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ORIGINAL ARTICLE

Post-operative outcomes in adult obstructive sleep apnea patients undergoing non-upper airway surgery: a systematic review and meta-analysis

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Abstract
Background: With the current obesity epidemic, obstructive sleep apnea (OSA) has become increasingly common. Several studies have reported on the risk of post-operative complications in OSA patients undergoing non-upper airway surgeries. The objective of our study was to systematically review the medical literature reporting the incidence of post-operative complications in patients with OSA.
Methods: We conducted a systematic review using the Cochrane Collaboration Methodology. We searched Medline via Ovid, Pubmed, Embase, and Evidence-Based Medicine Reviews databases from 1950 to 2012. We rated the quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. Meta-analysis was done using Review Manager Version 5.0.20.
Results: Our search resulted in 18 eligible studies. OSA was found to be associated with a significantly increased incidence of post-operative hypoxemia (odds ratio [OR]=3.06; 95 % confidence interval [CI] 2.35–3.97), respiratory complications (OR=2.77, 95 % CI 1.73–4.43), cardiac complications (OR=1.76 95 % CI 1.16–2.67), neurological complications (OR=2.65, 95 % CI 1.43–4.92), and unplanned intensive care unit (ICU) transfer (OR=2.97, 95 % CI 1.90–4.64). Re-intubation (OR=1.37, 95 % CI 0.65–2.91) was not significantly increased in patients with OSA. The association between OSA and post-operative outcomes remained unchanged with sub-group analysis including only studies that used polysomnography (PSG) for diagnosis.
Conclusions: OSA patients are at increased risk of post-operative complications from non-upper airway surgeries. Early diagnosis and treatment of OSA might decrease post-operative complications in these patients. There is a need for further studies to assess the benefit of peri-operative treatment of OSA on post-operative outcomes.

Keywords Sleep apnea · Sleep apnea syndromes · Surgical procedures · Operative · Intraoperative complications · Post-operative complications

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Introduction

Obstructive sleep apnea (OSA) is extremely common in middle aged men and women worldwide but particularly in North America. In one landmark study in 1993, 9 % of middle aged women and 24 % of men had an apnea–hypopnea index (AHI)>5 h^{-1} [1]. As the obesity epidemic continues, estimates of prevalence obtained in the 1990s may underestimate the current problem as obesity is a major risk factor for the development of sleep apnea [2, 3]. The Wisconsin group has recently compared sleep apnea prevalence from 1988 to 1994 and from 2007 to 2010 using data collected for the Wisconsin sleep cohort study. Prevalence has increased substantially during this period due largely to increases in obesity but also perhaps due to other factors [4]. Patients can be defined as having the sleep apnea syndrome based on an abnormal AHI on polysomnography associated with sleepiness or sleep apnea can be identified solely on the basis of an abnormal sleep study. OSA is associated with many comorbidities particularly hypertension, cardiovascular disease, cerebral vascular disease and the metabolic syndrome [5, 6]. These associations are seen even if sleep apnea is identified solely

on the basis of an abnormal AHI [7]. OSA is now recognized as a chronic disorder and guidelines are established for diagnosis and management of this condition to improve patient outcomes [8].

Recent studies have shown that sleep apnea is common in patients undergoing elective surgery [9–11]. The majority of patients with sleep apnea undergoing elective surgery have not been diagnosed prior to surgery. In one study, approximately 80 % of patients felt to have OSA pre-operatively had not been previously diagnosed [12].

Anesthetic agents and analgesics used for pain in the post-operative period may be particularly problematic in patients with OSA. These agents by relaxing upper airway muscles could exacerbate the patient's sleep apnea [13, 14]. There are reports of apnea/hypopnea episodes and respiratory arrest associated with opioid analgesics [15, 16]. There is no definitive data to attribute increased perioperative complications in OSA patients to the use of anesthetic agents and analgesics. However, given that these agents can cause airway collapsibility, immediate post-operative complications in the OSA patients may plausibly be attributed to these agents. The current guidelines, therefore, recommend avoidance of opioids, where possible, and cautious selection of the appropriate surgical setting [17].

There have been quite a few studies comparing the risk of post-operative complication rates in patients with and without sleep apnea [9, 12, 18–34]. The majority of studies have shown a higher post-operative complication rate in patients with sleep apnea. However, considerable heterogeneity has been noted between studies. A recent meta-analysis found that OSA was associated with a significantly higher risk of desaturation, intensive care unit (ICU) transfer, cardiovascular complications and acute respiratory failure [35]. However, three studies that met the inclusion criteria were not included in the meta-analysis [24, 30, 31]. These studies reported data on outcomes, such as hypoxemia, respiratory complications, cardiac complications, neurologic complications, and ICU transfer, and thus could substantially affect the effect estimates. Moreover, four studies included in the meta-analysis also reported on neurologic complications but this outcome was not analyzed in the prior meta-analysis.[18, 23, 27, 29]. There have been several studies published since then and thus substantial additional data is now available that should improve the precision of these estimates. As well, more recent data is now available to examine the incidence of neurological complications in patients with and without sleep apnea [36, 37]. For these reasons, we thought that a meta-analysis at this time would provide useful information to further refine the effects of sleep apnea on post-operative complications.

Polysomnography is the gold standard for the diagnosis of OSA. However, this test is expensive and resource-intensive. Thus, there has been considerable interest in developing questionnaires that identify patients at high risk for sleep apnea. These questionnaires might be particularly useful in identifying patients who are at high or low risk of sleep apnea before elective surgery as it is not practical to perform polysomnography on all patients undergoing elective surgery. A recent systematic review of screening questionnaires analyzed the characteristics of these questionnaires and provided a comprehensive review of validated screening questionnaires [38]. Accordingly, we included in our meta-analysis, patients who were diagnosed with or without sleep apnea by polysomnography as well as patients identified as high risk or low risk for sleep apnea based on a validated screening questionnaire. We performed a subgroup analysis looking only at the patients who were classified with or without sleep apnea by polysomnography.

Materials and methods

Eligibility criteria

We included observational studies (prospective and retrospective cohort studies, and case-control studies) that reported post-operative complications from non-upper airway surgery in adult patients. Studies conducted on pediatric or adolescent population, case reports, case series, and abstracts were excluded. Studies reporting complications from upper airway surgery and endoscopic procedures were also excluded. Studies that did not use a validated prediction model or diagnostic tool for OSA and those that established OSA diagnosis based on International Code Diseases (ICD)-9 codes were also excluded from the meta-analysis (Table 2). Post-operative complications resulting from surgery itself like bleeding and infection were excluded from analysis.

Search strategy

In August 2012, we electronically searched Medline (1950 onwards; access via Ovid), Embase (all years; access via Ovid), and Evidence-Based Medicine Reviews using a detailed search strategy with search terms outlined in Appendix 1. The search strategy was outlined by the authors after initial detailed discussion of the aim of the study and the research question. There was no restriction on the language in which studies were reported. Preliminary review of related studies and keywords for some of the best studies done in the field were used as well. The search strategy was reviewed and approved by two librarians who are experts in literature search field. As we proceeded further in the literature search, using the selected studies, we searched for “related articles” in

PubMed. We also manually searched the references of the included studies to confirm the inclusion of all related articles. In April 2013, we repeated the search for related articles in Pubmed, and to our knowledge, there are no other new publications that we did not include on our review.

Selection process

Using a standardized screening guide, two reviewers independently reviewed the titles and abstracts of the citations resulting from the search. Full text for the articles which were thought to be eligible by at least one of the reviewers was obtained. Each reviewer independently reviewed these full texts to judge eligibility to be included in our review. Any disparities within the two reviewers about including studies were discussed and resolved by a third reviewer.

Data abstraction

Two reviewers independently extracted data from the included studies using a standardized and pilot-tested data abstraction form. After completion, the reviewers tried to resolve differences in extracted data by discussion and, if not resolved, by discussion with the third reviewer. The pilot-tested form included study design, population, method used to diagnose or predict OSA, methodological characteristics of the study and results reported. We assessed for the validation of the tests used to establish a diagnosis of OSA and also the validity of any questionnaire used to predict OSA in the study population. Results from each study were assessed to exclude perioperative complications like bleeding and infection which are a result from the surgery as such. We recorded the effect measures derived from the regression models that adjusted for the maximum number of covariates. Results from the data abstraction from the included studies are shown in Table 1. We rated the overall quality of evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [39]. Overall quality of evidence from the included studies for most outcomes is estimated to be moderate to low.

Data analysis

We calculated the kappa statistic to evaluate the agreement between the two reviewers who assessed the studies full texts for inclusion eligibility. Meta-analysis was conducted for all the outcomes that were reported by at least three studies in which the population were either diagnosed with OSA by a polysomnography (PSG) or were predicted to have OSA using a validated questionnaire. Sub-group analysis was done on the patient population who were diagnosed with OSA using polysomnography. In studies that did not report actual number of incidents, percentages or other available data was used to calculate the number of events for the outcomes evaluated. For each outcome, we pooled the odds ratios (OR) of eligible studies using the generic inverse variance and the random effects model in Review Manager Version 5.0.20. The random effects model was used as the included studies evaluated different patient populations. We measured homogeneity across study results using the I^2 statistic. We checked for possible publication bias using inverted funnel plots.

Results

Our extensive electronic database search resulted in 5,127 articles. Appendix 2 shows an outline of the search process. One study [9] that used a nonvalidated questionnaire for OSA risk assessment and two other studies [19, 20] that used ICD codes for OSA diagnosis were reviewed in detail, but excluded from meta-analysis. A study conducted by Finkel et al. [12] used the ARES questionnaire to categorize patients into high-risk and low-risk OSA groups. However, the outcomes were monitored only in a sub-set of the high-risk group who were diagnosed with OSA after a PSG. Therefore, the study was excluded since the outcomes were not compared to a non-OSA group. Studies by Neligan et al. [33] and Rennotte et al. [32] were randomized controlled trials which did not compare the outcomes with a non-OSA group. The study by Hallowell et al. [26] was a quality improvement study. Changes in practice over time in terms of obtaining sleep studies and managing patients peri-operatively made the global estimates of post-operative complications inaccurate, and thus, the study could not be included in our analysis. Another study [40] was excluded since only an abstract form was available which provided insufficient information to calculate the number of events for evaluated outcomes. Iyer et al. [34] compared outcomes in severe OSA group and nonsevere (including non-OSA, mild OSA, and moderate OSA groups) OSA groups. The study was excluded due to the inability to extract data for the group without OSA as the reference population.

Our literature search resulted in 18 observational studies which reported the incidence of hypoxemia, re-intubation, respiratory complications, cardiac complications, neurological complications, unplanned ICU transfer, prolonged oxygen therapy, and length of hospital stay [9, 18–25, 27–31, 36, 37, 41, 42]. The patient population in these studies was categorized into those with a diagnosis or at high-risk for OSA vs. those without a diagnosis or at low-risk for OSA. Table 1 contains the methodological qualities and results

Table 1 Methodological characteristics of studies reporting (included in meta-analysis) the risk of post-operative outcomes in OSA patients

Study	Population	Outcomes reported and definitions (by each study)	Methodological features	Results
Ahmad et al. [25] Study design: Prospective cohort Funding: National Center for Research Resources, NIH Grant, Masimo	Setting and period: Patients scheduled to undergo laparoscopic bariatric surgery at Northwestern University Feinberg School of Medicine, Chicago OSA group: 31 patients, 21 % males, mean age 43±10 years Non-OSA group: 9 patients, all females, mean age 42±12 years Type of surgery: laparoscopic gastric bypass or banding	Hypoxemia or ODI: Number of desaturation episodes per hour Re-intubation: Cardiac complication: Any Length of hospital stay: Blinding of outcome adjudicator: Not reported	Selection bias: Small study sample Information bias: Objective Outcome evaluation: Yes Standardized OSA risk measurement: Yes, polysomnography Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: Type of bariatric surgery, use of CPAP by six patients post-operatively Loss to follow-up: None	Total number of hypoxemic episodes were 53 and 129 (P=0.52) in OSA and non-OSA groups, respectively. Respiratory complication (re-intubation) occurred in 1 patient (11.11 %) in non-OSA group compared to none in OSA group. None of the patients in either group experienced any cardiac complication. The difference in the length of hospital stay was not statistically significant among both groups (2.3 vs. 2.2 days; P=0.78).
Auckley et al. [31] Study design: Retrospective cohort Funding: Not reported	Setting and period: Patients who had elective surgery at Case Western Reserve University High-risk group: 15 patients Low-risk group: 66 patients Type of surgery: not reported	Need for supplemental O2: Respiratory complication: Hypoxia, hypercapnia, need for supplemental O_2, nCPAP, atelectasis ICU transfer: Blinding of outcome adjudicator: Not reported	Selection bias: Small sample size Information bias: Objective outcome evaluation: Yes, standardized OSA risk Measurement: Yes, Berlin questionnaire Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: Gender, age, co-morbidities Loss to follow up: Two patients	Respiratory complications occurred in four patients (26.7 %) in high-risk group compared to three patients (4.5 %) in low-risk group. One patient (6.7 %) in high-risk group required ICU transfer compared to none from low-risk group. Number of patients who needed supplemental oxygen was not statistically different among both groups (n=3 vs. 3).
Chung et al. [23] Study design: Prospective cohort Funding: Physician Services Foundation, Toronto, Canada	Setting and period: Pre-operative patients at Toronto Western Hospital, Canada OSA group: 147 patients, 56.5 % males, mean age 59±12 years Non-OSA group: 64 patients, 36 % males, mean age 56±13 years Type of surgery: general surgery, orthopedics, urology, plastic surgery, ophthalmology, or neurosurgery	Desaturation: SpO_2<95 % at any time and/or cyanosis Any respiratory complication: Includes desaturation, pulmonary edema, bronchospasm, and arrival in PACU intubated Any cardiac complication: Includes tachycardia, bradycardia, dysrhythmia, and myocardial ischemia Any neurologic complication: Includes confusion, agitation, and excessive drowsiness Prolonged oxygen therapy: Requirement of O_2 therapy after discharge from PACU ICU transfer: Length of hospital stay: Hospital stay after surgery Blinding of outcome adjudicator: Yes	Selection bias: Self-selection of patients may have been involved. Patients who had sleep symptoms might have selectively consented to PSG Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: Gender, age, BMI and co-morbidities Loss to follow-up: None	Number of patients with desaturations were significantly higher in OSA group compared to non-OSA group (20.6 % vs. 9.2 %, respectively; P=0.044). Number of patients experiencing any respiratory complication was significantly higher in OSA group compared to non-OSA group (22.6 % vs. 9.2 %, respectively; P=0.021). Incidence of any cardiac complication was not significantly different between OSA and non-OSA groups (6.9 % vs. 3.1 %, respectively; P=0.35). Patients with any neurologic complication was not significantly different (1.4 % vs. 0 % in OSA and non-OSA groups, respectively; P=1.00). Number of patients requiring prolonged oxygen therapy was significantly higher in OSA group compared to non-OSA group (14.3 % vs. 4.7 %, respectively; P=0.043). Length of hospital stay after surgery was not significantly different between both groups (2.15 vs. 1 days in OSA and non-OSA groups, respectively; P=0.25). Patients requiring unplanned ICU transfer was 2.7 % in OSA group and 0 % in non-OSA group.

Table 1 (continued)

Study	Population	Outcomes reported and definitions (by each study)	Methodological features	Results
Chung et al. [24] Study design: Prospective cohort Funding: Not reported	Setting and period: Patients who were difficult to intubate at four hospitals in Toronto, Canada OSA group: 22 patients, 81.8 % males, mean age 60±10 years Non-OSA group: 11 patients, 45.5 % males, mean age 50±17 years Type of surgery: not reported	Desaturation: SaO_2<90 % at any time and/or cyanosis and/or PaO_2 <60 Torr Respiratory complications: Desaturation; mild (SaO_2 90-95 %) or severe (SaO_2≤90 %) Cardiac complications: Myocardial infarction, myocardial ischemia, congestive heart failure, arrythmia Neurological complications: Somnolence, transient ischemic attack Unplanned ICU transfer: Oxygen requirement: After transfer to ward Blinding of outcome adjudicator: Not reported	Selection bias: Small study sample, High-risk population. Only 40 % of population agreed to undergo PSG Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: Gender, neck size, BMI, comorbid conditions Loss to follow-up: None reported	Desaturation occurred in 18 % of patients in OSA group and none of the non-OSA group patients. Respiratory complications occurred in five patients (22.7 %) in OSA group compared to one patient (9 %) in non-OSA group. No cardiac complications or unplanned ICU admissions occurred in either groups. Neurological complications occurred in 1 patient (4.5 %) in OSA group compared to none in non-OSA group. Oxygen requirement was noted 31.8 % patients in OSA group compared to none in non-OSA group (P=0.0674).
Flink et al. [36] Study design: Prospective cohort Funding: Grant from NIH and Dept. of Anesthesia, Duke University Medical Center	Setting and period: Patients undergoing elective knee Arthroplasty at Duke University Medical Center or the Durham VAMC, Durham, NC OSA group: 15 patients. 53.3 % males. Mean age 70.3±3.3 years Non-OSA group: 91 patients. 42.9 % males. Mean age 74±5.1 years Type of surgery: Elective knee replacement surgery	Delirium: Tested on post-op days 2 and 3, Diagnosed by a psychiatrist using DSM-IV criteria, DRS-R-98, CAM and nursing notes Blinding of outcome adjudicator: Not reported	Selection bias: Small study sample Information bias: Objective Outcome evaluation: Yes, standardized OSA risk measurement: Yes, polysomnography, except in three patients Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: Age, comorbidities Loss to follow-up: None	Among patients with OSA, 53.3 % (8/15) experienced post-operative delirium, compared with 20.9 % of patients without OSA (19/91) (P=0.0123, OR=4.3; 95 % CI 1.2–15.8).
Gali et al. [41] Study design: Prospective cohort Funding: Not reported	Setting and period: Patients in pre-operative evaluation clinic at Mayo Clinic Rochester, Minnesota between September 2004 and August 2005 High SACS group: 115 patients. 85.2 % males. Mean age 59.9± 9.8 years Low SACS group: 25 patients. 72 % males. Mean age 59.6±8.5 years Type of surgery: Plastic, Colorectal, Otorhinolaryngoscopic procedures, Gynecologic, Urologic, Orthopedic	Desaturations: <90 % on pulse oximeter while on supplemental O_2 of 4 l or less for 30 s Unplanned ICU transfer: Other than planned direct transfer from PACU to ICU Blinding of outcome adjudicator: None	Selection bias: High-risk population Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, Flemon's criteria/ SACS Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: BMI, neck circumference, type of analgesia Loss to follow-up: 22 patients	Desaturation following PACU discharge occurred in 41.7 % patients in high-risk group compared to 12 % patients in low-risk group. Unplanned ICU transfer occurred in 4.3 % patients in high-risk group and none of the patients in low-risk group (P=0.59).

Table 1 (continued)

Study	Population	Outcomes reported and definitions (by each study)	Methodological features	Results
Gali et al. [21] Study design: Prospective cohort Funding: Institutional and Anesthesia Dept. sources at Dept. of Internal Medicine, Mayo Clinic	Setting and period: Patients in pre-operative evaluation clinic at Mayo Clinic Rochester, Minnesota between October 2005 and September 2007 High Sleep Apnea Clinical Score (SACS) group: 221 patients. 86 % males. Mean age 59.9 ±10.5 years Low SACS group: 472 patients. 43 % males. Mean age 58.2±11.6 years Type of surgery: Orthopedic, Gynecologic, Urology, Thoracic, ENT, Plastic, General abdominal, Neurosurgical, other	Desaturations: Decrease in saturation of 4 % or greater for 10 s or more Respiratory complication: ICU transfer for respiratory indication like respiratory failure, need for respiratory therapy, need for CPAP, pneumonia Cardiac complication: New arrhythmia requiring treatment, myocardial infarction, myocardial ischemia ICU transfer: For respiratory indication Blinding of outcome adjudicator: Yes	Selection bias: High-risk population Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, Flemon's criteria/ SACS Confounding: No Matching: No Adjustment in analysis: Yes Loss to follow-up: None reported	The likelihood of post-operative desaturation was increased with a high SACS (OR=1.9; $P<0.001$). Post-operative respiratory events occurred in 9 % patients from high-risk group and 2.8 % patients from low-risk group ($P<0.001$). Post-operative cardiac events occurred in 1.8 % of patients from high-risk group compared to 1.9 % from low-risk group ($P=0.869$). 7.2 % of patients in high-risk group and 1.9 % of patients in low-risk group required ICU admission for respiratory indication.
Gupta et al. [29] Study design: Retrospective case-control Funding: Not reported	Setting and period: Patients undergoing joint replacement surgery at Mayo Clinic, Rochester, Minnesota between January 1995 and December 1998 OSA group: 101 patients. 69.3 % males. Mean age 68.1±7.3 years Non-OSA group: 101 patients. 69.3 % males. Mean age 69.4 years Type of surgery: Hip or knee replacement	Hypoxemia: $SpO_2<90$ % and >4 % reduction, with witnessed four apneic episodes or not explained by other events Re-intubation: Delirium: As noted by caregivers Unplanned ICU transfer: Cardiac events: Including myocardial infarction, myocardial ischemia, arrhythmia Length of hospital stay: Prolonged O_2 therapy: Blinding of outcome adjudicator: not reported	Selection bias: Control group did not undergo PSG Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography except for 17 patients who underwent overnight oximetry Confounding: No Matching: Yes Adjustment in analysis: Yes Loss to follow-up: None	Number of patients with hypoxemia was not significantly different (21 % in OSA group vs. 8 % in non-OSA group; $P=0.08$). Difference in re-intubation was not statistically significant between OSA and non-OSA groups (2 % vs. 0 %, respectively; $P=0.16$). Incidence of cardiac events was not significantly different in OSA and non-OSA groups (16 % vs. 9 %, respectively). Delirium was noted in 10 % of OSA group patients vs. 3 % of non-OSA group patients; $P=0.07$). Patients requiring unplanned ICU transfer was significantly higher (20 %) in OSA group compared to 6 % in non-OSA group ($P=0.003$). Hospital stay was significantly longer for OSAS patients at a mean SD of 6.8±2.8 days compared to 5.1± 4.1 days in non-OSA group patients ($P<0.007$). Significantly more patients with OSAS required supplemental oxygen for a longer duration ($P=0.001$) than non-OSA group patients.
Hallowell et al. [26] Study design: Retrospective cohort Funding: Not reported	Setting and period: Patients who underwent Bariatric surgery from 1998 through December 2005 at Case Medical Center, Cleveland, OH OSA group: 454 patients (186+268) Controls: 436 total Type of surgery: Gastric bypass	Respiratory distress: ICU transfer: Blinding of outcome adjudicator: Not reported	Selection bias: Selective election of patients for PSG before 2003 Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography Confounding: Yes Matching: No Adjustment in analysis: No Confounding variables: Demographic variables, CPAP use Loss to follow-up: None reported	Respiratory distress was reported in 1.1 % of OSA patients and 1.6 % of patients without OSA diagnosis. In OSA group, 4.4 % needed ICU transfer compared to 5.3 % of patients without OSA diagnosis.

Table 1 (continued)

Study	Population	Outcomes reported and definitions (by each study)	Methodological features	Results
Hwang et al. [22] Study design: Prospective cohort Funding: Not reported	Setting and period: Elective surgery patients at North Shore University Hospital, New York between July 2004 and November 2006 ODI4%≥5: 98 patients, 56 % males ODI4%<5: 74 patients, 40.5 % males Type of surgery: Abdominal, thoracic, gynecologic, vascular, neurological, urological, cardiothoracic, orthopedic, ENT	Desaturation: Decrease in oxygen saturation requiring addition or increase in supplemental oxygen Cardiovascular complications: Length of hospital stay: Blinding of outcome adjudicator: Yes	Selection bias: Only patients with clinical features of OSA were preselected for nocturnal oximetry Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, nocturnal pulse oximetry Confounding: No Matching: Yes, except for BMI Adjustment in analysis: Yes Loss to follow-up: None reported	Desaturation was reported in 6 % of ODI4%≥5 group patients, and 1.4 % of ODI4%<5 group patients. Cardiovascular complication occurred in 3 % of patients in ODI4%≥5 group compared to 1.4 % in ODI4%<5 group. Length of hospital stay was not significantly different between both groups; actual numbers not reported.
Kaw et al. [27] Study design: Retrospective case-control study Funding: RPC Grant 2005-1037	Setting and period: Patients who underwent open heart surgery between Jan. 1995 and Dec. 2000, at Cleveland Clinic, Ohio OSA group: 37 patients, 78.4 % male, mean age 61 years (56–69 range) Non-OSA group: 185 patients, 78.4 % male, mean age 61 years (55–69 range) Type of surgery: CABG/valve surgery	Pulmonary complications: Re-intubation: Cardiac complication: Neurologic complication: Length of hospital stay: Blinding of outcome adjudicator: Not reported	Selection bias: Very small patient sample Information bias: Objective outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography in OSA group only (controls did not undergo PSG to exclude OSA diagnosis) Confounding: No Matching: Yes Adjustment in analysis: Yes Loss to follow-up: None reported	Pulmonary morbidity was reported in 5.4 % patients in OSA group and 7 % in non-OSA group ($P=0.99$). Cardiac morbidity was reported in 0 % patients in OSA group and 1.1 % in non-OSA group ($P=0.99$). Neurologic morbidity occurred in 0 % patients in OSA group and 2.7 % in non-OSA group ($P=0.59$). Hospital length of stay was not significantly different with medians of 11 and 9 days in OSA and non-OSA groups respectively. Incidence of re-intubation was not significantly different: 13.5 % vs. 8.6 % in OSA and non-OSA groups, respectively.
Kaw et al. [43] Study design: Retrospective cohort Funding: RPC Grant 2005-1037	Setting and period: Patients who underwent pre-operative assessment at Cleveland Clinic, Ohio between Jan. 2002 and Dec. 2006 OSA group: 282 patients, 44.6 % males, mean age 55.9±12.2 years Non-OSA group: 189 patients, 19.6 % males, mean age 46.3± 14.3 years Type of surgery: Abdominopelvic, ENT, GYN, neurosurgical, orthopedic, thoracic, urologic, vascular, other	Hypoxemia: oxygen saturation <90 % or >4 % reduction from last recorded value or respiratory failure or if confirmed by arterial blood gas Respiratory failure: Need for prolonged mechanical ventilation (>24 h), endotracheal re-intubation or tracheostomy Re-intubation: Cardiac complications: Atrial fibrillation, myocardial infarction, congestive heart failure Delirium: ICU transfer: Length of hospital stay: Blinding of outcome adjudicator: Not reported	Selection bias: None Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography Confounding: No Matching: No Adjustment in analysis: Yes Loss to follow-up: None reported	OSA was associated with a higher incidence of post-operative hypoxemia (12.4 % vs. 2.1 % patients in OSA and non-OSA groups, respectively; $P=0.009$). Delirium occurred in 3.4 % of OSA group patients compared to none from non-OSA group. Respiratory failure was reported in 4.9 % patients in OSA group compared to 2.1 % in non-OSA group. Need for re-intubation was reported in 1.4 % of OSA group patients and 0.5 % of non-OSA group patients. OSA diagnosis was associated with higher ICU transfer (6.7 % vs. 1.6 % in OSA and non-OSA groups, respectively; $P=0.049$). Presence of OSA was associated with a longer hospital stay (OR, 1.65; $P=0.049$).
Mador et al. [37] Study design: Retrospective cohort Funding: None	Setting and period: Patients who underwent surgery and a sleep study from 2000 to 2010, at VAMC, Buffalo, NY	Desaturation: SpO_2<90 % requiring O_2 supplementation or up-titration Re-intubation:	Selection bias: Predominantly male study population Information bias: Objective	29.9 % of patients with OSA had oxygen desaturation compared to 16.3 % patients in non-OSA group ($P=0.012$).

Table 1 (continued)

Study	Population	Outcomes reported and definitions (by each study)	Methodological features	Results
	OSA group: 284 patients, 95.8 % males, mean age 62.13±10 years Non-OSA group: 86 patients, 88.4 % males, mean age 59.68±9.8 years Type of surgery: CABG, cholecystectomy, colorectal surgery, total hip replacement, total knee replacement, prostatectomy	Respiratory complications: Oxygen desaturation, acute hypercapnea, bronchospasm, arrival to PACU/ICU intubated, re-intubation Cardiac complications: Dysrhythmia, ischemia, infarction, pulmonary edema, tachycardia, bradycardia, hypertension, hypotension Neurological complications: Confusion, agitation, excessive daytime drowsiness (as noted by caregivers) Unplanned ICU transfer: Length of hospital stay: Since surgery Blinding of outcome adjudicator: Not reported	Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography Confounding: No Matching: No Adjustment in analysis: Yes Loss to follow-up: None	There was no significant difference in the number of patients who required re-intubation among OSA and non-OSA groups (2.82 % vs. 2.33 %, respectively; $P=1.00$). Patients with OSA had higher incidence of respiratory complications compared to patients without OSA (40.5 % vs. 23.3 %, respectively). There was no significant difference in total cardiac complications in OSA patients compared to non-OSA group (64.8 % vs. 57 %). No significant difference in neurological complications in OSA patients compared to control group (7.4 % vs. 2.3 %, respectively; $P=0.46$). Unplanned ICU transfers were not significantly different in OSA patients compared to non-OSA group (4.6 % vs. 4.6 %, respectively; $P=1.00$). Length of hospital stay was not significantly different in OSA patients compared to non-OSA group (median of 5 vs. 5, respectively; $P=0.27$).
Mooe et al. [30] Study design: Prospective cohort Funding: Grants from Swedish National Association for Heart and Lung Patients, the Swedish Heart Lung Foundation, the Norrland Heart Fund and the Medical Faculty	Setting and period: Patients accepted for bypass surgery at Norrland University Hospital, Sweden OSA group: 72 patients, mean age 62.0±7.7 years Non-OSA group: 30 patients, mean age 61.3±8.7 years Type of surgery: CABG	Atrial fibrillation: Detected by continuous telemonitoring during first 4–5 post-op days and verified by a 12-lead EKG Length of hospital stay: Blinding of outcome adjudicator: Not reported	Selection bias: None Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography Confounding: No Matching: No Adjustment in analysis: Yes Loss to follow-up: None	Atrial fibrillation was diagnosed in 32 % vs. 18 % of patients in OSA and non-OSA groups, respectively ($P=0.11$). Length of hospital stay was significantly higher in patients with OSA compared to non-OSA patients (14.6±12.1 days vs. 11.0±2.6 days; $P<0.01$).
Sabers et al. [28] Study design: Case-control study Funding: Mayo Foundation	Setting and period: Patients who underwent outpatient surgical procedures at Mayo Clinic Rochester from Jan 1997 through December 2000 OSA group: 234 patients, 73.1 % males, mean age 57.0±12.8 years Non-OSA group: 234 patients, 73.1 % males, mean age 56.9±13.1 years Type of surgery: partial meniscectomy, transurethral excision of lesion or tissue of bladder, dilation and curettage, surgical extraction of tooth, repair of umbilical hernia	Respiratory complications: Reported bronchospasm, airway obstruction, difficult mask ventilation, other Atrial fibrillation: Blinding of outcome adjudicator: Not reported	Selection bias: Relatively healthy population of patients undergoing outpatient surgery. Control group did not undergo PSG to exclude OSA. Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, polysomnography only in OSA group Confounding: No Matching: Yes Adjustment in analysis: Yes Loss to follow-up: Two patients	Bronchospasm (re-intubation) occurred in 0.4 % patients vs. none in OSA and non-OSA groups, respectively. Incidence of difficult mask ventilation (hypoxemia) occurred in 0.4 % vs. none in OSA and non-OSA groups, respectively. Atrial fibrillation occurred in 0 vs. 0.4 % patients in OSA and non-OSA groups, respectively.

Table 1 (continued)

Study	Population	Outcomes reported and definitions (by each study)	Methodological features	Results
Vasu et al. [42] Study design: Historical cohort Funding: Not reported	Setting and period: Patients about to undergo elective surgery for three consecutive days in May 2008, at Thomas Jefferson University Hospital, PA High-risk for OSAS: 56 patients, 67.9 % males, mean age 64.7 years Low-risk for OSAS: 79 patients, 27.8 % males, mean age 53 years Type of surgery: Orthopedic, head and neck, abdominal, gynecologic, genitourinary, ENT, cardiothoracic, vascular, others	Post-operative desaturation: Decrease in oxyhemoglobin saturation requiring increase in flow rate of supplemental O_2 or transfer to ICU Respiratory failure: Hypoxemia, atelectasis, pulmonary embolism, pneumonia Cardiac event: New-onset atrial fibrillation, systemic hypotension, myocardial infarction ICU transfer: Length of hospital stay: Blinding of outcome adjudicator: Not reported	Selection bias: None Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: Yes, STOP-BANG questionnaire Confounding: No Matching: No Adjustment in analysis: Yes Loss to follow-up: None	Hypoxemia occurred in 10.7 % vs. 0 patients in OSA and non-OSA groups, respectively. Cardiac complications occurred in 5.4 % of patients vs. none in OSA and non-OSA groups, respectively. 7 % patients in OSA group required ICU transfer compared to none from non-OSA group. Length of hospital stay was significantly longer for patients at high risk for OSAS compared with patients at low risk (3.6 days vs. 2.1 days; $P=0.003$).

ODI oxygen desaturation index, *OSA* obstructive sleep apnea, *PSG* polysomnography, *PACU* post anesthesia care unit, *ICU* intensive care unit, *DSM-IV* diagnostic and statistical manual of mental disorders, *DRS-R-98* delirium rating scale-revised-98, *CAM* confusion assessment method, *SACS* sleep apnea clinical score, *BMI* body mass index, CPAP continuous positive airway pressure, *IDDM* insulin-dependent diabetes mellitus

reported by the 15 studies included in our meta-analysis [18, 21–25, 27–31, 36, 37, 41, 42]. Polysomnography was used to confirm the diagnosis in most studies [18, 23, 24, 27–31, 36, 37], while others used nocturnal oximetry [22] or validated questionnaires like Berlin questionnaire [25], Flemon's criteria [21, 41] or STOP-BANG questionnaire [42] to assess the risk for OSA. Table 2 contains the methodological qualities and results reported by the three studies included in our systematic review but excluded from the meta-analysis as outlined above [9, 19, 20]. Various post-operative outcomes were reported as the number of patients with the outcome in both comparison groups. Agreement between the reviewers for study eligibility was excellent (kappa= 0.946). Using GRADE approach, the quality of evidence from the studies included in our review was found to be moderate to low.

Hypoxemia

A total of 12 studies that compared post-operative hypoxemia or oxygen desaturations in patients with and without OSA were included in analysis [18, 21–24, 27–29, 31, 37, 41, 42]. All these studies reported the outcome as number of patients experiencing post-operative hypoxemia in both the groups. Study conducted by Ahmad et al. [25] reported the number of hypoxemic events in each group rather than number of patients experiencing the event. Therefore, results from this study could not be included in the analysis. Auckley [31] reported the number of patients requiring supplemental oxygen, and these patients were assumed to have hypoxia, and data used for analysis. The overall OR for the outcome is 3.06 (95 % CI 2.35–3.97; I^2=0 %), indicating that hypoxemia is significantly higher in OSA patients after non-upper airway surgery. Subgroup analysis including only the studies that used polysomnography [18, 23, 24, 27–29, 37] showed an OR of 2.75 (95 % CI 1.89–4.00; I^2=0 %) with the significance still persistent (Fig. 1).

Re-intubation

Data from six observational studies was included in the analysis of incidence of re-intubation [18, 25, 27–29, 37]. All the included studies used PSG to diagnose OSA. Meta-analysis with the reported data resulted in OR of 1.37 (95 % CI 0.65–2.91; I^2=0 %). Results indicate that the incidence of re-intubation in patients with OSA was not significantly higher (Fig. 2).

Respiratory complications

Results from ten studies have been included in the analysis to compare the incidence of any respiratory complication in OSA group vs. non-OSA group [21–25, 27, 28, 31, 37, 42].

Table 2 Methodological characteristics of studies (excluded from meta-analysis) reporting the risk of post-operative outcomes in OSA patients

Study	Population	Outcomes reported, definitions (by each study)	Methodological features	Results
Liao et al. [20] Study design: Retrospective matched cohort Funding: University Health Network Foundation, Physician Services Foundation and University of Toronto, Canada	Setting and period: Patients who underwent elective surgery at University Health Network, Toronto between Jan. 1, 1990 and Dec. 31, 2005 OSA group: 240 patients, 77 % males, mean age 57 years Non-OSA group: 240 patients, 77 % males, mean age 57 years Type of surgery: Cardiac, ENT, orthopedic, general, urology, gynecology, spine, plastic, other	Severe desaturation: Sa $O_2 \leq 90$ % Respiratory failure: Need for mechanical ventilation Respiratory complication: Any post-operative respiratory event ranging from desaturation to bronchospasm to re-intubation Total cardiac complication: arrhythmia or ischemia or change in BP or arrest Total neurological complication: Any change in neurologic function Unplanned ICU admission: Defined Total hospital stay: Defined Blinding of outcome adjudicator: Not reported	Selection bias: OSA patients were identified by ICD-10 code. Information bias: Objective Outcome evaluation: yes, standardized OSA risk Measurement: No, ICD-10 code Confounding: No Matching: Yes Adjustment in analysis: Yes Loss to follow-up: None reported	Overall incidence of post-operative complications in the OSA group compared with non-OSA group (44 % vs. 28 %, $P<0.01$) Total respiratory complication in OSA group compared to non-OSA group (33 % vs. 22 %, $P<0.01$) with incidence of post-operative desaturation in OSA group compared to non-OSA group (17 % vs. 8 %) ICU admissions in OSA group compared to non-OSA group (40 % vs. 28 %, $P<0.01$) Total cardiac complications in OSA group compared to non-OSA group (15 % vs. 11 %, $P<0.22$) Total neurological complications in OSA group compared to non-OSA group (6 % vs. 5 %, $P<0.55$)
Memtsoudis et al. [19] Study design: Retrospective cohort Funding: Hospital for Special Surgery Anesthesiology, Young Investigator Award, Center for Education and Research in Therapeutics (CERTs) (AHRQ RFA-HS-05-14) and Clinical Translational Science Center (CTSC)	Setting and period: Patients who underwent orthopedic and general surgical procedures from National Inpatient Sample data for each year between 1998 and 2007 OSA group: 65,774 patients underwent orthopedic procedures (54.07 % males, mean age 63.14 years), and 51,509 patients had general surgery (47.56 % males, mean age 53.41 years). Non-OSA group: 2,544,667 patients underwent orthopedic procedures (38.84 % males, mean age 64.37 years) and 3,389,753 patients had general surgery (39.24 % males, mean age 52.55 years). Type of surgery: Orthopedic procedures, general surgery	Adult respiratory distress syndrome (ARDS): Not defined Intubation/mechanical ventilation: Not defined Pulmonary embolism (PE): Not defined Blinding of outcome adjudicator: Not reported	Selection bias: A large nationally representative sample was used Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: No; ICD-9 code Confounding: No Matching: Yes Adjustment in analysis: Yes Loss to follow-up: None	Patients with OSA developed pulmonary complications more frequently than their matched controls after both orthopedic and general surgical procedures. Aspiration pneumonia in OSA patients compared to non-OSA patients after general surgical procedures: OR 1.37 (1.33–1.41) and after orthopedic surgeries OR 1.41 (1.35–1.47) ARDS in OSA patients compared to non-OSA patients after general surgical procedures": OR 1.58 (1.54–1.62) and after orthopedic surgeries OR 2.39 (2.28–2.51) PE in OSA patients compared to non-OSA patients after general surgical procedures: OR 0.90 (0.84–0.97) and after orthopedic surgeries OR 1.22 (1.15–1.29) Intubation/mechanical ventilation in OSA patients compared to non-OSA patients after general surgical procedures: OR 1.95 (1.91–1.98) and after orthopedic surgeries OR 5.20 (5.05–5.37)

Table 2 (continued)

Study	Population	Outcomes reported, definitions (by each study)	Methodological features	Results
Steirer et al. [9] Study design: Retrospective cohort Funding: In part by the International Anesthesia Research Society	Setting and period: 2139 Consecutive patients undergoing outpatient surgery at John Hopkins University Baltimore, MD from May 2004 to May 2006. High-risk group: 103 patients, 65 % males, mean age 58.7 years. Low-risk group: 2,036 patients, 30 % males, mean age 47.6 years. Type of surgery: Otolaryngological, gynecological, orthopedic, plastic, general, neurological, and urological surgeries.	Increased oxygen requirement: Not defined Cardiac dysrhythmias: Not defined Naloxone use: Not defined Need for ventilator assistance: Not defined Re-intubation: Not defined Unplanned admission: Defined Discharge home: Not defined Blinding of outcome adjudicator: Not reported	Selection bias: Data was available for 2,139 patients out of the consecutive 3,553 patients. Information bias: Objective Outcome evaluation: Yes, standardized OSA risk Measurement: No, Maislin questionnaire (not validated) Confounding: Yes Matching: No Adjustment in analysis: No Loss to follow-up: None	Choice of regional anesthesia over general anesthesia was associated with high-risk OSA group ($P<0.001$) Intra-operative use of ephedrine, labetalol, metoprolol and succinylcholine was associated with high-risk OSA group ($P<0.001$) Prolonged supplemental oxygen and lower post-operative oxygen saturation were associated with high-risk OSA group ($P<0.016$). Tachycardia was associated with high-risk OSA group ($P<0.026$).

ODI oxygen desaturation index, *OSA* obstructive sleep apnea, *PSG* polysomnography, *ICU* intensive care unit, *BMI* body mass index, *CPAP* continuous positive airway pressure

Included studies reported incidence of one or more respiratory complications varying from hypoxemia to re-intubation (detailed description in Table 1). Data from studies that reported only a single respiratory complication was included in the analysis of this outcome. Two other studies [29, 41] reported the number of patients experiencing each respiratory complication. However, these studies did not report the total number of patients experiencing at least one of the respiratory complications, and therefore, the results could not be included in the meta-analysis. Analysis resulted in an overall OR of 2.77 (95 % CI 1.73–4.43; I^2=23 %) showing a statistically significant increased risk in the OSA group. Subgroup analysis including only studies that used polysomnography [23–25, 27, 28, 37] did show a significantly increased incidence in OSA group compared to control group; OR of 2.03 (95 % CI 1.13–3.64; I^2=22 %; Fig. 3).

Cardiac complications

Twelve observational studies reported various post-operative cardiac complications including dysrhythmias, abnormal heart rate, myocardial infarction and ischemia, hypotension, and congestive heart failure [18, 21–25, 27–30, 37, 42]. Included studies reported the incidence of one or more cardiac complications as reported in the data extraction tables. Data from studies that reported a single cardiac complication was also included in the analysis of this group of outcomes. Study by Kaw et al. [18] reported incidence of individual cardiac outcomes, such as myocardial ischemia and infarction, but did not report the total number of patients experiencing any type of cardiac complication. We attempted to obtain the data from the author and did not get any response. However, a recent meta-analysis by the same author [35] included the data which was not reported in the original paper. Numbers from this study have been included in our meta-analysis. Data analysis showed a significantly increased incidence of the outcome in the OSA group with an OR of 1.76 (95 % CI 1.16–2.67; I^2= 0 %). Subgroup analysis showed a persistent significantly increased incidence in patients diagnosed with OSA using only PSG [18, 23–25, 27–30, 37]; OR of 1.83 (95 % CI 1.16–2.90 I^2=0 %; Fig. 4).

Neurological complications

Seven studies compared the incidence of post-operative neurological complications like delirium, agitation, confusion, and excessive drowsiness [18, 23, 24, 27, 29, 36, 37]. All the included studies used PSG to diagnose OSA. Statistical analysis revealed a significantly increased incidence of the outcome in patients with OSA (OR=2.65; 95 % CI 1.43–4.92; I^2=0 %; Fig. 5).

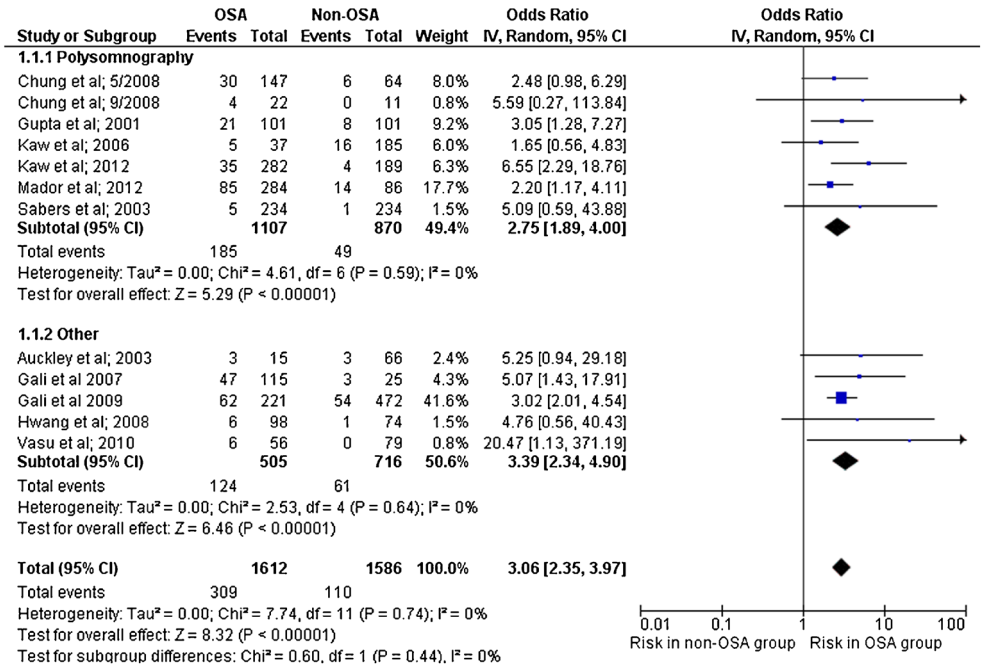

Fig. 1 Association between OSA and post-operative hypoxemia

Unplanned ICU transfer

Number of patients requiring post-operative unplanned ICU transfer was compared and reported by ten observational studies [18, 21, 23, 24, 27, 29, 31, 37, 41, 42]. Most of the studies reported number of patients requiring unplanned ICU transfer, whereas others [18, 21, 26, 27, 42] reported number of ICU transfers. Review of the descriptions provided in these studies does suggest that these ICU transfers were unplanned. For study by Kaw et al. [27], our attempt to get additional data from the authors failed. Therefore, we included the numbers reported by the same authors in their recent meta-analysis [35]. Chung et al. [24] reported no unplanned ICU transfers in both the groups. Meta-analysis of the data yielded an OR of 2.97 (95 % CI 1.90–4.64; I^2=1 %). Subgroup analysis after exclusion of the studies that used a questionnaire to predict occurrence of OSA [21, 31, 41, 42] still showed a significantly increased incidence in the sleep apnea group; OR of 2.36 (95 % CI 1.26–4.45; I^2=21 %; Fig. 6).

Other outcomes

Length of hospital stay

Eight studies reported results comparing the length of post-operative hospital stay in OSA vs. non-OSA patients. Statistically significant increased duration of stay was reported by three studies [29, 30, 43], whereas the results from five other studies [22, 25, 27, 37, 44] showed no significant effect of OSA on the outcome, as reported in Table 1. Due to inconsistency in the way the data were reported, analysis for a combined effect could not be done.

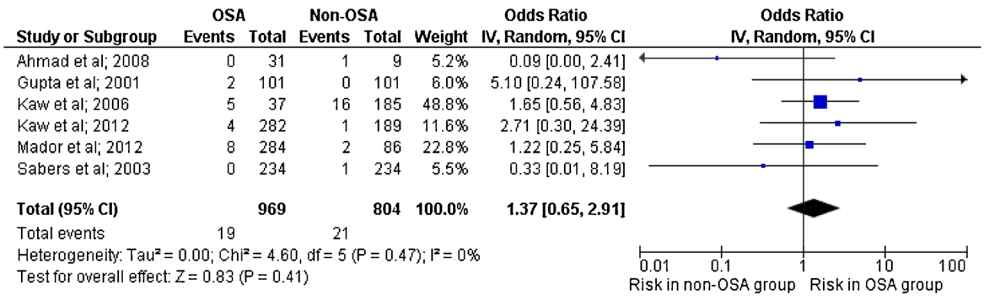

Fig. 2 Association between OSA and reintubation

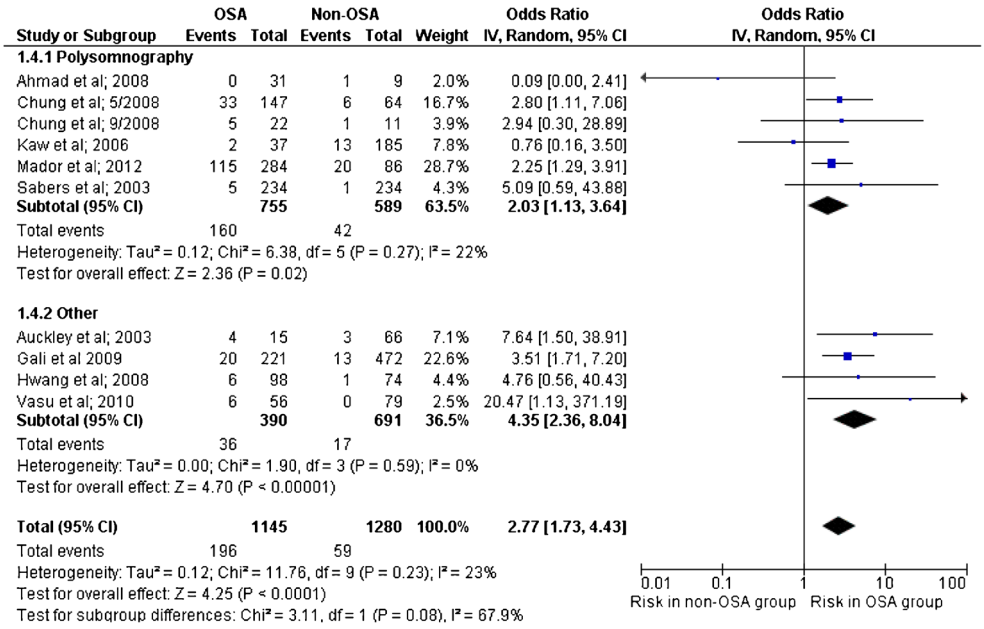

Fig. 3 Association between OSA and post-operative respiratory complications

Prolonged oxygen therapy

Three studies reported the effect of diagnosis or risk of OSA on the need for oxygen therapy after transfer out of post-operative recovery unit (PACU) [23, 24, 29]. All the studies found that patients with OSA or at high risk of OSA required prolonged oxygen therapy post-operatively, compared to patients without OSA or at low risk of OSA.

Discussion

The principal findings of our study is that patients with OSA or at high risk of OSA are more prone to adverse perioperative outcomes including respiratory, cardiac, neurological complications, and unplanned ICU transfer . Subgroup analysis including only studies in which sleep apnea was diagnosed by polysomnography yielded similar results.

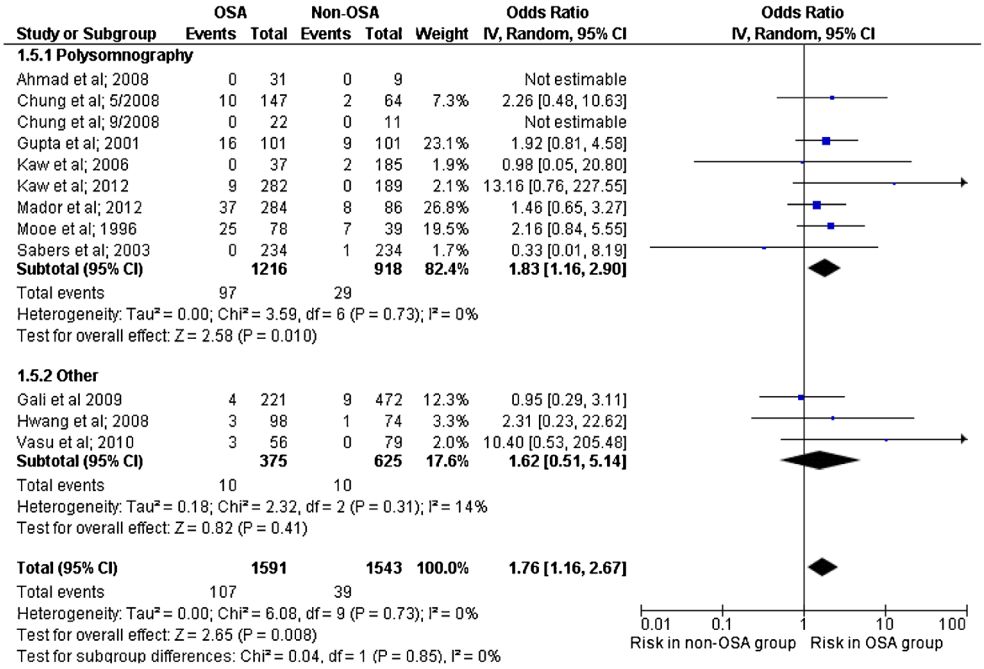

Fig. 4 Association between OSA and post-operative cardiac complications

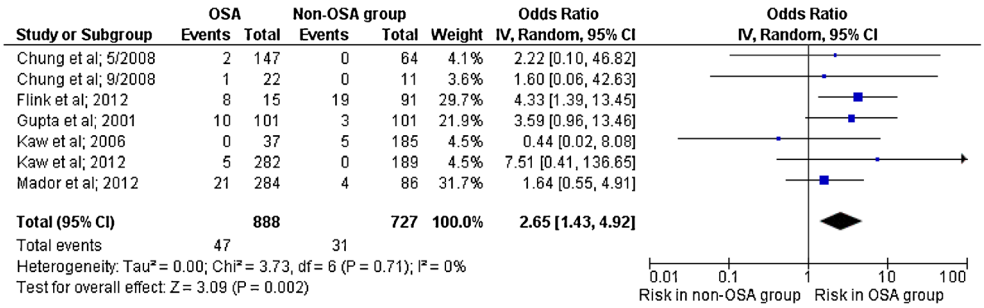

Fig. 5 Association between OSA and post-operative neurologic complications

Respiratory complications

Not surprisingly, patients with sleep apnea had a greater risk of having hypoxemia post-operatively than those without sleep apnea. Since many of the studies were retrospective in nature, episodes of hypoxemia may have been missed that would have been detected with a more systematic prospective approach. However, there is no reason why hypoxemia would be preferentially missed in the non OSA group so that the differences between groups are significant, and the overall magnitude of the problem may have even been underestimated. Hypoxemia by itself is more of a sign than a complication per se. Nevertheless, hypoxemia is clearly undesirable and can potentially precipitate more serious complications including respiratory failure, re- intubation, cardiac ischemia or cardiac arrhythmias. If persistent, it must also be treated. Thus, its presence complicates the post-operative period and may be a harbinger of more serious complications. We also found that patients with sleep apnea had a greater risk of being on oxygen for a prolonged period of time.

We found no increase in the rate of re-intubation in patients with OSA. Similar results have been reported previously [35]. Our analysis included two additional studies including over 400 patients while excluding one study where re-intubation rates were incompletely reported.

Total respiratory complications were increased in patients with sleep apnea. The type of respiratory complications measured varied substantially between studies which decreased the utility of this measure. When only studies that included polysomnography were included, this variable remained statistically significant. Further studies preferably with a prospective study design are needed before definitive statements can be made about the effect of sleep apnea on total respiratory

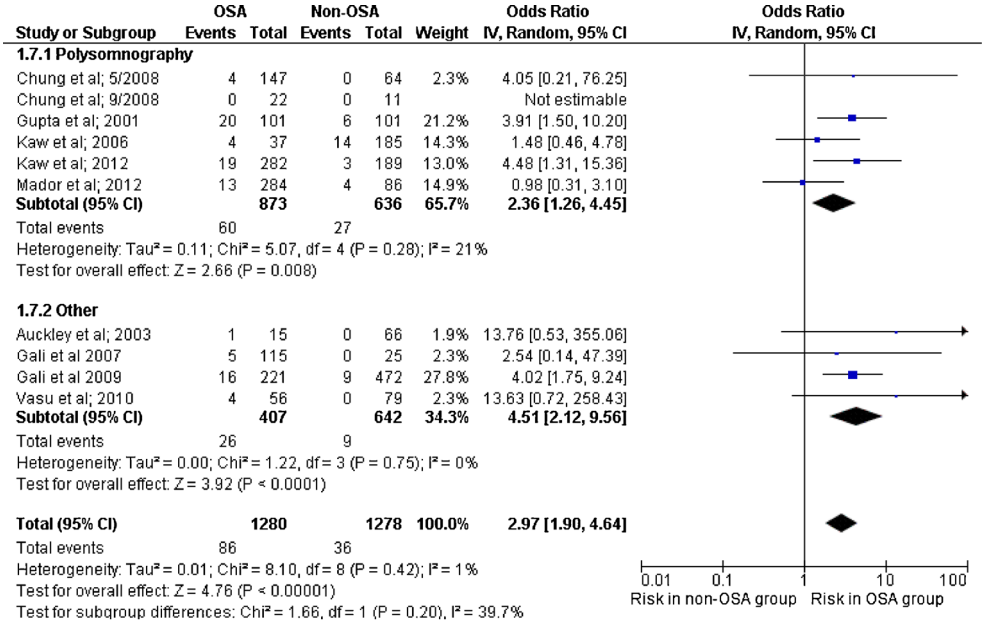

Fig. 6 Association between OSA and post-operative unplanned ICU transfer

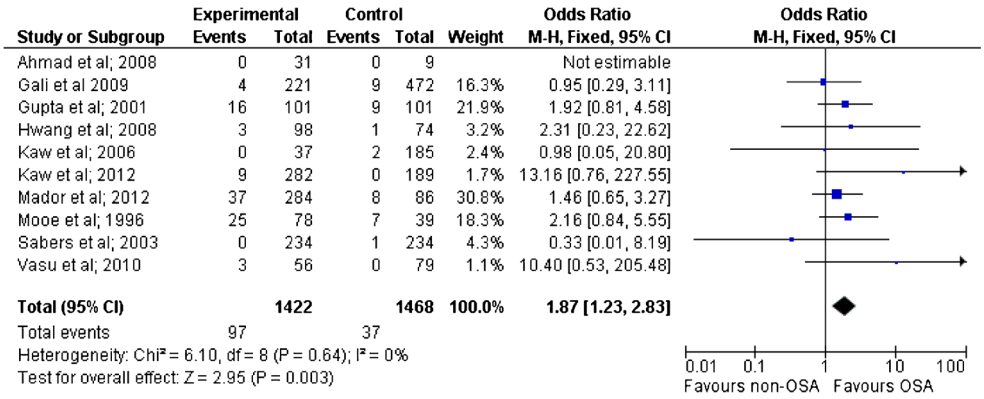

Fig. 7 Association between OSA and post-operative cardiac complications; no confounders

complications. However, it does appear that hypoxemia (sustained requiring treatment) is more common in patients with sleep apnea. In a huge administrative database study, patients with sleep apnea had a greater risk of aspiration pneumonia, adult respiratory distress syndrome, and mechanical ventilation after orthopedic and general surgeries [19]. This latter study would indirectly suggest an increased re-intubation rate in patients with sleep apnea. Since re-intubation was relatively uncommon in all the studies we included in our meta-analysis, our study may not have had sufficient power to adequately assess this outcome even though there were almost 1,800 patients included in the analysis.

Cardiac complications

We found an increased risk of cardiac complications in patients with OSA compared to those without. This was present even when only studies where sleep apnea was confirmed by polysomnography were included in the analysis. Reporting of cardiac events varied between studies and as a result some studies had very few cardiac events reported. Despite these issues, cardiac events were clearly increased in the sleep apnea group. However, patients with sleep apnea also are more obese, have greater incidence of coronary artery disease and diabetes all of which may influence the incidence of cardiac complications post-operatively. Most studies adjusted for these confounders when examining post-operative risk while some did not. We conducted a sub group analysis including results from the studies that matched patient characteristics or adjusted for them during analysis [18, 21, 22, 25, 27–30, 37, 42]. Results showed significantly increased incidence of post-operative cardiac complications in patients with OSA (OR= 1.87; 95 % CI 1.23–2.83; I^2=0 %; Fig. 7). Thus, sleep apnea does appear to increase the post-operative risk of cardiac complications.

Neurologic complications

We found an increased risk of neurologic complications including delirium, agitation, confusion, and excessive drowsiness in patients with OSA. Since, these symptoms were detected retrospectively in many of the studies; their true incidence was likely underestimated. None of the studies included reported any morbidity or mortality attributable to these neurologic complications. It is worth noting though that neurologic complications like delirium in the elderly surgical patient in the immediate post-operative period have the potential to significantly complicate the patients' post-operative course leading to a prolonged hospital stay or other adverse outcomes [45].

Unplanned ICU transfer

We found an increased risk of ICU transfer in patients with sleep apnea. There was a difference in reporting among studies with some studies reporting only unplanned ICU transfers [21, 23, 24, 29, 37, 41], while others reported all ICU transfers [18, 27, 31, 42]. However, in those studies in which ICU transfer was not specified as unplanned, it does appear that ICU transfers were really unplanned based on the descriptions provided in the studies. In one study, all patients were transferred to the ICU overnight who had severe sleep apnea (planned transfer) [23]. Since unplanned ICU transfer was the outcome reported, the number of unplanned ICU transfers would be underestimated in the sleep apnea group since there could be no unplanned transfers in those with severe sleep apnea. In a quality improvement study by Hallowell et al. [26] in patients undergoing gastric surgery for morbid obesity, there were a number of measures introduced for patients with sleep apnea that reduced ICU transfers starting in 2004–2005. This suggests that focused interventions in such patients and active surveillance for sleep apnea

may lead to a reduction in post-operative complications. Length of hospital stay was significantly increased in three out of the eight studies where it was reported. Unfortunately, due to the way the data was reported, pooling of data to calculate the overall effect could not be calculated.

Limitations of study

The studies on which this meta-analysis is based were not of high methodological quality which lends caution to our conclusions. The criteria used to identify respiratory, cardiac, and neurologic complications varied substantially among studies which could make pooling of the data problematic. Despite this limitation, analysis did not show substantial heterogeneity among studies supporting our decision to pool the data. We evaluated for possible publication bias by looking at the funnel plots in meta-analysis. We cannot exclude the possibility of publication bias for two outcomes, namely, post-operative hypoxemia and unplanned ICU transfer. Another limitation is the retrospective nature of some of the studies which relies on reporting of complications in the chart by clinicians who may have different definitions for the complications noted. While there should not be a selective difference in reporting between patients with and without sleep apnea, the retrospective nature likely leads to systematic underreporting of complications compared to a prospective study using validated tools for daily measurement. This is especially important for subjective outcomes such as delirium, whereas re-intubation or unplanned ICU transfer should be less affected by this methodological concern. Another important point is that meta-analysis is by design a univariate analysis and not adjusted for confounding variables that are likely different between patients with and without OSA and may be influencing the observed association between OSA and post-operative outcomes. However, most of the individual studies on which the meta-analysis is based attempted to correct for confounders, such as body weight, diabetes, coronary artery disease, etc., and still found a significant effect for OSA on post-operative outcomes [18, 21, 22, 27–30, 37, 42]. Finally, length of stay is influenced by many factors other than medical acuity such as availability of sub-acute rehabilitation beds in patients after hip replacement that may mask real differences between patients with and without sleep apnea.

Implications for clinical practice

The increased risk of post-operative complications in patients with OSA suggests that identification of patients at high risk for OSA pre-operatively might be clinically worthwhile. Identifying treatment algorithms for patients with sleep apnea to reduce post-operative complication rates will require further investigation. However, increased vigilance and monitoring of such patients may lead to a reduction in post-operative complications [21, 32, 33, 46]. Whether specific treatment with CPAP in patients at high risk for sleep apnea naïve to CPAP therapy will improve post-operative outcomes remains to be investigated but a recent pilot study did not show beneficial effects [47]. Another consideration is the venue for surgical procedures. Ambulatory stand-alone centers are becoming increasingly utilized for surgical procedures that do not require post-operative inpatient care. If sleep apnea patients are operated at these sites then they must be equipped to handle acute airway collapse in the post-operative recovery room and be staffed to handle potentially longer and more difficult recovery periods [48]. The ideal setting and monitoring for patients with sleep apnea is also an area that requires further study.

In conclusion, patients with sleep apnea or at high risk for sleep apnea have an increased post-operative risk for respiratory, cardiac, and neurologic complications as well as an increased risk of ICU transfer.

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Contributions of authors: Dr. Gaddam contributed to drafting the protocol, designing the search strategy, developing the forms, study selection, revising the article critically for important intellectual content, data abstraction, data analysis, data interpretation, drafting of the manuscript, and approving the final version of manuscript.

Dr. Gunukula contributed to developing the forms, study selection, revising the article critically for important intellectual content, data abstraction, drafting of the manuscript, and approving the final version of manuscript.

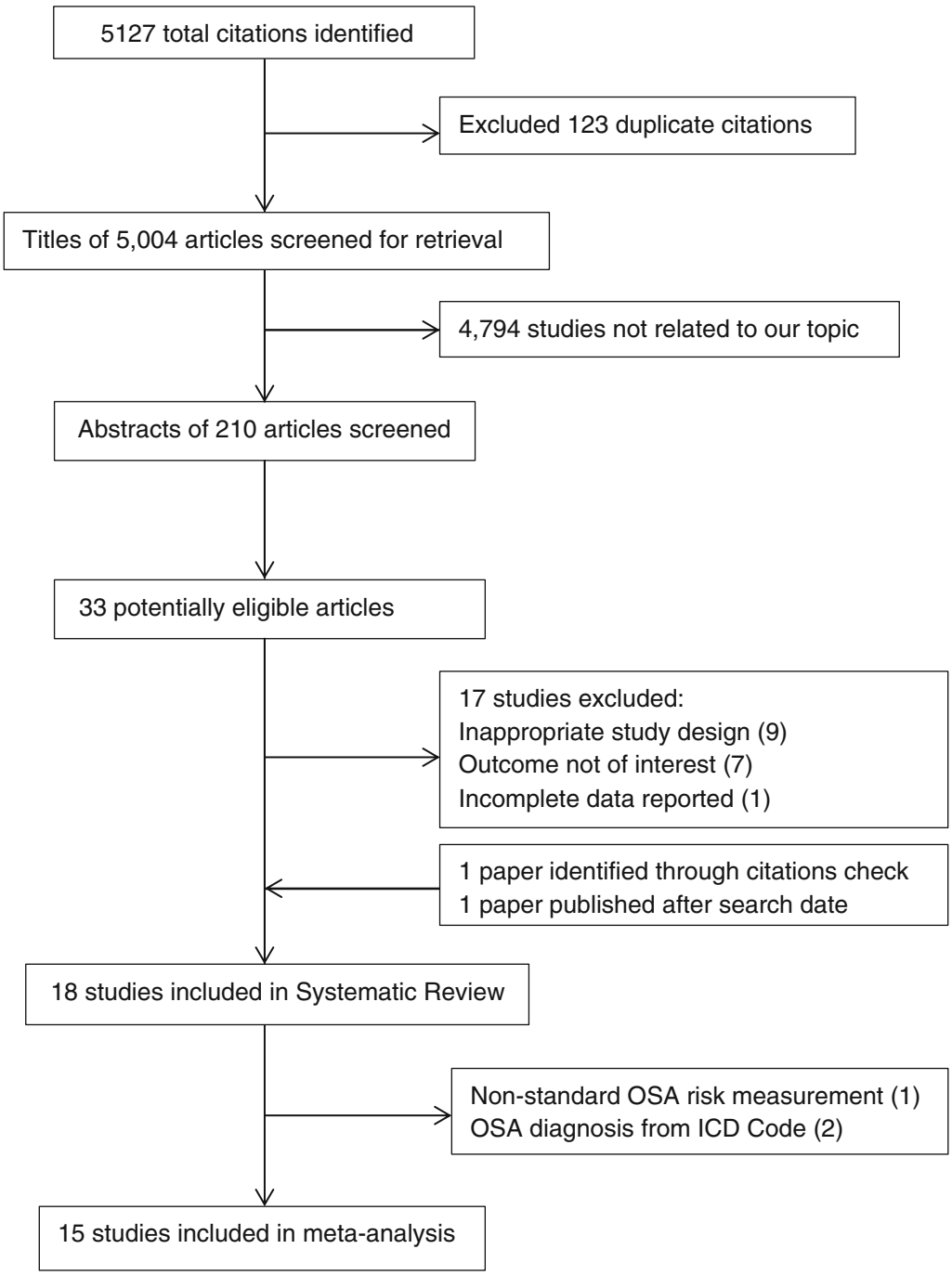
Dr. Mador contributed to drafting the protocol, designing the search strategy, study selection, data interpretation, drafting of the manuscript, and approving the final version of manuscript.

Conflict of interest None

Appendix 1 Search terms used

Apnea, complications, intraoperative, intraoperative complications, operative period, perioperative, perioperative period, post-operative, post-operative complications, procedures, sleep, sleep apnea, sleep apnea syndromes, surgical, surgical procedures operative, surgical procedures, operative

Appendix 2 Study flow diagram



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