

## Safety of gastrointestinal endoscopy with conscious sedation in obstructive sleep apnea

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### Abstract

#### AIM

To perform a systematic review and meta-analysis to assess the safety of conscious sedation in patients with obstructive sleep apnea (OSA).

#### METHODS

A comprehensive electronic search of MEDLINE and EMBASE was performed from inception until March 1, 2015. In an effort to include unpublished data, abstracts from prior gastroenterological society meetings as well as other reference sources were interrogated. After study selection, two authors utilizing a standardized data extraction form collected the data independently. Any disagreements between authors were resolved by consensus among four authors. The methodological quality was assessed using the Newcastle Ottawa tool for observational studies. The primary variables of interest included incidence of hypoxia, hypotension, tachycardia, and bradycardia. Continuous data were summarized as odds ratio (OR) and 95%CI and pooled using generic inverse variance under the random-effects model. Heterogeneity between pooled studies was assessed using the  $I^2$  statistic.

#### RESULTS

Initial search of MEDLINE and EMBASE identified 357 citations. A search of meeting abstracts did not yield any relevant citations. After systematic review and exclusion consensus meetings, seven studies met the a priori determined inclusion criteria. The overall methodological

quality of included studies ranged from moderate to low. No significant differences between OSA patients and controls were identified among any of the study variables: Incidence of hypoxia (7 studies, 3005 patients; OR = 1.11; 95%CI: 0.73-1.11;  $P = 0.47$ ;  $I^2 = 0\%$ ), incidence of hypotension (4 studies, 2125 patients; OR = 1.10; 95%CI: 0.75-1.60;  $P = 0.63$ ;  $I^2 = 0\%$ ), incidence of tachycardia (3 studies, 2030 patients; OR = 0.94; 95%CI: 0.53-1.65;  $P = 0.28$ ;  $I^2 = 21\%$ ), and incidence of bradycardia (3 studies, 2030 patients; OR = 0.88; 95%CI: 0.63-1.22;  $P = 0.59$ ;  $I^2 = 0\%$ ).

### CONCLUSION

OSA is not a significant risk factor for cardiopulmonary complications in patients undergoing endoscopic procedures with conscious sedation.

**Key words:** Conscious sedation; Obstructive sleep apnea; Endoscopy; Complications; Safety; Meta-analysis

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**Core tip:** Patients with obstructive sleep apnea (OSA) often receive monitored anesthesia care in lieu of conscious sedation due to a perceived elevated risk of complications. However, prior studies have failed to note any clinically significant variations in cardiopulmonary parameters in OSA patients when compared to controls during endoscopy but studies have been underpowered due to small sample sizes. The objective was to perform a systematic review and meta-analysis to assess the safety of conscious sedation in patients with OSA. This meta-analysis showed OSA is not a significant risk factor for cardiopulmonary complications in patients undergoing endoscopic procedures with conscious sedation.

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## INTRODUCTION

Obstructive sleep apnea (OSA) is an increasingly common disorder. Because of a presumed elevated risk, endoscopic evaluation in patients with OSA may be delayed, denied or achieved at a higher level of care resulting in substantial healthcare expenses. In the general population, adverse events during endoscopy are rare with an approximate adverse event rate of 0.1% and 0.2% for upper gastrointestinal and lower gastrointestinal procedures respectively<sup>[1-4]</sup>. Non-significant variations in cardiopulmonary parameters are usually noted during routine endoscopy and have been well studied<sup>[5-7]</sup>. Several published studies, including a recently reported prospective study evaluating the risk of cardiopulmonary

complications in patients with OSA undergoing endoscopy with conscious sedation have not supported the need for extra precaution<sup>[8]</sup>. We recently published a prospective analysis in the veteran population undergoing upper and lower endoscopy which did not find any significant cardiopulmonary variation in control and OSA patients<sup>[8]</sup>.

Despite their comparable findings, these conclusions are limited by small sample sizes in conjunction with low adverse event rates. No systematic reviews or meta-analyses have been performed on this topic to date. The present study aims to systematically review the literature and perform a meta-analysis of all selected published and unpublished data meeting search criteria on patients with OSA undergoing endoscopic procedures.

## MATERIALS AND METHODS

### Selection criteria

A comprehensive electronic search of MEDLINE and EMBASE was performed from inception until March 1, 2015. A total of 119 MEDLINE references were identified using the following search strategy: (apnea OR "sleep apnea") OR sleep apnea) OR obstructive sleep apnea) OR "obstructive sleep apnea") OR sleep disordered breathing) OR "sleep disordered breathing") AND (sedation) OR conscious sedation) OR "conscious sedation") OR moderate sedation) OR "moderate sedation") AND endoscopy. A total of 238 EMBASE references were identified using the following strategy: Endoscopy AND (Apnea OR (sleep AND disordered AND breathing) OR "sleep disordered breathing" OR "obstructive sleep apnea" OR "sleep apnea" OR (sleep AND apnea) OR (obstructive AND sleep AND apnea) AND (Sedation OR "conscious sedation" OR (conscious AND sedation) OR "moderate sedation" OR (moderate AND sedation) AND human. Two authors evaluated the combined 357 candidate studies independently. Studies performed on patients with obstructive sleep apnea undergoing endoscopy with conscious sedation and at least one the following variables of interest were considered for inclusion: Incidence of hypoxia, hypotension, tachycardia, and bradycardia.

### Data collection

Two authors extracted all data independently utilizing a standardized data extraction form. Once the data was entered into a dataset, a random data check was performed for accuracy. All disagreements between authors were resolved by consensus with a third author. Data were collected on study and patient characteristics, OSA groups, use of conscious sedation and the incidences of hypoxia, hypotension, tachycardia, and bradycardia when available. The methodological quality was assessed using the Newcastle Ottawa tool for observational studies<sup>[9]</sup>. The primary variables of interest included incidence of hypoxia, hypotension, tachycardia, and bradycardia. The systematic review was performed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

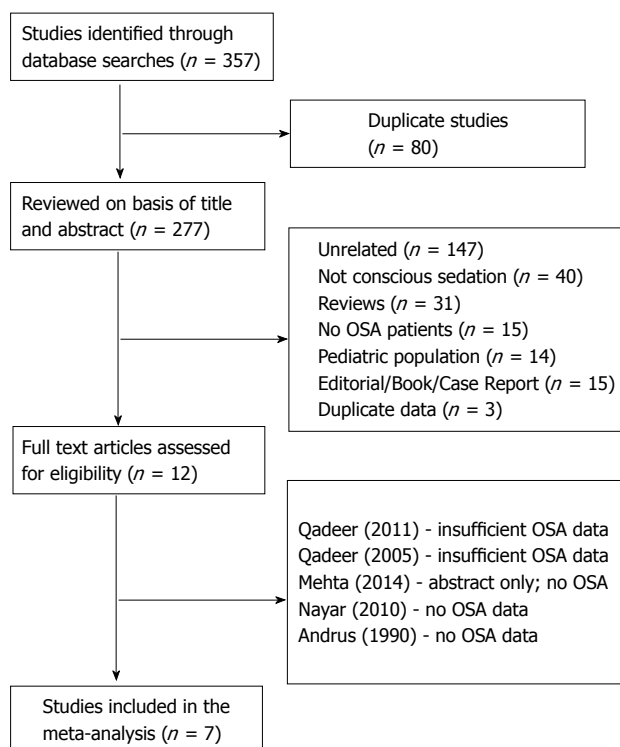


Figure 1 Flow diagram of study selection<sup>[22-25]</sup>. OSA: Obstructive sleep apnea.

guidelines<sup>[10]</sup>.

### Statistical analysis

Continuous data were summarized as odds ratio (OR) and 95%CI and pooled using generic inverse variance under the random-effects model. Heterogeneity between pooled studies was assessed using  $I^2$  statistic and categorized as low (< 30%), moderate (30%-50%), or high (> 50%)<sup>[11]</sup>. All analyses were performed using Review Manager 5.1 software<sup>[12]</sup>.

### Biostatistics

The statistical methods of this study were performed and reviewed by a biomedical statistician, Ambuj Kumar, MD, MPH from Comparative Effectiveness Research, Morsani College of Medicine, University of South Florida, Tampa, FL, United States.

## RESULTS

### Study selection

A comprehensive search of MEDLINE and EMBASE identified 357 eligible citations. In an effort to capture unpublished data, conference abstracts from the last 3 meetings (2013-2015) of the American College of Gastroenterology and Digestive Disease Week were also reviewed. No studies were identified to meet inclusion criteria. The following sites were also interrogated for possible study inclusion: ClinicalTrials.gov, Roche clinical trial protocol registry ([www.roche-trials.com](http://www.roche-trials.com)), Novartis clinical trials database ([www.novctrd.com](http://www.novctrd.com)), Australian New Zealand Clinical Trials Registry (ANZCTR), and the

metaRegister of Controlled Trials. No additional studies were identified for inclusion.

After systematic review and exclusion consensus meetings, seven studies met the a priori determined inclusion criteria (Figure 1). None of the references from the included studies yielded additional studies eligible for inclusion. The overall methodological quality of the included studies ranged from moderate to low as assessed by the Newcastle Ottawa tool for observational studies<sup>[9]</sup>.

### Hypoxia

Seven studies identified for inclusion contained data on the incidence of hypoxia. A total of 3005 patients were included for analysis. No significant differences between OSA patients and controls were identified with regards to the incidence of hypoxia (OR = 1.11; 95%CI: 0.73-1.11;  $P = 0.47$ , Figure 2). The heterogeneity among the studies was low ( $I^2 = 0\%$ ).

### Hypotension

Four studies identified for inclusion contained data on the incidence of hypotension. A total of 2125 patients were included for analysis. No significant differences between OSA patients and controls were identified with regards to the incidence of hypotension (OR = 1.10; 95%CI: 0.75-1.60;  $P = 0.63$ , Figure 3). The heterogeneity among the studies was low ( $I^2 = 0\%$ ).

### Tachycardia

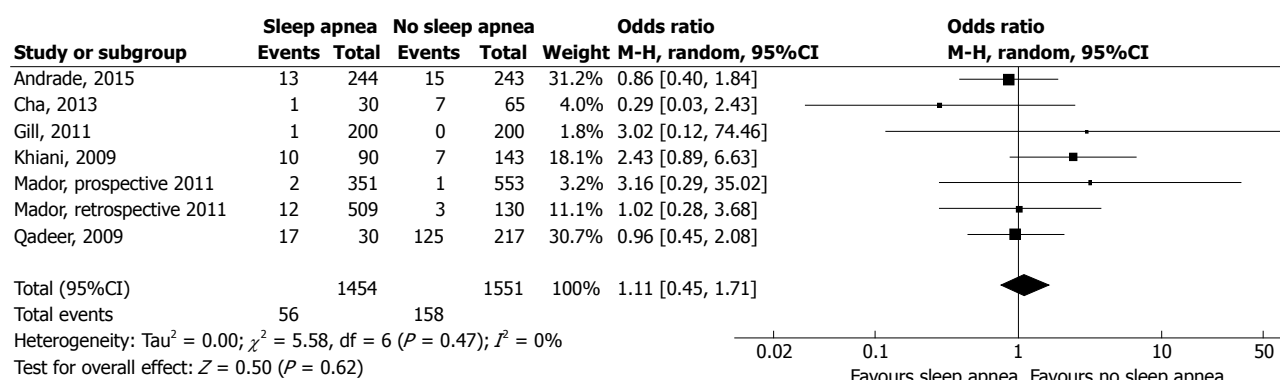
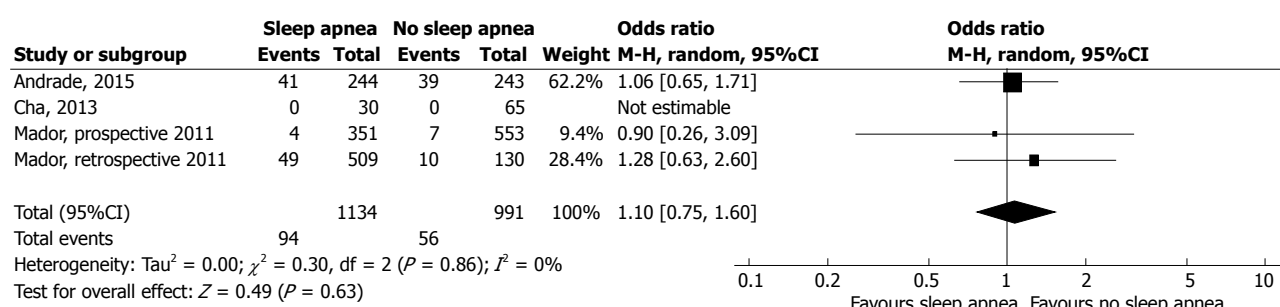
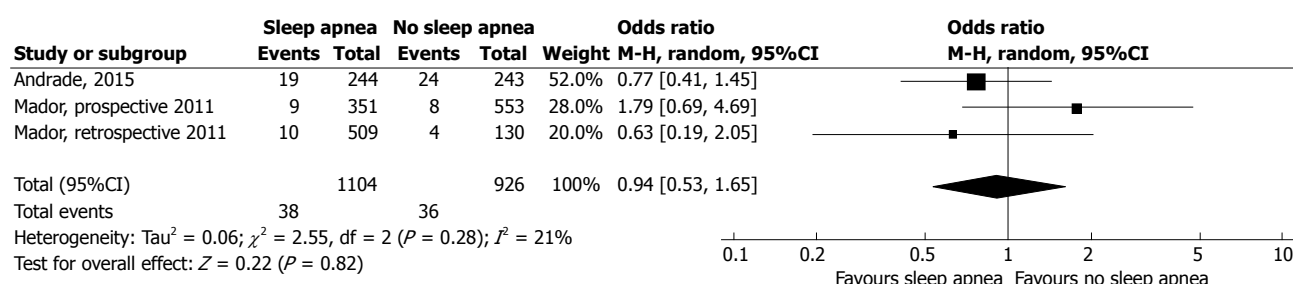
Three studies identified for inclusion contained data on the incidence of tachycardia. A total of 2030 patients were included for analysis. No significant differences between OSA patients and controls were identified with regards to the incidence of tachycardia (OR = 0.94; 95%CI: 0.53-1.65;  $P = 0.28$ , Figure 4). The heterogeneity among the studies was low ( $I^2 = 21\%$ ).

### Bradycardia

Three studies identified for inclusion contained data on the incidence of bradycardia. A total of 2030 patients were included for analysis. No significant differences between OSA patients and controls were identified with regards to the incidence of bradycardia (OR = 0.88; 95%CI: 0.63-1.22;  $P = 0.59$ , Figure 5). The heterogeneity among the studies was low ( $I^2 = 0\%$ ).

## DISCUSSION

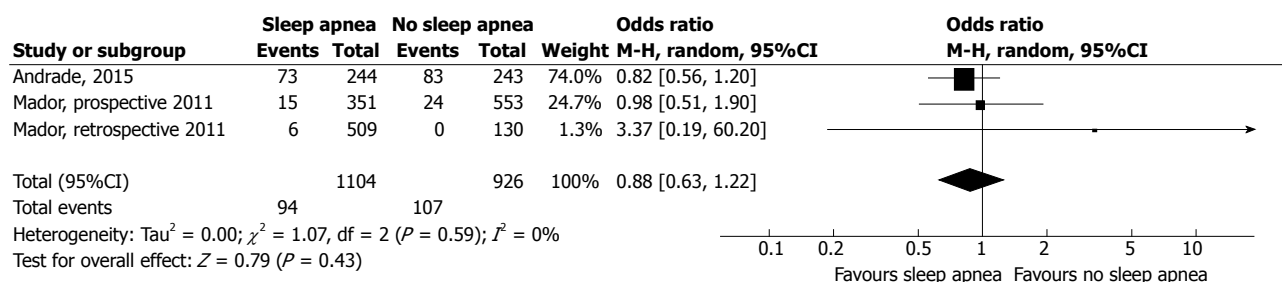
OSA is a growing problem in the United States especially among the veteran population. Moderate to severe OSA is estimated to affect approximately 13% of men and 6% women between the ages of 30-70<sup>[13]</sup>. Per the ASGE sedation guidelines, patient with OSA are considered to be at a higher risk regarding sedation-related cardiopulmonary complications in relation to upper and lower endoscopy<sup>[14]</sup>. These patients are routinely recommended MAC anesthesia for endoscopic

Figure 2 Incidence of hypoxia<sup>[8,17-21]</sup>.Figure 3 Incidence of hypotension<sup>[8,17,20,21]</sup>.Figure 4 Incidence of tachycardia<sup>[8,20,21]</sup>.

evaluation. Cardiopulmonary complications are the most feared unfavorable events among patients with OSA including episodes of tachycardia, bradycardia, hypotension, and hypoxia<sup>[5-7]</sup>. It is believed that OSA patients especially tend to have poor respiratory drive and effort which can be exacerbated by sedation<sup>[15,16]</sup>. Contrary to that belief, our meta-analysis and review does not show any significant difference in regards to hypoxia in OSA patients. It is also well studied that sedation tend to lower overall mean blood pressure. When looking at cardio-circulatory parameters including bradycardia, tachycardia and hypotension, our review failed to show any significant difference in regards to those parameters. Therefore, in patients undergoing endoscopy with conscious sedation, OSA does not seem to be a clinically important risk factor for unfavorable outcomes. In short, significant differences between OSA patients and controls were not identified among any of

the study variables: Incidence of hypoxia, hypotension, tachycardia or bradycardia. This is in correlation with regards to the recent publication from our institution highlighting the cardiopulmonary parameters in the OSA and non-OSA patients<sup>[8]</sup>. OSA patients are perceived as high risk for endoscopy and are offered monitored anesthesia care routinely although this meta-analysis suggests otherwise. Moving forward, endoscopists should be cognizant that OSA does not predispose patients to higher risk compared to non OSA patients. In addition, using conscious sedation for OSA patients may reduce overall healthcare burden with cost saving measures as MAC anesthesia care has not necessarily shown any overall reduction in adverse events. A major limitation of the study includes the overall methodological quality of the included studies ranged from moderate to low. Further, for patients undergoing endoscopic procedures with conscious sedation, OSA does not appear to be a



Figure 5 Incidence of bradycardia<sup>[8,20,21]</sup>.

significant risk factor for cardiopulmonary complications. Future prospective studies must be conducted to evaluate the cost effectiveness and safety of endoscopy with MAC in the OSA population.

## COMMENTS

### Background

Patients with obstructive sleep apnea (OSA) often receive monitored anesthesia care in lieu of conscious sedation due to a perceived elevated risk of complications. However, prior studies have failed to note any clinically significant variations in cardiopulmonary parameters in OSA patients when compared to controls during endoscopy but studies have been underpowered due to small sample sizes. The authors aim was to perform a systematic review and meta-analysis to assess the safety of conscious sedation in patients with obstructive sleep apnea (OSA).

### Research frontiers

This meta-analysis has demonstrated that OSA does not appear to be a significant risk factor for cardiopulmonary complications in patients undergoing endoscopy. Future prospective studies are needed to look at both the safety and cost-effectiveness of endoscopy with MAC in the OSA population.

### Innovations and breakthroughs

This meta-analysis showed OSA is not a significant risk factor for cardiopulmonary complications in patients undergoing endoscopic procedures with conscious sedation, which has typically been the standard of care. These results further open the consideration of endoscopy without MAC in patients with OSA but future prospective studies are needed to look at both the safety and cost-effectiveness of endoscopy with MAC in the OSA population.

### Applications

These findings can be considered by endoscopists when performing endoscopy with MAC in the OSA population in assessing their risk for procedural cardiopulmonary complications.

### Terminology

Conscious sedation - The use of a sedative during a medical procedure that allows for a quick recovery; OSA - A sleep disorder that causes breathing to start and stop during sleep due to airway obstruction during sleep; Endoscopy - A procedure which uses an endoscope, or a long flexible tube with a camera to examine the upper GI tract.

### Peer-review

The author gave a systematic review and meta-analysis about the safety of gastrointestinal endoscopy with conscious sedation in patients with OSA. The manuscript was concise and helpful for us to be cognizant that OSA does not appear to be a clinically significant risk factor for adverse outcomes in patients undergoing endoscopy with conscious sedation.

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