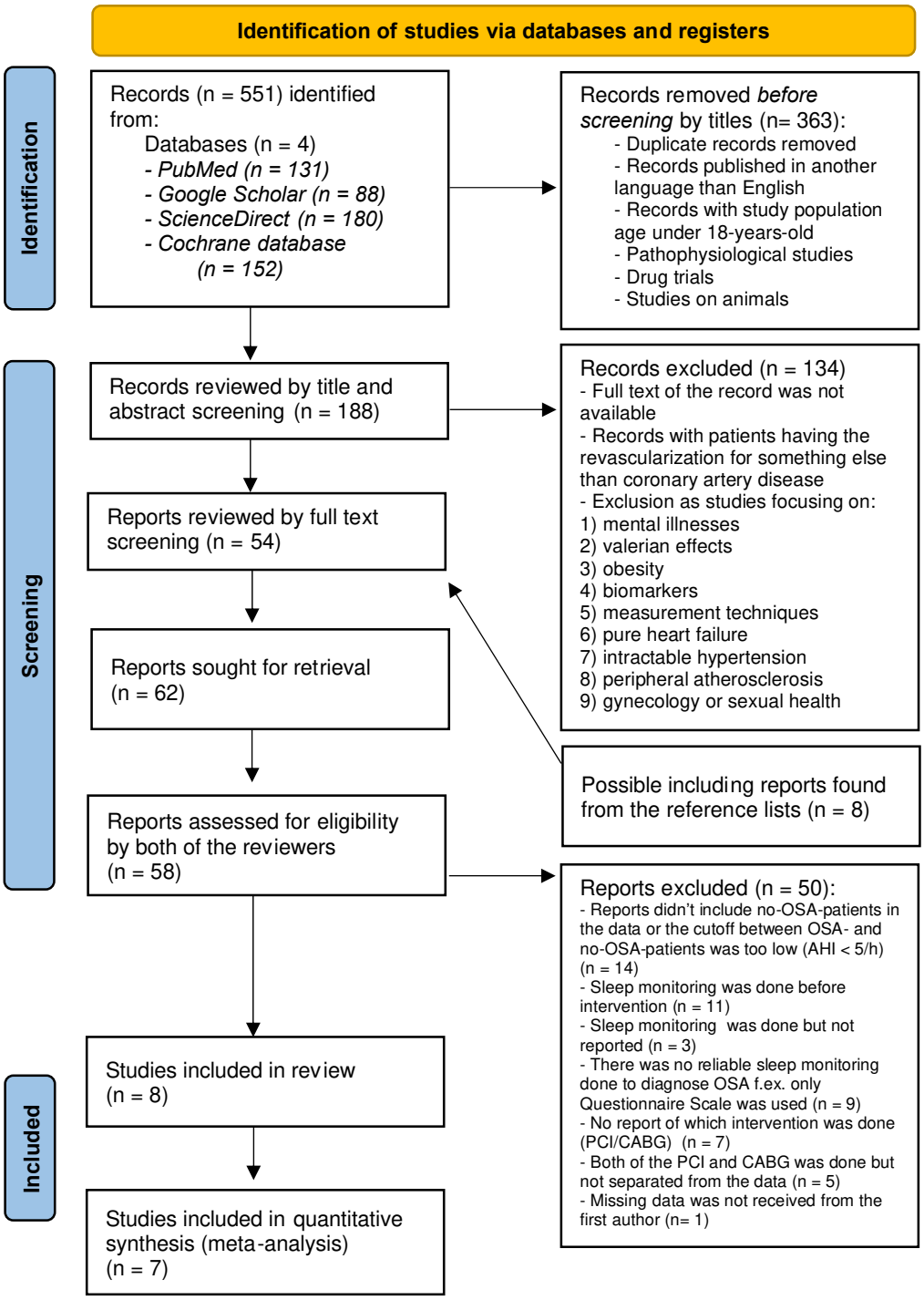

Figure 1. PRISMA flow diagram
OSA, obstructive sleep apnea; AHI, apnea-hypopnea index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting surgery.

Table 1. Study characteristics

First author (year)	**Study design**	**Country**	**Sample size *n***	**PCI/ CABG /No**	**Outcome**	**Age** (years) ***mean (SD)***	**Male sex *n*** (%)	**BMI** (kg/m²) ***mean (SD)***	**Sleep monitoring** (device)	**PSG done after ACS** (days)	**AHI cutoff** (events /h)	**OSA vs. no-OSA *n*** (%)	**AHI OSA vs. no-OSA** (events /h) ***mean (SD)*** *p value*	**SpO_2 lowest OSA vs. no-OSA** (%) ***mean (SD)*** *p value*
Buchner et al. (2022)	POS *(sub-analysis)*	Germany	41	PCI	Patho-physiology of the heart	**56 (10)* ***54 (11)*	35 (85.4)	**29.3 (3.4)* ***26.7 (2.5)*	PSG (Alice System)	4 ± 1	≥ 15	21 (51.2) 20 (48.8)	31 (13) 6 (3) *p = 0.001*	83 (4) 86 (4) *p = 0.100*
Calcaianu et al. (2019)	POS	France	53	PCI	Patho-physiology of the heart	59 (9.6)	43 (81.1)	28.5 (4.2)	PSG (Cidelec)	60	≥ 15	39 (73.6) 14 (26.4)	42.3 (13.4) 15.1 (3.9) *p < 0.001*	- - -
Lee et al. (2011)	PLCS	Singapore	105	PCI	MACE	52.7 (9.8)	103 (98)	24.9 (3.3)	Home (Somte)	3.5 ± 1.5	≥ 30	44 (42) 61 (58)	48.6 (13.4) 14.4 (8.2) *p < 0.001*	- - -
Liu et al. (2022)	POS	China	119	PCI	Patho-physiology of the heart	**55.4 (12.0)* ***56.3 (11.2)*	104 (87.4)	**26.9 (3.4)* ***25.4 (2.9)*	Hospital, portable device (ApneaLink Air)	(during hosp-italiza-tion)	≥ 15	60 (50.4) 59 (49.6)	28.7 (5.25) 7.5 (1.33) *p < 0.001*	82.4 (6.9) 86.6 (4.6) *p = 0.016*

Table 1. Study characteristics (continue)

First author (year)	**Study design**	**Country**	**Sample size *n***	**PCI/ CABG /No**	**Outcome**	**Age** (years) ***mean (SD)***	**Male sex** *n* (%)	**BMI** (kg/m²) ***mean (SD)***	**Sleep monitoring** (device)	**PSG done after ACS** (days)	**AHI cutoff** (events /h)	**OSA vs. no-OSA** ***n*** (%)	**AHI OSA vs. no-OSA** (events /h) ***mean (SD)*** *p value*	**SpO_2 lowest OSA vs. no-OSA** (%) ***mean (SD)*** *p value*
Loo et al. (2014)	POS	Asian (multi-center)	68	PCI	MACCE	54.2 (8.8)	59 (86.8)	25.5 (3.8)	Home (Embletta)	14	≥ 15	24 (35.3) 44 (64.7)	24.0 (8.78) 4.9 (3.65) *p < 0.001*	82.5 (7.75) 89.0 (5.75) *p < 0.001*
Peker et al. (2022)	RCT *(sub analysis)*	Sweden	147	CABG	Patho-physiology of the heart	**65.3 (7.8)* ***63.5 (9.5)*	107 (86.3)	**28.5 (3.9)* ***25.4 (3.6)*	Home (HSAT)	73 ± 30	≥ 15 < 5	106 (72.1) 18 (12.2)	32.3 (16.3) 3.2 (1.3)	79.3 (9.1) 86.5 (8.8)
Schiza et al. (2012)	LS	Greece	52	No	Prevalence and time course of OSA	55.8 (13)	40 (76.9)	28.5 (4.9)	PSG (Alice 5)	3	≥ 10	28 (53.8) #22 (42.3)	19.7 (6.9) #4.9 (1.93)	84.5 (3.7) -
Zhang et al. (2023)	POS	China	590	No	MACCE	**59.0 (9.8)* ***56.8 (10.0)*	470 (79.7)	**28.07 (3.58)* ***26.12 (3.51)*	Hospital, portable device (ApneaLink Air)	(during hospi-taliza-tion)	≥ 15	288 (48.8) 302 (51.2)	28.4 (14.07) 7.9 (4.44) *p < 0.001*	82 (6.67) 87 (2.96) *p < 0.001*

POS, prospective observational study; PLCS, prospective, longitudinal cohort study; RCT, randomized controlled trial; LS, longitudinal study; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting surgery; No, no coronary intervention; MACE, major adverse cardiac event; MACCE, major adverse cardiac and/or cerebrovascular event; BMI, body mass index; PSG, polysomnography; ACS, acute coronary syndrome; AHI, apnea-hypopnea index; AHI cutoff, participants divided in OSA- or no-OSA-groups based on PSG results; OSA, participants who suffer from obstructive sleep apnea based on the PSG result; no-OSA, participants who do not have obstructive sleep apnea based on PSG results; SpO2 lowest, the lowest score of oxygen saturation based on PSG results.

Age and BMI reported only in *OSA- and **no-OSA-groups, not together [29–31,44] #Schiza did not report no-OSA-group's PSG results but they were in their different report[33]

Table 2. Sleep monitoring results in different intervention groups

Intervention (PCI/CABG/no)	**PCI**	**CABG**	**No coronary intervention**
Sample size, n	386	147	642
OSA group			
n (%)	188 (48.7)	106 (72.1)	316 (49.2)
age (years)	55.2 ± 1.8	65.3 ± 7.8	59.0 ± 0.3
BMI (kg/m^2)	26.6 ± 3.6	28.5 ± 3.9	27.4 ± 4.2
AHI (events /h)	34.9 ± 4.6	32.3 ± 16.3	24.1 (19.7-28.4)
lowest SpO_2 (%)	82.5 (82.4-83.0)	79.3 ± 9.1	83.3 (82.0-84.5)
no-OSA group			
n (%)	198 (51.3)	18 (12.2)	324 (50.4)
age (years)	54.0 ± 9.9	63.5 ± 9.5	57.4 ± 11.0
BMI (kg/m^2)	25.5 ± 3.1	25.4 ± 3.6	26.6 ± 3.8
AHI (events /h)	9.6 ± 4.8	3.2 ± 1.3	6.4 (4.9-7.9)
lowest SpO_2 (%)	86.6 (86.0-89.0)	86.5 ± 8.8	87.0*

Results presented with categorical variables as counts (n) and percentages and continuous variables, which followed normal distribution as mean ± SD and non-normally distributed variables as median (interquartile range; IQR). *Only one data received from the articles.

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting surgery; OSA, participants who suffer from obstructive sleep apnea based on the PSG result; PSG, polysomnography; no-OSA, participants who do not have obstructive sleep apnea based on PSG results; AHI, apnea-hypopnea index; lowest SpO_2, the lowest score of oxygen saturation based on PSG results.

Meta analysis, AHI in obstructive sleep apnea

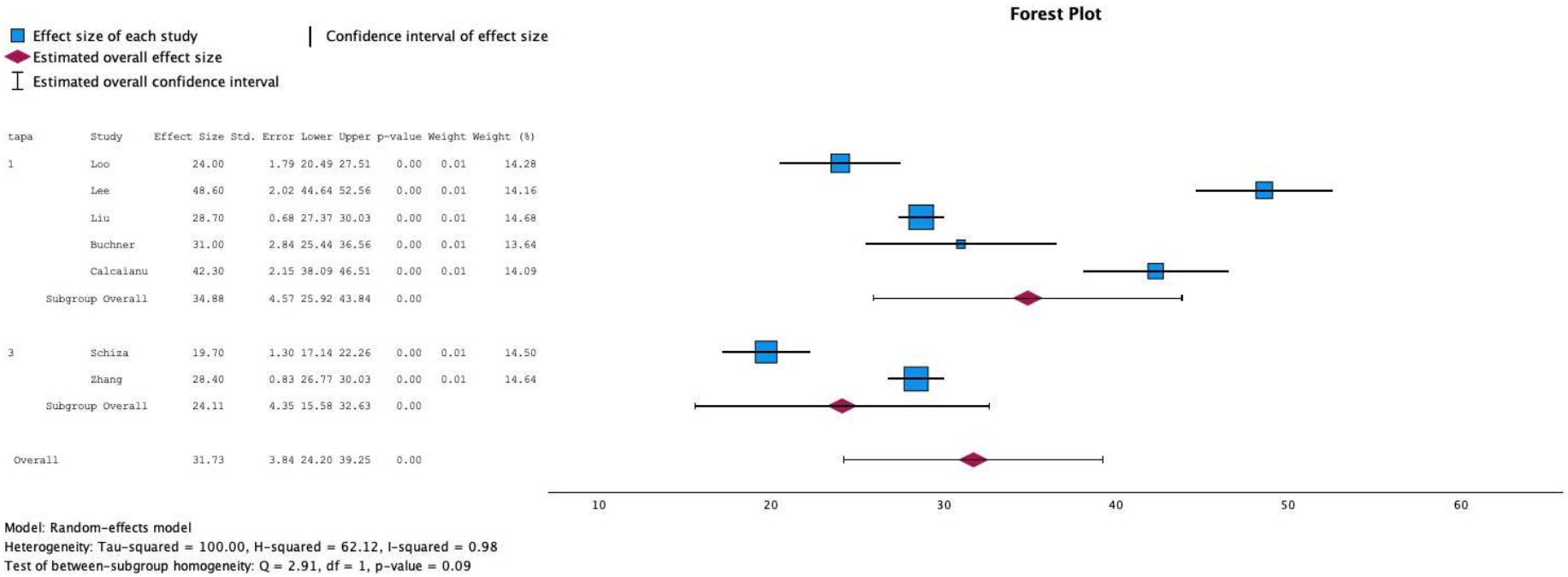

Figure 2. Forest plot comparing OSA patients AHI (events/h) between PCI (tapa 1) and no intervention (tapa 3) groups

Meta- analysis, Lowest saturation in obstructive sleep apnea patients

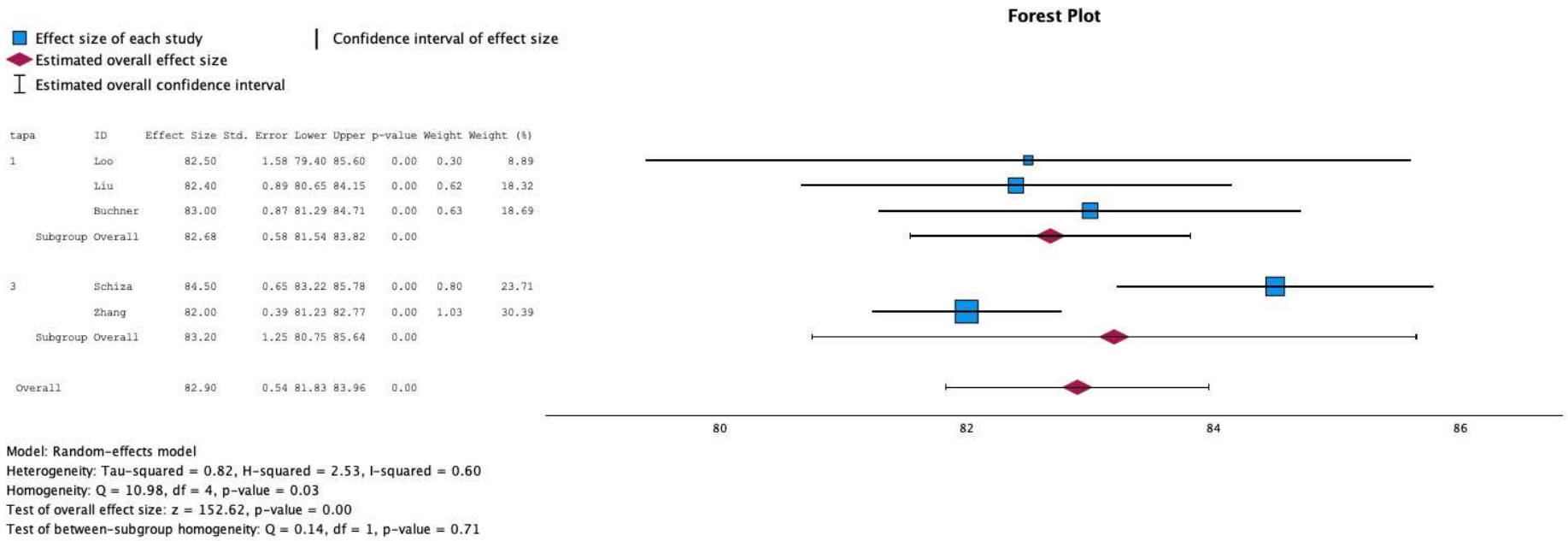

Figure 3. Forest plot comparing OSA patients lowest SpO_2 (%) during study night between PCI (tapa 1) and no intervention (tapa 3) groups

Supplementary material
Appendix A. The search terms

Table A. 1. The search terms used in each database

Database	*Search terms*
PubMed	"coronary artery disease [Mesh]" AND ("coronar* arter* bypass" OR "Coronary Artery Bypass"[Mesh] OR "heart bypass" OR "cabg") OR (" Percutaneous Coronary Intervention" [Mesh] "percutaneous" AND "coronar*" OR "heart" AND "intervent*" OR "PCI") AND ("respirator* disorder*" OR "sleep apn*" OR "obstructive sleep apn*" OR "sleep apnea, obstructive" [Mesh] OR "Sleep Apnea Syndromes"[Mesh] OR "Respiration Disorders"[Mesh])
Google Scholar	"coronary artery disease" AND ("respirator* disorder*" OR "sleep apn*" OR "obstructive sleep apn*" OR "sleep apnea, obstructive" OR "Sleep Apnea Syndromes") AND ("coronar* arter* bypass" OR "Coronary Artery Bypass" OR "cabg" OR " Percutaneous Coronary Intervention" OR "percutaneous coronar*" OR "PCI") AND ("clinical trial" OR "randomized controlled trial")
ScienceDirect	"coronary artery disease" AND ("obstructive sleep apn?a" OR "Sleep Apnea Syndromes" OR "Sleep disord! breath!") AND ("coronar! arter! bypass" OR "cabg" OR "percutaneous coronar! intervention" OR "PCI")
Cochrane database	(coronar* NEXT arter* NEXT bypass OR heart NEXT bypass OR cabg OR PCI OR percutaneous NEXT coronar* NEXT intervent* OR coronar* NEXT revascular*) AND (sleep NEXT apne* NEXT syndrom* OR sleep NEXT apne* OR respirati* NEXT disord*)

Appendix B. More detailed additional exclusion criteria

Table B. 1. List of additional exclusion criteria

	ADDITIONAL EXCLUSION CRITERIA
1	Treatment interventions, for example pre-operational evaluation
2	Heart failure
3	Hypertension
4	Pathophysiological research
5	Obesity and sleep disorders
6	Peripheral atherosclerosis
7	Gynecologic patients
8	Children
9	Pre-clinical studies and medicine research
10	Device research
11	Transplant patients
12	Valve surgery and OSA
13	Anatomical disorders, for example pectus excavatum

Table B. 2. List of excluded articles that might appear to meet the inclusion criteria

	Excluded article/study First author (publication year)	**Reason for exclusion**
1	Ooi (2023)	The participants had angina but did not have obstructive Coronary Artery Disease based on the coronary angiography
2	Uchôa (2015)	The sleep study (polysomnography and portable monitoring) was performed before CABG
3	Low (2013)	The study population included stable CAD participants who did not have a revascularization procedure
4	Summerer (2021)	The study population was divided based to CRS Grading of Coronary Collaterals and the OSA or no-OSA participants was not separated from the data
5	Sánchez-de-al-Torres (2020)	There was no statement which revascularization technique was done to the participants
6	Nakashima (2013)	The AHI cutoff between the OSA and no-OSA participants was ≥ 5 events/h
7	Berger (2013)	Participants were stratified according to oxygen desaturation index (ODI) into two subgroups and there was no data of AHI results
8	Glantz (2012)	There was both PCI and CABG done in the study population but there was no division between these groups based on revascularization technique
9	Morra (2017)	There was PCI, CABG and medical intervention done in the study population but there was no division between these groups based on revascularization technique
10	Lee (2010)	The sleep study results were not reported (AHI or lowest SpO2)
11	Fan (2019)	There was both PCI and CABG done in the study population but there was no division between these groups based on revascularization technique
12	Bauça (2017)	There was no statement which revascularization technique was done to the participants
13	Cheong (2021)	There was no statement which revascularization technique was done to the participants

CABG, coronary artery bypass grafting surgery; CAD, coronary artery disease; CRS, Cohen-Rentrop Score; OSA, participants who suffer from obstructive sleep apnea based on the sleep study result; no-OSA, participants who do not have obstructive sleep apnea based on sleep study results; AHI, apnea-hypopnea index; AHI cutoff, participants divided in OSA- or no-OSA-groups based on sleep study results; PCI, percutaneous coronary intervention; lowest SpO2, the lowest score of oxygen saturation based on sleep study results; SDB, sleep-disordered breathing

Appendix C. Funnel plots

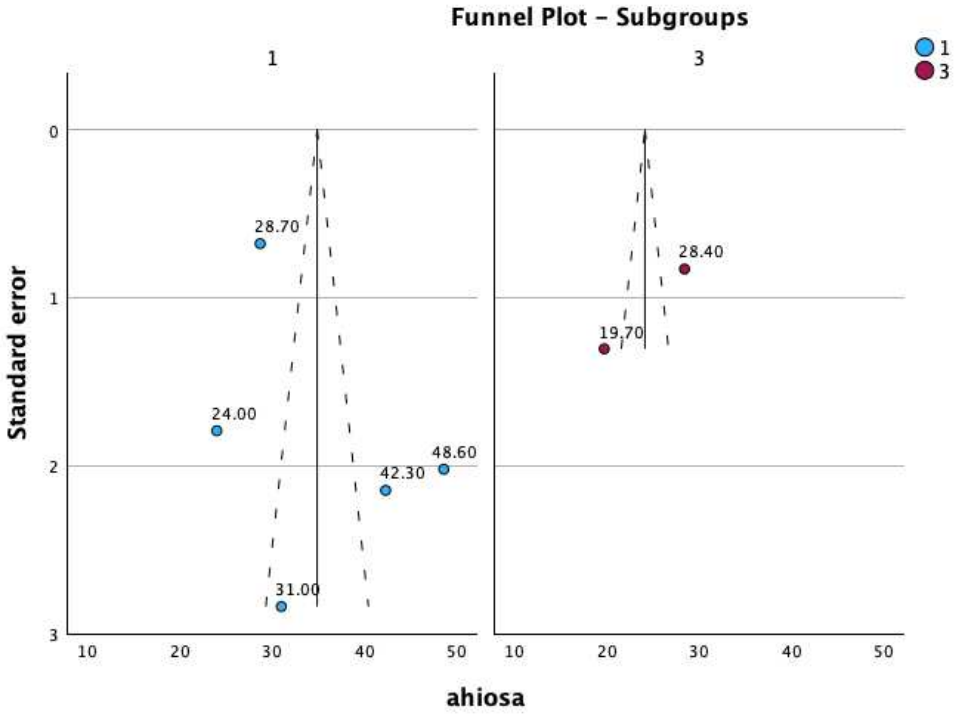

Figure C. 1. Funnel plot 1, AHI in OSA patients

AHI, apnea-hypopnea index; OSA, participants who suffer from obstructive sleep apnea based on the PSG result; PSG, polysomnography; ahiosa; OSA participants mean AHI

Subgroups 1= PCI, percutaneous coronary intervention; 3= No intervention

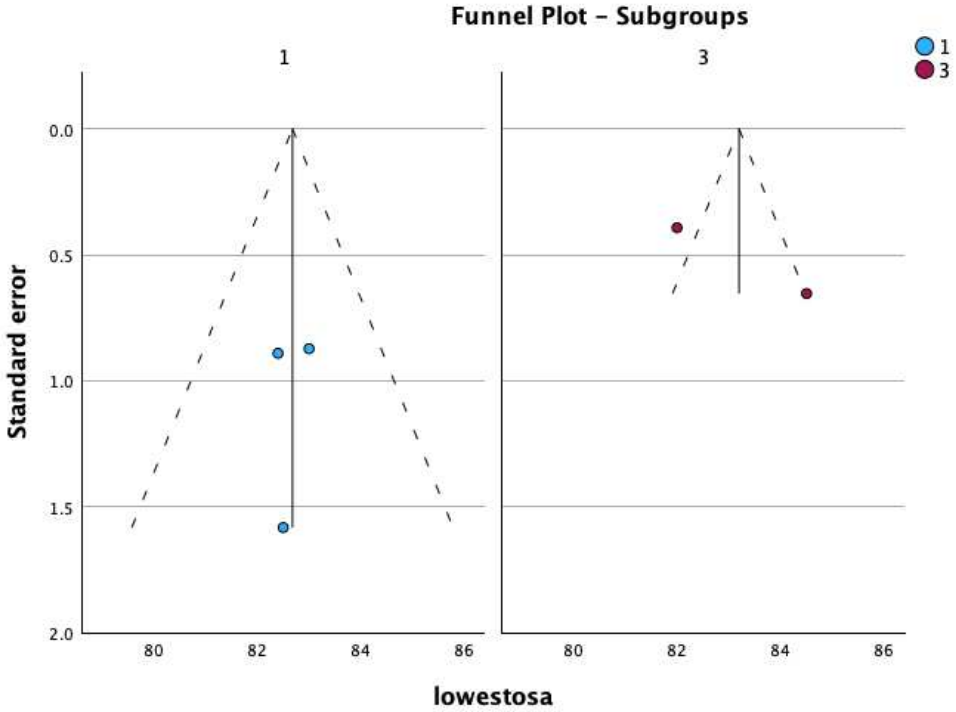

Figure C. 2. Funnel plot 2, Lowest saturation in OSA patients

Lowest saturation, the lowest score of oxygen saturation based on PSG results; OSA, participants who suffer from obstructive sleep apnea based on the PSG result; PSG, polysomnography; lowestosa, OSA participants mean lowest saturation.

Subgroups 1= PCI, percutaneous coronary intervention; 3= No intervention

Appendix D. Risk of bias assessment

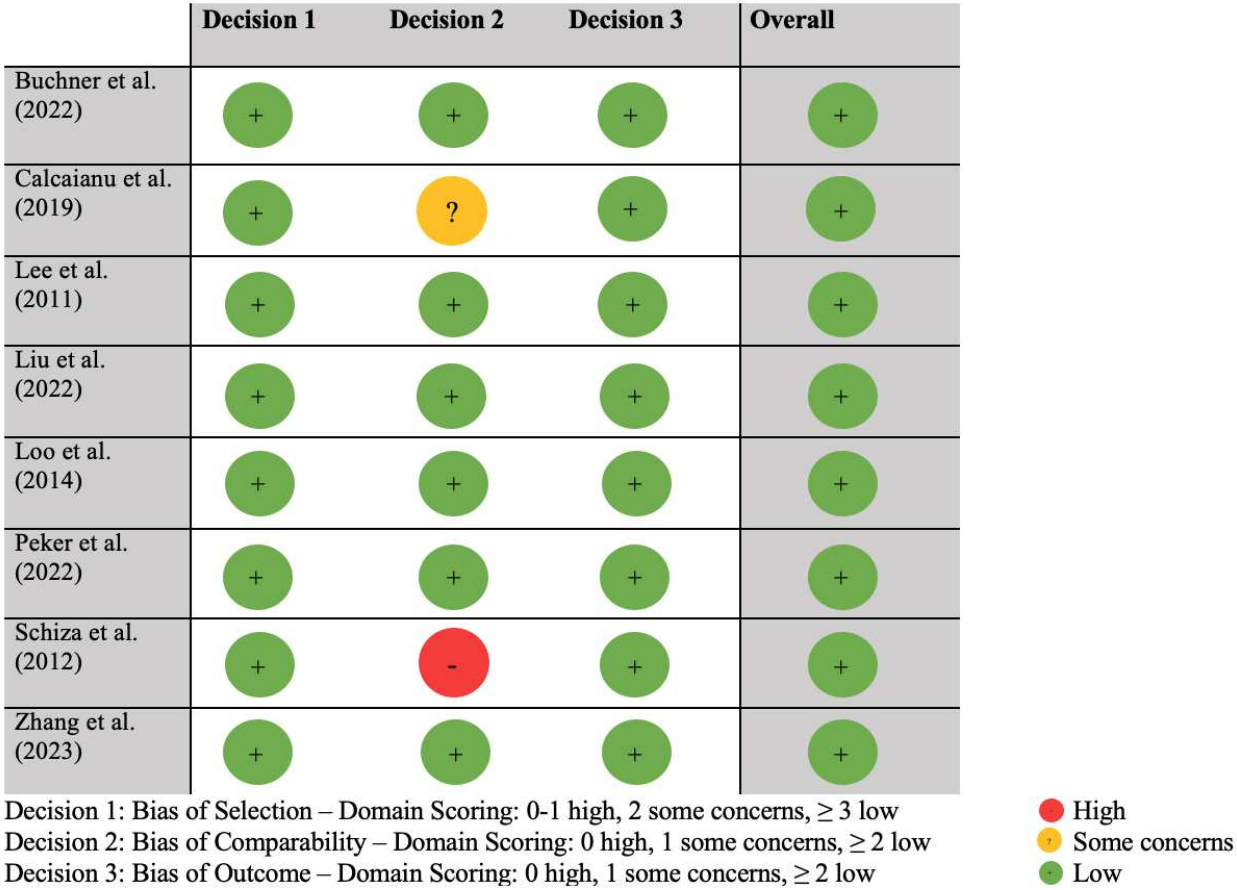

Figure D. 1. Risk of bias assessment of each article using Newcastle-Ottawa Scale