Postoperative Outcomes in Obstructive Sleep Apnea Patients Undergoing Cardiac Surgery: A Systematic Review and Meta-Analysis of Comparative Studies

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BACKGROUND: Obstructive sleep apnea (OSA) is a common comorbidity in patients undergoing cardiac surgery and may predispose patients to postoperative complications. The purpose of this meta-analysis is to determine the evidence of postoperative complications associated with OSA patients undergoing cardiac surgery.

METHODS: A literature search of Cochrane Database of Systematic Reviews, Medline, Medline In-process, Web of Science, Scopus, EMBASE, Cochrane Central Register of Controlled Trials, and CINAHL until October 2016 was performed. The search was constrained to studies in adult cardiac surgical patients with diagnosed or suspected OSA. All included studies must report at least 1 postoperative complication. The primary outcome is major adverse cardiac or cerebrovascular events (MACCEs) up to 30 days after surgery, which includes death from all-cause mortality, myocardial infarction, myocardial injury, nonfatal cardiac arrest, revascularization process, pulmonary embolism, deep venous thrombosis, newly documented postoperative atrial fibrillation (POAF), stroke, and congestive heart failure. Secondary outcome is newly documented POAF. The other exploratory outcomes include the following: (1) postoperative tracheal intubation and mechanical ventilation; (2) infection and/or sepsis; (3) unplanned intensive care unit (ICU) admission; and (4) duration of stay in hospital and ICU. Meta-analysis and meta-regression were conducted using Cochrane Review Manager 5.3 (Cochrane, London, UK) and OpenBUGS v3.0, respectively. **RESULTS:** Eleven comparative studies were included (n = 1801 patients; OSA versus non-OSA: 688 vs 1113, respectively). MACCEs were 33.3% higher odds in OSA versus non-OSA patients (OSA versus non-OSA: 31% vs 10.6%; odds ratio [OR], 2.4; 95% confidence interval [CI], 1.38–4.2; P = .002). The odds of newly documented POAF (OSA versus non-OSA: 31% vs 21%; OR, 1.94; 95% CI, 1.13–3.33; P = .02) was higher in OSA compared to non-OSA. Even though the postoperative tracheal intubation and mechanical ventilation (OSA versus non-OSA: 13% vs 5.4%; OR, 2.67; 95% CI, 1.03–6.89; P = .04) were significantly higher in OSA patients, the length of ICU stay and hospital stay were not significantly prolonged in patients with OSA compared to non-OSA. The majority of OSA patients were not treated with continuous positive airway pressure therapy. Meta-regression and sensitivity analysis of the subgroups did not impact the OR of postoperative complications for OSA versus non-OSA groups.

CONCLUSIONS: Our meta-analysis demonstrates that after cardiac surgery, MACCEs and newly documented POAF were 33.3% and 18.1% higher odds in OSA versus non-OSA patients, respectively. (Anesth Analg 2017;XXX:00–00)

KEY POINTS

- **Question:** To determine the evidence of postoperative complications associated with obstructive sleep apnea (OSA) patients undergoing cardiac surgery.
- **Findings:** Our meta-analysis demonstrates that after cardiac surgery, major adverse cardiac or cerebrovascular events and newly documented postoperative atrial fibrillation were 33.3% and 18.1% higher odds in OSA versus non-OSA patients, respectively.
- **Meaning:** OSA is an important risk factor for the postoperative complications in patients undergoing cardiac surgery. Further research on the optimal perioperative management of cardiac surgical patients at high risk for OSA is needed.

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Copyright © 2017 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the International Anesthesia Research Society. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. DOI: 10.1213/ANE.00000000002558 IDepartment of Anesthesia & Perioperative Medicine, Western University, London, ON, Canada.

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Reprints will not be available from the authors.

Address correspondence to Frances Chung, MD, FRCPC, Department of Anesthesiology and Pain Medicine, Toronto Western Hospital, University Health Network, 399 Bathurst St, Toronto, Ontario, M5T 2S8, Canada. Address e-mail to frances.chung@uhn.ca. bstructive sleep apnea (OSA) is a common sleep disordered breathing characterized by upper airway collapse resulting in recurrent episodes of arousal from sleep and intermittent hypoxemia. Its prevalence in the adult population ranges from 9% to 25%.¹ In the cardiac surgical population, prevalence of mild OSA (apneahypopnea index [AHI] ≥5) and moderate–severe OSA (AHI ≥15) is 74% and 48%, respectively.²

The association between OSA and the adverse postoperative outcomes has been well documented in patients undergoing various types of elective surgeries.³⁻⁵ In cardiac surgery, it is unclear whether patients with OSA are at higher risk of adverse events compared to patients without OSA. Several new studies reported positive association between OSA and increased postoperative complications.^{2,6–10} However, varying methodologies and limitations of data on the types of outcomes have impeded meaningful conclusions in cardiac surgical patients. For example, Foldvary-Schaefer et al² found no significant association between OSA and adverse postoperative outcomes, but Kaw et al¹¹ reported that OSA was significantly associated with a higher incidence of encephalopathy, postoperative infection, and increased length of stay (LOS) in the intensive care unit (ICU).

In view of the absence of randomized controlled studies and inconsistencies in the postoperative outcomes reported in recently published studies, we conducted a meta-analysis of comparative studies to determine whether adult OSA patients undergoing cardiac surgery are at increased risk for postoperative complications versus non-OSA patients.

METHODS

This study was planned in accordance with the Metaanalysis Of Observational Studies in Epidemiology guideline for observational studies.¹²

Literature Search Strategy

With the assistance of an expert librarian, an electronic search was conducted to identify all studies in Medline (1946 to October 2016), Medline In-process (up to March 2016), EMBASE (1946 to October 2016), Cochrane Central Register of Controlled Trials (up to October 2016), Cochrane Database of Systematic Reviews (2005 to October 2016), PubMed-NOT-Medline (1945 to October 2016), Web of Science (1900 to October 2016), Scopus (1960 to October 2016), and CINAHL (1983 to October 2016). The search included the combination of the following MESH key words: "cardiovascular diseases," "cardiovascular surgical procedures," "cardiac surgery," "heart surgery," "sleep apnea syndromes," "obstructive sleep apnea," "sleep disordered breathing," "intraoperative complications," "postoperative complications," "odds ratio," "cohort studies," "morbidity," "mortality," "risk," and "treatment outcome."

Study Selection Criteria

Our investigation was constrained to cohort-controlled publications of adult (>18 years) patients with versus without OSA undergoing cardiac surgery published in the English language. Information must be available on at least 1 postoperative complication. OSA must be diagnosed by polysomnography (PSG) or screened as "high-risk OSA" by screening questionnaire. Manuscripts without report on control group (ie, patients without OSA) and published in a non-English language were excluded.

Study Retrieval

Study titles and abstracts were evaluated to recognize whether inclusion/exclusion criteria were met. Two investigators (M.N. and G.H.) independently reviewed the search results in a stepwise manner. Relevant studies were first selected by title review of the search results. Abstracts of the selected studies were screened to determine if the inclusion/exclusion criteria were fulfilled. Then, the full text of the selected manuscript was considered and pertinent information was collected. The primary or the review articles were collected to perform the manual citation search. Any dissimilarities with article selection were solved by consulting the senior author (F.C.).

Data Extraction

Two investigators (M.N. and G.H.) extracted data and compiled the results. Any discrepancies in data collection were solved by consulting the senior author (F.C.). The following data were gathered from individual studies: sample size of OSA and non-OSA patients, method of diagnosing/screening for OSA, type of surgery, age, gender, body mass index, preexisting medical conditions, and postoperative complications. We contacted individual authors via e-mail for further study results including data on mean and standard deviation where only medians and interquartile ranges were reported.

Outcome Definition

The primary outcome is major adverse cardiac or cerebrovascular events (MACCEs) up to 30 days after surgery, which is the composite outcome of the following events: death from all-cause mortality, myocardial infarction, myocardial injury, nonfatal cardiac arrest, revascularization process, pulmonary embolism, deep venous thrombosis, newly documented postoperative atrial fibrillation (POAF), stroke, and congestive heart failure.8 The secondary outcome is newly documented POAF. The other exploratory outcomes include the following: (1) postoperative tracheal intubation and mechanical ventilation; (2) infection and/or sepsis; (3) unplanned ICU admission; and (4) duration of stay in hospital and ICU. Myocardial infarction was defined as evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Detection of an increase or decrease of cardiac enzymes with at least 1 value above the 99th percentile upper reference limit and with at least one of the following: ischemic symptoms; new ST-T wave changes or new left bundle branch block; pathological O waves; new regional wall motion abnormality; and intracoronary thrombus by angiography. Newly documented POAF was defined as any patient developing atrial fibrillation after the cardiac surgery and before the hospital discharge. Death was defined as cumulative incidence of all-cause mortality. Tracheal intubation and mechanical ventilation were defined as any patient who was placed on the ventilator or positive airway pressure due to respiratory failure, hypoxia, or pneumonia in the postoperative period.

Study Quality Assessment

Two investigators (M.N. and G.H.) evaluated study quality in accordance with the Meta-analysis Of Observational Studies in Epidemiology guidelines and Newcastle–Ottawa scale.^{12,13} The key points of study quality reviewed included the following: (1) a clear identification of the study population; (2) a clear definition of the outcomes and outcome assessment; (3) no selective loss of patients during followup; and (4) important confounders and/or prognostic factors identified. Each point was evaluated using yes/no. If one of these key points was not clearly mentioned in a study, it was considered a no.

Statistical Analysis

Summary Measures. The measure of association for postoperative outcomes was the weighted odds ratio (OR) with 95% confidence interval (CI) for dichotomous outcomes and the weighted mean difference (WMD) with 95% CI for the continuous outcomes. The Mantel-Haenszel method was used to combine dichotomous events, and the inverse variance method was used to combine continuous events. To address the multiplicity issues due to several outcomes in our meta-analyses, we also performed sensitivity analyses using small continuity corrections (Mantel-Haenszel), mixed-effect logistic regression, and the Bayesian approach. To measure whether stability in solutions was achieved on the final-reported model, a false discovery rate on the observed P values across all outcomes was also calculated as a sensitivity analysis. The OR for the individual studies was estimated and then pooled across studies using randomeffects modeling. The results were displayed as forest plots using Review manager (RevMan, version 5.3.; Copenhagen, Denmark). P < .05 was considered statistically significant.

Heterogeneity across studies was investigated for each adverse event by calculating *I*². Funnel plot was visualized to rule out the publication bias, and Egger regression test was done to confirm the absence of publication bias.

Meta-regression was performed to measure the impact of study type, study quality, medical comorbidities, outcome definitions, loss of patients to follow-up, and confirmation of OSA on the effect size for composite postoperative complications. OpenBUGS v3.0 was used for meta-regression analysis. (The protocol for conducting this review is attached in Supplemental Digital Content 1, File S1, http://links.lww.com/AA/C71.)

RESULTS

The initial search conceded 3426 citations. After inspecting title and abstracts, 3391 titles were excluded due to not meeting the preset inclusion criteria. Of the remaining 35 studies, 24 were excluded for various reasons. Figure 1 summarizes our literature search strategy. Eleven studies with a total of 1801 patients (688 OSA versus 1113 non-OSA) were included in the final analysis.^{2,6,8–11,14–18} Eight studies investigated patients undergoing coronary artery bypass grafting,^{6,8,10,14–18} and 3 studies investigated patients undergoing cardiac procedures including coronary artery bypass grafting, valve replacements, and/or repairs.^{2,9,11} Table 1 describes the baseline characteristics of included studies, and Supplemental Digital Content 2, File S2, http://links. lww.com/AA/C72 compares the baseline characteristics between OSA and non-OSA patients. Supplemental Digital Content 3, File S3, http://links.lww.com/AA/C73 provides the systematic review in tabular column.

Most studies included newly diagnosed or suspected OSA patients by sleep studies or questionnaire (Table 2). In total, 79% (607/771) were newly diagnosed and untreated OSA patients. The use of preoperative continuous positive airway pressure (CPAP) was usually not reported (Table 2). Only 2 of 11 studies reported preoperative CPAP use in 34% and 63% of OSA patients, respectively.^{9,18} In all studies, the use of the postoperative CPAP therapy was not mentioned. The quality of the included studies is summarized in Supplemental Digital Content 4, File S4, http://links.lww.com/AA/C74 and Newcastle–Ottawa scale scoring system in Supplemental Digital Content 5, File S5, http://links.lww.com/AA/C75.

Primary Outcome

Supplemental Digital Content 6, File S6, http://links.lww. com/AA/C76 provides the details regarding the postoperative complications extracted from each study for calculating

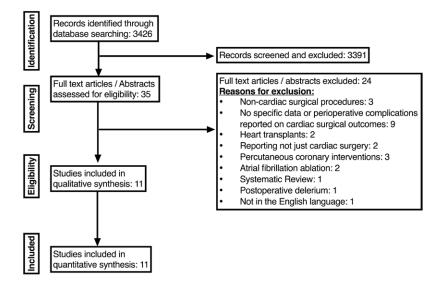


Figure 1. Flow diagram of search strategy used for meta-analysis.

Study Type Location of OSA Non-OSA Non-OSA Non-OSA<				Diagnosis	Gro	Groups (n)	Age ()	Age (y ± SD)	Gende	Gender: Male (%)) IMB	BMI (kg/m²)
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Study ID	Study Type	Location	of OSA	OSA	Non-OSA	OSA	Non-OSA	OSA	Non-OSA	OSA	Non-OSA
PC United States PSG, clinical 20 65 65 ± 6 65 ± 10 100 100 100 100 RC United States PSG, clinical 37 185 62 ± 9 61 ± 10 78 77 PC United States BQ 33 40 NA NA <td>Mooe et al¹⁴</td> <td>PC</td> <td>Sweden</td> <td>PSG</td> <td>78</td> <td>39</td> <td>62 ± 7</td> <td>61 ± 8</td> <td>80</td> <td></td> <td>NA</td> <td>NA</td>	Mooe et al ¹⁴	PC	Sweden	PSG	78	39	62 ± 7	61 ± 8	80		NA	NA
	Bhama et al ¹⁵	PC	United States	PSG, clinical	20	65	65 ± 6	65 ± 10	100	100	NA	NA
RC United States PSG 37 185 62±9 61±10 78 77 PC United States BQ 81 40 60±9 59±9 69 31 PC Turkey BQ 33 40 NA NA NA NA NA PC Turkey BQ 33 40 NA NA <td></td> <td></td> <td></td> <td>documentation</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>				documentation								
PC United States BQ 81 40 60±9 59±9 69 31 PC Turkey BQ 33 40 NA NA <td>Kaw et al¹¹</td> <td>RC</td> <td>United States</td> <td>PSG</td> <td>37</td> <td>185</td> <td>62 ± 9</td> <td>61 ± 10</td> <td>78</td> <td>77</td> <td>31 ± 6</td> <td>31 ± 7</td>	Kaw et al ¹¹	RC	United States	PSG	37	185	62 ± 9	61 ± 10	78	77	31 ± 6	31 ± 7
PC Turkey BQ 33 40 NA NA <th< td=""><td>Sharma¹⁷</td><td>PC</td><td>United States</td><td>BQ</td><td>81</td><td>40</td><td>60 ± 09</td><td>59 ± 9</td><td>69</td><td>31</td><td>>30 = 70%</td><td>>30 = 30%</td></th<>	Sharma ¹⁷	PC	United States	BQ	81	40	60 ± 09	59 ± 9	69	31	>30 = 70%	>30 = 30%
PC Iran BQ 25 36 61±11 57±10 72 83 Il ¹⁸ PC Canada PSG, BQ 132 145 63±10 66±10 80 76 er et al ² PC United States PSG, BQ 132 145 63±10 66±10 80 76 PC United States PSG 37 30 59±8 55±6 84 63 RC United States PSG, clinical 72 473 67±10 65±14 79° 66° PC Singatore PSG, clinical 72 473 67±10 65±14 79° 66°	Mungan et al ¹⁶	PC	Turkey	BQ	33	40	NA	NA	NA	NA	NA	NA
at al ¹⁸ PC Canada PSG, BQ 132 145 63±10 66±10 80 76 aefer et al ² PC United States PSG 45 28 69±12 NA 64 NA PC United States PSG 37 30 59±8 55±6 84 63 RC United States PSG, clinical 72 473 67±10 65±14 79° 66° Accumentation Adocumentation 72 473 67±10 65±14 79° 66° PC Singabore PAT device 128 32 61±8 63±8 86 81	Amra et al ⁶	PC	Iran	BQ	25	36	61 ± 11	57 ± 10	72	83	29 ± 4^{a}	26 ± 3^{a}
aefer et al ² PC United States PSG 45 28 69±12 NA 64 NA PC Brazil PSG 37 30 59±8 55±6 84 63 RC United States PSG, clinical 72 473 67±10 65±14 79° 66° documentation documentation 72 473 67±10 65±14 79° 66° PC Singapore PAT device 128 32 61±8 66° 81	van Oosten et al ¹⁸	PC	Canada	PSG, BQ	132	145	63 ± 10	66 ± 10	80	76	31 ± 6^{a}	26 ± 3^{a}
PC Brazil PSG 37 30 59±8 55±6 84 63 RC United States PSG, clinical 72 473 67±10 65±14 79° 66° documentation 72 473 67±10 65±14 79° 66° PC Singapore PAT device 128 32 61±8 63±8 86 81	Foldvary-Schaefer et al ²	PC	United States	PSG	45	28	69 ± 12	NA	64	NA	26 ± 6	NA
RC United States PSG, clinical 72 473 67 ± 10 65 ± 14 79 ^a 66 ^a documentation documentation 2 61 ± 8 63 ± 8 86 81 PC Singapore PAT device 128 32 61 ± 8 63 ± 8 86 81	Uchôa et al ⁸	PC	Brazil	PSG	37	30	59 ± 8	55 ± 6	84	63	29 ± 4	27 ± 3
documentation PC Singapore PAT device 128 32 61 ± 8 63 ± 8 86 81	Wong et al ⁹	RC	United States	PSG, clinical	72	473	67 ± 10	65 ± 14	79ª	66ª	31 ± 7^{a}	27 ± 5^{a}
PC Singapore PAT device 128 32 61±8 63±8 86 81				documentation								
	Zhao et al ¹⁰	PC	Singapore	PAT device	128	32	61 ± 8	63 ± 8	86	81	26 ± 4^{a}	23 ± 3^{a}

the composite postoperative outcome (MACCEs). Figure 2A summarizes the results on the MACCEs. Overall, MACCEs were 33.3% higher odds in the OSA patients when compared to the non-OSA patients (OSA versus non-OSA: 31.1% vs 10.6%; OR, 2.4; 95% CI, 1.38–4.2; P = .002; heterogeneity $I^2 = 64\%$) (Figure 2A). The influential analysis found that Wong et al9 and Uchôa et al8 contributed the maximum heterogeneity to our meta-analysis. When these 2 studies were removed and the summary estimate was recalculated, heterogeneity decreased to 3% and final estimate decreased to 1.73 (95% CI, 1.23–2.42; P = .002) without affecting the final inference (not shown in the figure). The credibility of the results was further tested by excluding the POAF events in the composite outcome (MACCEs) and recalculating the summary estimate. The OR slightly decreased to 2.3 (95% CI, 1.11-4.75; P = .02) and heterogeneity decreased to 41%, without altering the final inference of our results (not shown in the figure). Funnel plot, Egger regression test (P = .95), and Beggs test (P = .69) did not indicate the presence of publication bias for the composite postoperative outcomes.

Secondary Outcome

The newly documented POAF was 18.1% higher odds in the OSA patients versus the non-OSA patients (OSA versus non-OSA: 31% vs 21%; OR, 1.94; 95% CI, 1.13–3.33; P = .02; heterogeneity $l^2 = 45\%$) (Figure 2B). No evidence of publication bias was observed.

Exploratory Outcomes

The risk of postoperative tracheal intubation was significantly higher by 7.6% in the OSA patients versus the non-OSA patients (OSA versus non-OSA: 13% vs 5.4%; OR, 2.67; 95% CI, 1.03–6.89; P = .04; heterogeneity $I^2 = 59\%$) (Supplemental Digital Content 7, Figure, panel A, http://links.lww.com/ AA/C77). Neither the funnel plot nor Egger test suggested publication bias. There were no significant differences in the infection or sepsis (Supplemental Digital Content 7, Figure, panel B, http://links.lww.com/AA/C77) and ICU readmissions (Supplemental Digital Content 7, Figure, panel C, http://links.lww.com/AA/C77). Both the ICU LOS stay (WMD 0.48 day; 95% credible interval, 0.02-1.00; P = .08; heterogeneity $I^2 = 0\%$) and hospital LOS (WMD 0.56 day; 95% CI, -0.19 to 1.3; P = .14; heterogeneity $I^2 = 21\%$) were not significantly prolonged in patients with OSA versus non-OSA. In both outcomes of ICU and hospital LOS, the heterogeneity was low without any publication bias (Supplemental Digital Content 8, Figure 2, http://links. lww.com/AA/C78).

Meta-regression Analysis

The meta-regression analysis based on the various characteristics like study type, study quality, medical comorbidities, loss of patients to follow-up, and confirmation of OSA (PSG versus Berlin questionnaires) did not impact the OR of postoperative complications for OSA versus non-OSA groups (Table 3).

Multiple-Effect Measures

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Using multiple-effect measures for this meta-analysis did not reveal significant difference in pooled risk estimates

Table 2. Diagnosis of OSA and Pre-/Postoperative CPAP Use in Patients With OSA

Study ID	Screening and/or Diagnostic Tool	OSA or High-Risk OSA	n	Newly dx OSA Patients	OSA Patients on Preoperative CPAP Use (n)	OSA Patients on Postoperative CPAP	Comments	
Mooe et al ¹⁴	PSG	OSA	78	Yes	NA	NA		
Bhama et al ¹⁵	PSG, clinical documentation	OSA	20	No	NA	NA		
Kaw et al ¹¹	PSG	OSA	37	No	Low adherence	NA		
Sharma ¹⁷	BQ	High-risk OSA	81	Yes	NA	NA	No patients with previously dx OSA	
Mungan et al ¹⁶	BQ	High-risk OSA	33	Yes	NA	NA		
Amra et al ⁶	BQ	High-risk OSA	25	Yes	NA	NA	No patients with previously dx OSA	
van Oosten et al ¹⁸	PSG, BQ	Confirmed OSA	35	No	22 (63%)			
		High-risk OSA	97	Yes	None	NA		
Foldvary-Schaefer et al ²	PSG	OSA	45	Yes	None	None	Patients with OSA + CPAP therapy or oral appliance excluded	
Uchôa et al ⁸	PSG	OSA	37	Yes	None	None	No patients with previously dx OSA	
Wong et al ⁹	PSG, clinical documentation	OSA	72	No	32 (44%)	NA		
Zhao et al ¹⁰	PAT device	OSA	128	Yes	None	NA	Patients with OSA + CPAP therapy excluded	
Total OSA Patients	Previously dx/S Patients		OSA Patients on Preoperative CPAP; n (%)			OSA Patients on Postoperative CPAP		
688	16	64 (24)		5	4 (7)		None	

Abbreviations: BQ, Berlin questionnaire; CPAP, continuous positive airway pressure; dx, diagnosed; n, sample size; NA, not available; OSA, obstructive sleep apnea; PAT, peripheral arterial tone; PSG, polysomnography; RC, retrospective cohort.

by outcomes. We have added the results of only Bayesian approach into each forest plot for comparisons (data for other methods were not shown) and used the most conservative pooled estimate for reporting in our analyses. The corresponding corrected probabilities related to false discovery rate did not change much across multiple outcomes (Figure 2; Supplemental Digital Content 7 and 8, Figure, http://links.lww.com/AA/C77, Figure, http://links.lww.com/AA/C78). The rate of false-positives (type I error) among all tests with *P* values <.15 is only 2.8%.

DISCUSSION

The association between OSA and postoperative complications has been established in various types of elective surgeries.³⁻⁵ In cardiac surgery, the evidence whether patients with OSA are at increased risk for complications compared to patients without OSA is inconsistent.^{2,6–10} Due to varying methodologies and small sample size on outcomes, they failed to provide the strong evidence to characterize the OSA as an independent risk factor. To date, this is the first meta-analysis comparing the incidence of postoperative complications between OSA and non-OSA patients undergoing cardiac surgery. We found that MACCEs were 33.3% higher odds in the OSA patients when compared to the non-OSA patients. Moreover, OSA patients undergoing cardiac surgery are nearly 2-fold higher to develop POAF (OR, 1.94). There was no significant difference in the number of ICU readmissions, infection or sepsis, ICU LOS, and hospital LOS. In the absence of randomized controlled studies on this topic, the use of meta-regression analysis signifies an excellent method to determine the best possible evidence on this topic.

Despite improved standard of care in anesthesia and surgery, postoperative adverse events remain a important problem in OSA patients undergoing surgical procedures.^{5,19-22} Two meta-analyses on 13 and 17 studies, respectively, found that adverse cardiopulmonary events were increased by 2–3-fold in OSA patients after surgery versus non-OSA patients.^{3,4} A recent systematic review of 61 studies reporting on 413,304 OSA and 8,556,279 control patients supported the same results.5 These studies were mainly focused on noncardiac surgical procedures. Recently, OSA was found to be independently associated with postoperative major adverse cardiac and cerebrovascular events after percutaneous coronary intervention.23 There is a strong association between OSA and atrial fibrillation in patients undergoing various elective surgeries.²² In prospectively collected outcomes of 190 patients with OSA (confirmed by PSG), after cardiac surgery, POAF was associated with AHI in univariate analysis but not after results were adjusted for obesity and other confounders.²⁴ Our meta-analysis on 7 studies found that OSA increased the risk of newly documented POAF after cardiac surgery by nearly 2-fold (OR, 1.94), supporting previous findings.25

In the literature, there are inconsistencies in the results on the association between OSA and postoperative mortality. D'Apuzzo and Browne²⁶ found that the risk of postoperative in-hospital mortality increased by 2-fold in OSA patients undergoing total hip and knee revision arthroplasty. Conversely, Mokhlesi et al²² found that patients with OSA undergoing elective orthopedic, abdominal, and cardiovascular surgeries had a decreased risk of in-hospital mortality. The study results may differ depending on whether patients at high risk for OSA were recognized, and subsequent monitoring or CPAP therapy was implemented.

A Major Adverse Cardiac or Cerebrovascular Events (MACCE)

	OS/	4	Non-O	DSA		Odds Ratio			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	М-Н,	Random, 95% CI	
Mooe et al. 1996	25	78	7	39	11.2%	2.16 [0.84, 5.55]	1996			
Kaw et al. 2006	1	37	4	185	4.6%	1.26 [0.14, 11.58]	2006			
Bhama et al. 2006	0	20	4	65	2.9%	0.33 [0.02, 6.46]	2006	· · · · ·	<u> </u>	
Sharma et al. 2012	23	81	14	40	12.3%	0.74 [0.33, 1.65]	2012			
Mungan et al. 2013	19	33	13	40	11.1%	2.82 [1.08, 7.33]	2013			
Amra et al. 2014	2	25	2	36	5.2%	1.48 [0.19, 11.26]	2014			
Van Oosten et al. 2014	60	132	43	145	14.6%	1.98 [1.21, 3.24]	2014			
Wong et al. 2015	13	72	18	473	12.6%	5.57 [2.60, 11.95]	2015			
Foldvary-Schaefer et al. 2015	6	45	3	28	7.7%	1.28 [0.29, 5.60]	2015	-		
Zhao et al. 2015	33	128	3	32	9.0%	3.36 [0.96, 11.75]	2015			
Uchoa et al. 2015	32	37	7	30	8.9%	21.03 [5.93, 74.62]	2015			→
Total (95% CI)		688		1113	100.0%	2.41 [1.38, 4.20]			-	
Total events	214		118							
Heterogeneity: Tau ² = 0.49; Ch	i ² = 28.1	0, df =	10 (P =	0.002)	; I ² = 649	6				50
Test for overall effect: Z = 3.09	(P = 0.0)	02)						0.02 0.1	1 10	50
Devenier Develop Officiale Of				F4 00 4	- 4 001			Low-risk	F	ligh-risk

Bayesian Random-Effects, 95% Credible Interval: 2.49 [1.26 to 4.38] Predictive Interval: 2.41 [0.43 to 13.3] Corrected probability related to false discovery rate 0.014

B Newly Documented Postoperative Atrial Fibrillation (POAF)

	OS/	λ	Non-C	DSA		Odds Ratio		Od	ds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Ra	ndom, 95% Cl		
Mooe et al. 1996	25	78	7	39	17.0%	2.16 [0.84, 5.55]	1996				
Sharma et al. 2012	13	81	10	40	17.3%	0.57 [0.23, 1.45]	2012		+		
Mungan et al. 2013	19	33	13	40	16.8%	2.82 [1.08, 7.33]	2013				
Van Oosten et al. 2014	60	132	43	145	27.4%	1.98 [1.21, 3.24]	2014				
Amra et al. 2014	2	25	2	36	5.9%	1.48 [0.19, 11.26]	2014			_	
Uchoa et al. 2015	10	37	0	30	3.2%	23.29 [1.30, 416.35]	2015				• • •
Zhao et al. 2015	32	128	3	32	12.2%	3.22 [0.92, 11.29]	2015			—	
Total (95% CI)		514		362	100.0%	1.94 [1.13, 3.33]			-		
Total events	161		78								
Heterogeneity: Tau ² = 0.	21; Chi ² :	= 10.93	1, df = 6	(P = 0)	.09); I ² =	45%				-	
Test for overall effect: Z								0.02 0.1	1	10	50
Powerien Dendem Effec	ha 05% 0	ve dible		4 00 54	1 4 4 - 0 00			Low-risk			

Bayesian Random-Effects, 95% Credible Interval: 1.98 [1.14 to 3.29] Predictive Interval: 1.94 [0.49 to 7.67]

Corrected probability related to false discovery rate <0.047

Figure 2. Meta-analysis of composite postoperative events (MACCEs) (A) and newly documented POAF (B) between OSA and non-OSA patients undergoing cardiac surgery. The odds ratio of each included study is plotted. A pooled estimate of overall odds ratio (diamonds) and 95% CIs (width of diamonds) summarizes the effect size using the random-effects model. CI indicates confidence interval; df, degrees of freedom; MACCEs, major adverse cardiac or cerebrovascular events; M-H, Mantel–Haenszel; OSA, obstructive sleep apnea; POAF, postoperative atrial fibrillation.

Table 3. Meta-regression and Sensitivity Analysis of Subgroups for OSA and Postoperative Composite Outcomes

	Study Characteristics	Point Estimate		Meta-regressio	n
Measure or Outcome	(No. of Studies)	(95% Crl)	1 ²	Coefficient (SE)	P value
Study type	Prospective (9) ^{2,6,8,10,14–18}	2.19 (1.14-4.14)	64%	-0.51 (-2.35 to 1.34)	.548
	Retrospective (2)9,11	4.41 (0.18-41.88)	36%		
Confirmation of OSA	PSG (5) ^{2,8,10,11,14}	3.27 (1.19-9.01)	65%	-0.84 (-2.32 to 0.63)	.264
	Berlin questionnaire (3)6,16,17	1.4 (0.53–3.71)	55%		
Quality of study	Good (5) ^{8,10,14,17,18}	2.57 (0.74-10.62)	80%	0.24 (-1.23 to 1.70)	.724
	Poor-moderate (6) ^{2,6,9,11,15,16}	2.91 (1.21-5.87)	31%		
Loss of patients	Yes (1)17	0.74 (0.33-1.65)		-1.36 (-3.17 to 0.45)	.123
due to follow-up	No (10) ^{2,6,8–11,14–16,18}	2.88 (1.70-4.89)	53%		
Medical comorbidities	Yes (5) ^{8-10,17,18}	3.29 (1.29-8.40)	84%	0.66 (-0.52 to 1.84)	.274
	No (6) ^{2,6,11,14-16}	1.93 (1.11-3.36)	0%		

Study quality scores were obtained from the Ottawa–Newcastle quality checking. Study was considered good when assigned score was ≥8 of 9. P values are based on random-effects model.

Abbreviations: Crl, credible interval; OSA, obstructive sleep apnea; PSG, polysomnography.

The ICU LOS for OSA patients was not significantly (mean difference, 0.48) longer than non-OSA patients. Nearly half a day longer, ICU LOS for OSA patients suggests that OSA patients may require greater ventilatory support and longer monitoring. OSA patients might have a longer intubation time than non-OSA patients, prolonging the ICU LOS.^{26,15} Prolonged ICU stay leads to higher health care costs and greater consumption of limited resources.²⁷ Similarly, the length of hospital LOS was not significantly prolonged in OSA patients compared to non-OSA patients. The variations in the hospital LOS in the individual studies may be due to varying discharge criteria across different hospitals and changing practice principles with time as well as possible cohort bias.

The high prevalence but low recognition of OSA among patients presenting for cardiovascular surgery may put patients at increased risk of postoperative complications.^{2,5,28} PSG is the gold standard for diagnosing OSA, but it is time consuming, labor intensive, and costly. The Society of Anesthesia and Sleep Medicine has recommended the use of a screening tool to identify OSA in the surgical patients in the preoperative period.²⁹ The STOP-Bang questionnaire, a validated screening tool for OSA, can be incorporated into preoperative clinical practice to risk-stratify surgical patients.³⁰ The process may mitigate postoperative complications using postoperative monitoring and CPAP therapy.

The majority of OSA patients in our meta-analysis were untreated before surgery given that 79% (607/771) of the OSA patients were newly diagnosed or screened as high risk "at the beginning of the studies." Only 7% (54/771) of the OSA patients were on preoperative CPAP. None of the OSA patients were reported to be on postoperative CPAP. The high percentage of newly diagnosed OSA patients strengthens the evidence that OSA is highly prevalent in the cardiac surgical population but largely remains unrecognized. It raises the question whether the perioperative management of these newly diagnosed OSA patients is adequate in view of the increased risk of postoperative complications.

CPAP therapy is the most effective therapy for OSA, and perioperative CPAP use may optimize the condition of surgical patients with OSA.31 A recent meta-analysis found that the AHI was reduced by 25 events/h and LOS was 0.4 days less in treated OSA patients versus untreated OSA patients.³² The benefits of CPAP therapy in surgical patients were supported by 2 recent publications.^{33,34} In a retrospective-matched cohort analysis of postoperative outcomes in diagnosed versus undiagnosed OSA undergoing various surgeries, surgical patients with diagnosed OSA and a CPAP prescription had >50% decreased risk of cardiovascular complications (cardiac arrests and shock) versus patients with undiagnosed OSA.33 In another cohort study of adult patients undergoing vascular and general surgeries, patients with untreated OSA were at an increased risk of cardiopulmonary complications versus OSA patients with CPAP therapy.³⁴ Further work is needed in this area.

Most of the outcomes showed low-to-moderate heterogeneity across the studies, providing high credence to the robustness of the results. Furthermore, the study quality assessment, subgroup analysis, and meta-regression failed to show significant changes in the results, supporting the stability of the results.

There are some limitations to the findings of this metaanalysis due to the absence of randomized controlled trials. The criteria in which patients are categorized as patients with known or suspected OSA varies widely ranging from sleep studies (PSG, portable polygraph),^{2,8-11,14} sleep questionnaires,6,16-18 and clinical documentation.9,15 The cutoff value of AHI ≥5 is used in most studies with the exception of 2 using an AHI cutoff ≥15.^{2,8} Variation also exists between studies on reporting of various comorbidities and definition of postoperative outcomes. Several of these comorbidities that are associated with postoperative complications after cardiac surgery were not fully controlled as confounders. Selection bias and treatment bias, inherent to the observational studies, may exist. Our meta-analysis may be underpowered for some of the postoperative outcomes, increasing the chances of the type II error. Many of these limitations, multiplicity of the data, and other unknown confounding factors may have introduced some bias in the mean estimate and its dispersion.

In conclusion, our meta-analysis demonstrates that after cardiac surgery, MACCEs and newly documented POAF were 33.3% and 18.1% higher odds in OSA versus non-OSA patients, respectively. Further research on the optimal perioperative management of cardiac surgical patients at high risk for OSA is needed.

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DISCLOSURES

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