Relationship between Chronic Intermittent Hypoxia and Intraoperative Mean Arterial Pressure in Obstructive Sleep Apnea Patients Having Laparoscopic Bariatric Surgery

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ABSTRACT

Background: Recurrent nocturnal hypoxemia in obstructive sleep apnea enhances sympathetic function, decreases baroreceptor sensitivity, and weakens peripheral vascular responses to adrenergic signals. The authors hypothesized that the percentage of total sleep time spent at oxyhemoglobin saturation (Sao_2) less than 90% and minimum nocturnal Sao_2 on preoperative polysomnography are associated with decreased intraoperative mean arterial pressure.

Methods: The authors examined the records of all patients who had laparoscopic bariatric surgery at Cleveland Clinic between 2005 and 2009 and an available polysomnography study. The authors assessed the relationships between the percentage of total sleep time spent at Sao_2 less than 90% and minimum nocturnal Sao_2, and the time-weighted average of mean arterial pressure. The authors used multivariable regression models to adjust for prespecified clinical confounders.

Results: Two hundred eighty-one patients were included in the analysis. The average change in the time-weighted average of mean arterial pressure was −0.02 (97.5% CI, −0.08, 0.04) mmHg for each 1% absolute increase in the percentage of sleep time spent at Sao_2 less than 90% ($P = 0.50$). The average change was −0.13 (97.5% CI, −0.27, 0.01) mmHg, for each 1% absolute decrease in the minimum Sao_2 ($P = 0.04$ > significance criterion of 0.025, Bonferroni correction). An unplanned analysis estimated 1% absolute decrease in minimum Sao_2 was associated with −0.22 (98.75% CI, −0.39, −0.04) mmHg, change in mean arterial pressure ($P = 0.002$) in the time period between endotracheal intubation and trocar insertion.

Conclusion: Recurrent nocturnal hypoxemia in obstructive sleep apnea is not a risk marker for intraoperative hypotension.
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OBSTRUCTIVE sleep apnea (OSA) is common and characterized by repeated partial or complete airway collapse during sleep, potentially leading to severe oxyhemoglobin desaturation.[1] Approximately 30% of the general population suffers from OSA,[2] while a similar fraction of surgical patients[3] are at high risk for the disease, with most of them lacking a formal diagnosis.[3–5] OSA has been linked to cardiovascular[6,7] and metabolic[8] morbidity, while a diagnosis of moderate-to-severe disease (≥15 apnea /hypopnea events per hour of sleep) has been identified as an independent risk factor for all-cause and cardiovascular mortality.[9,10] As in other studies linking OSA to cardiovascular morbidity,[11,12] these investigations suggest that nocturnal intermittent hypoxia, rather than sleep fragmentation, is the responsible risk-increasing element.

Patients suffering from OSA present with a chronic enhancement in sympathetic adrenergic activity[13,14] that is considered one of the major mechanisms in the development of cardiovascular morbidity in this population.[15] This excess in adrenergic signaling is associated with an almost twofold increase in blood pressure variability,[16] a significant attenuation of baroreflex sensitivity,[17,18] and decreased peripheral

What We Already Know about This Topic

- Approximately 30% of the general population suffers from obstructive sleep apnea. Patients suffering from obstructive sleep apnea present with a chronic enhancement in sympathetic adrenergic activity that is considered one of the major mechanisms in the development of cardiovascular morbidity in this population. Thus, obstructive sleep apnea patients may have increased risk for intraoperative and postoperative morbidity consequent to hemodynamic instability.
- This study investigated whether nocturnal intermittent hypoxia consequent to obstructive sleep apnea, as quantified by the percentage of total sleep time spent at Sao_2 less than 90% and the minimum nocturnal Sao_2, is associated with decreased intraoperative mean arterial pressure in patients undergoing laparoscopic bariatric surgery.

What This Article Tells Us That Is New

- Recurrent nocturnal hypoxemia in obstructive sleep apnea is not a risk marker for intraoperative hypotension in patients undergoing laparoscopic bariatric surgery.

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vascular adrenergic responses,[19] in OSA patients compared to normal subjects. Both animal and human experiments demonstrate that the magnitude of these alterations in cardiovascular homeostatic mechanisms is proportional to the severity of the disease as measured by the number of apnea/hypopnea events per hour of sleep and the associated extent of recurrent hypoxemia.

The severity of nocturnal arterial desaturation was found to be the strongest predictor of baroreceptor sensitivity depression in OSA subjects.[17] In a rat model of chronic intermittent hypoxia, the resulting sympathetic overactivity was associated with a paradoxical decrease in the pressor response to adrenergic signals[20] suggesting peripheral adaptation to chronic adrenergic overstimulation. Consistent with these observations is a recent report that patients at high risk for OSA (based on a validated risk prediction model) were more likely to receive vasopressors to maintain hemodynamic goals intraoperatively than low-risk patients.[21]

Even short periods of low intraoperative mean arterial pressure (MAP) are strongly associated with postoperative morbidity and associated organ damage.[22] Impaired cardiovascular homeostasis may render OSA patients more vulnerable to hypotensive stimuli during a general anesthetic.[23,24] Furthermore, defects in blood flow autoregulation mechanisms for vital target organs like the brain[25,26] may decrease the ability of subjects with OSA to cope with low perfusion insults. OSA patients may thus especially be at risk for intraoperative and postoperative morbidity consequent to hemodynamic instability including cardiovascular events and transfers to intensive care settings.[27–29]

We thus retrospectively examined the intraoperative blood pressure in patients who had laparoscopic bariatric surgery. Specifically, we tested the hypothesis that nocturnal intermittent hypoxia consequent to OSA, as quantified by the percentage of total sleep time spent at oxyhemoglobin saturation (Sa_{O_2}) less than 90% and the minimum nocturnal Sa_{O_2}, are associated with decreased intraoperative MAP.

Materials and Methods

With approval from the Cleveland Clinic Institutional Review Board (Cleveland, Ohio), we undertook a retrospective observational study using data from the Cleveland Clinic Perioperative Health Documentation System. This registry contains the complete anesthesia record for all noncardiac surgery patients, and is linked to the full electronic medical record and about a dozen other data sources.

We used deidentified information from electronic records and the paper charts of patients who had laparoscopic bariatric surgery at the Cleveland Clinic Main Campus between June 2005 and December 2009, to retrospectively examine the relationship between the severity of chronic intermittent hypoxia, as measured by overnight polysomnography, and intraoperative MAP in patients suffering from OSA.

Patients

Eligible were all patients who had laparoscopic bariatric procedures between June 2005 and December 2009 and had a diagnosis of OSA with a polysomnography study performed within two preoperative years. We excluded patients who did not have a polysomnography report available and/or those whose polysomnography reports were missing critical exposure variables such as the percentage of total sleep time spent at Sa_{O_2} less than 90%, or minimum nocturnal Sa_{O_2}. We also excluded patients missing any of the prespecified potential confounders. Patients with severe cardiopulmonary disease associated with respiratory insufficiency and/or requiring oxygen supplementation during daytime or sleep, were also excluded.

Sleep studies were performed and evaluated, according to consensus and practice guidelines published by the American Academy of Sleep Medicine.[30–33] Briefly, 14-channel polysomnography included monitoring the electroencephalogram, electro-oculogram, electromyogram, oronasal flow by thermocouples and nasal pressure, thoracic and abdominal movement by inductance plethysmography, and oxyhemoglobin saturation by pulse oximetry (Sa_{O_2}). The apnea/hypopnea and arousal indices were estimated by dividing the number of all events occurring during sleep with the total sleep time calculated as the sum of all sleep stage periods.

Anesthetic Management

General anesthesia was induced with propofol, fentanyl, and rocuronium or succinylcholine, and maintained with a volatile anesthetic in an oxygen/air mixture. Fentanyl, morphine, alfentanil, remifentanil, or hydromorphone was titrated to patients' vital signs. Vasopressors such as ephedrine, phenylephrine, or epinephrine were used to maintain blood pressure within 20% of preoperative level. Intraabdominal pressure during the pneumoperitoneum was automatically controlled at a level equal to, or less than 15 mm H_2O. Epidural analgesia was not used.

Outcomes and Exposures

Time-weighted average intraoperative MAP was the main outcome in our analysis. Intraoperative blood pressure data were acquired from an electronic anesthesia record-keeping system, which continuously records minute-by-minute data from physiologic monitors during the intraoperative period. When an arterial catheter was used, blood pressure was recorded every minute. When noninvasive blood pressure monitoring was employed, blood pressure was recorded at 1- to 5-min intervals. We removed blood pressure artifacts, which were identified by out of range, abrupt change, and moving average methods.

Our main exposure variables were the percentage of total sleep time spent at Sa_{O_2} less than 90% and the minimum nocturnal Sa_{O_2} listed in polysomnography reports, two parameters indicating the nocturnal oxygenation status of

the patients with OSA. Investigators scrutinized the paper charts of patients with a diagnosis of sleep-disordered breathing and recovered any existing polysomnography reports. When polysomnography details were not included in the medical charts, the investigators contacted the respective sleep laboratories and recovered the full reports. From the polysomnography reports, the total sleep time spent at Sa_{O_2} less than 90%, the minimum nocturnal Sa_{O_2}, and the apnea/hypopnea index (events per hour of sleep) were recorded.

Exposure variables that were of interest because of their confounding potential were identified in our electronic registry and recorded. These included patients age, sex, and race, as well as morphometric characteristics like body height and weight that were used to estimate the body mass index [= (weight in kg)/(height in m)^2]. Important comorbid conditions including smoking status, hypertension, coronary artery disease, and diabetes, as well as the use of antihypertensive medications and continuous positive airway pressure for management of OSA were also determined from electronic or paper medical records. And finally, we also recorded the type of bariatric surgery and various intraoperative variables including surgery duration, anesthetic drug doses/gas concentrations, opioid use, as well as the amount of fluids and the type and doses of vasopressors that were given intraoperatively.

Statistical Analysis

All patients with available information on the examined exposure parameters and outcomes were included in the analysis. We assessed the relationships between nocturnal recurrent hypoxemia (severity measured by the percentage of total sleep time spent at Sa_{O_2} less than 90% and the minimum nocturnal Sa_{O_2}) and intraoperative time-weighted average of MAP (a total of two analyses), each with a multivariable regression model. The time-weighted average of MAP is equal to the sum of the portion of each time interval in-between two adjacent MAP measurements multiplied by the average of the corresponding two MAP measurements and divided by the time interval between the first and the last MAP measurements. We prespecified the following 11 potential confounders including age, sex, race, body mass index, smoking status, diabetes mellitus, hypertension, coronary artery disease, preoperative use of antihypertensive medications, continuous positive airway pressure therapy, and type of bariatric surgery (*i.e.*, laparoscopic gastroenterostomy *vs.* others). All the above potential confounders were considered for inclusion in each model using a backward selection procedure (alpha-to-stay = 0.20). A Bonferroni correction was used to adjust for multiple testing; the significance criterion for each individual analysis was *P* value less than 0.025 (*i.e.*, 0.05/2).

Intraoperative opioids were converted to IV morphine equivalents using published conversion tables.[34] The total amount of anesthetic gas (including isoflurane, desflurane, and sevoflurane) was estimated by multiplying the end-tidal gas concentration by the duration of volatile administration in hours, and then dividing by the corresponding potency (*i.e.*, 1.17 vol % for isoflurane, 1.8 vol % for sevoflurane, and 6.6 vol % for desflurane).

Secondary Analyses. We also evaluated the relationship between percentage of total sleep time spent at Sa_{O_2} less than 90% and minimum nocturnal Sa_{O_2}, and intraoperative use of vasopressor (yes *vs.* no), including ephedrine, epinephrine, and phenylephrine, each using a multivariable logistic regression. Among patients who received vasopressor, we further assessed the relationship between percentage of total sleep time spent at Sa_{O_2} less than 90% and minimum nocturnal Sa_{O_2}, and the total dose of vasopressor, using a multivariable regression model. The dose of ephedrine was converted to phenylephrine using a potency ratio between phenylephrine (μg) and ephedrine (mg) of 125, as suggested previously.[35] Subsequently, the total dose of vasopressor (phenylephrine equivalent) was calculated by adding of the dose of ephedrine and the dose of phenylephrine. Two patients given epinephrine were not included in this analysis. All the above mentioned potential confounders were considered for inclusion in each model through the use of a backward selection procedure (alpha-to-stay = 0.20).

We also conducted four unplanned exploratory analyses focusing on the associations between the percentage of total sleep time spent at Sa_{O_2} less than 90% and minimum nocturnal Sa_{O_2}, and the intraoperative time-weighted average of MAP, separately for the time periods spanning from endotracheal intubation to trocar insertion and from trocar insertion until the end of case, using the same statistical methods as in the primary analysis. A Bonferroni correction was used to adjust for multiple testing; the significance criterion for each individual analysis was thus *P* value less than 0.0125 (*i.e.*, 0.05/4).

The Statistical Analysis Software version 9.3 (SAS Institute, Cary, NC) was used for all analyses.

Results

One thousand six hundred forty-one adult patients had laparoscopic bariatric surgery at the Cleveland Clinic Main Campus between June 6, 2005 and December 30, 2009. Among 335 who had an overnight polysomnography performed, 54 patients with missing minimum nocturnal Sa_{O_2}, percentage of total sleep time at Sa_{O_2} less than 90%, and/or other covariates were excluded from the analyses, yielding a final set of 281 patients (table 1 and fig. 1). More than 71% of our patients had a polysonography study performed within 1 yr preoperatively, and 52% of the tests were done within 6 months before surgery.

After removing artifacts (2% of all measurements), the median of number of MAP measurements between endotracheal intubation and end of the case was 59 [Q1, Q3: 47, 91]. The observed mean (SD) of the intraoperative time-weighted average of MAP was 89 (11) mmHg. The observed median of percentage of total sleep time spent at Sa_{O_2} less than 90% was 8.1% [1.4, 26.9] and median of minimum

Table 1. Morphometrics, Polysomnography Variables, and Clinical Characteristics (N = 281*)

Variable	Summary Statistics
Age (yr)	47 ± 11
Sex (female), No. (%)	201 (72)
Race, No. (%)	
Caucasian	216 (77)
African American	57 (20)
Others	8 (3)
Body mass index (kg/m^2)	46 [42, 52]
Polysomnography parameters	
Time spent at Sa_{O_2} <90% (% of total sleep time)	8.1 [1.4, 26.9]
Minimum nocturnal Sa_{O_2} (%)	82 [74, 86]
AHI	
AHI < 5	38 (14)
5 ≤ AHI < 15	68 (24)
15 ≤ AHI < 30	64 (23)
AHI ≥ 30	108 (39)
Smoking status (smokers), No. (%)	141 (50)
Diabetes, No. (%)	97 (35)
Hypertension, No. (%)	175 (70)
Coronary artery disease, No. (%)	26 (9)
Antihypertensive medication, No. (%)	67 (24)
Continuous positive airway pressure therapy, No. (%)	178 (63)
Intraoperative	
Type of gastric surgery, No. %	
Gastroenterostomy	225 (80)
Gastric restrictive procedure	51 (18)
Gastroplasty	3 (1)
Removal of gastric restrictive device	1 (<1)
Duration of surgery (hours)	4.2 [3.7, 4.9]
From ET intubation to trocar insertion (hours)	0.5 ± 0.1
From trocar insertion to end of case (hours)	3.5 ± 1.1
TWA of MAP during surgery (mmHg)	89 ± 11
From ET intubation to trocar insertion (mmHg)	79 ± 12
From trocar insertion to end of case (mmHg)	90 ± 12
TWA of heart rate during surgery (beats/min)	76 ± 10
From ET intubation to trocar insertion (beats/min)	76 ± 13
From trocar insertion to end of case (beats/min)	76 ± 10
Antihypertensive medications, No. (%)	76 (31)
Usage of vasopressors, No. (%)	153 (54)
Usage of ephedrine, No. (%)	97 (63)
Ephedrine (mg)	10 [10, 20]
Usage of epinephrine, No. (%)	2 (1)
Epinephrine (mg)	0.01 [0.01, 0.01]
Usage of phenylephrine, No. (%)	109 (71)
Phenylephrine (μg)	200 [100, 400]
Amount of anesthetic gas (MAC hours)	2.8 [2.1, 3.4]
Propofol at induction (mg)	200 [200, 250]
Opioids (IV morphine equivalent) (mg)	30 [25, 40]
Crystalloids (l)	3.0 ± 0.9
Colloids (l)	0.5 ± 0.4

* Out of 335 patients who had nocturnal polysomnography, 54 patients with missing total time Sa_{O_2} <90% and/or other covariates were excluded from the analyses. One patient had missing amount of anesthetic gas; three patients had missing AHI value. Statistics are reported as mean ± SD, median [1st, 3rd quartile], or No. (%).

AHI = apnea/hypopnea index; ET = endotracheal; MAC = minimum alveolar concentration; MAP = mean arterial pressure; Sa_{O_2} = oxyhemoglobin saturation; TWA = time-weighted average.

nocturnal Sa_{O_2} was 82% [74, 86]. The unadjusted associations are displayed in figure 2.

We found that neither percentage of total sleep time spent at Sa_{O_2} less than 90% (P = 0.50) nor minimum nocturnal Sa_{O_2} (P = 0.04 > Bonferroni-corrected significance criterion of 0.025) was associated with intraoperative time-weighted average of MAP (table 2). The estimated average change in time-weighted average of MAP was −0.02 (97.5% CI, −0.08 to 0.04) mmHg for each 1% absolute increase in the percentage of total sleep time spent at Sa_{O_2} less than 90%, after adjusting for smoking and coronary artery disease (retained *via* the model selection procedure). The estimated average change was −0.13 (97.5% CI, −0.27 to 0.01) mmHg, for each 1% absolute decrease in the minimum nocturnal Sa_{O_2}, after adjusting for smoking and coronary artery disease. For example, in a minimum nocturnal Sa_{O_2} reduction from 92 to 74%, the time-weighted average of MAP would decrease 2.3 mmHg (−2.3 [97.5% CI, −4.8 to 0.1]).

Secondary Analyses

One hundred fifty-three (54%) patients were given vasopressor intraoperatively. Receiving vasopressor was not significantly associated with either percentage of total sleep time spent at Sa_{O_2} less than 90% (P = 0.86) or minimum nocturnal Sa_{O_2} (P = 0.39). The estimated odds ratio of receiving vasopressor was 1.00 (97.5% CI, 0.99 to 1.01) for each 1% absolute increase in percentage of total sleep time spent at Sa_{O_2} less than 90% and 1.01 (0.98 to 1.04) for each 1% absolute decrease in minimum nocturnal Sa_{O_2}. Age, body mass index, smoking, coronary artery disease, hypertension, and type of bariatric surgery were adjusted for in both analyses.

Among the 154 patients given vasopressor, 97 received ephedrine with median dose of 10 [10, 20] mg; two patients were given epinephrine; and 109 patients received phenylephrine with a median dose of 200 [100, 400] μg. The estimated total dose of vasopressor in phenylephrine equivalents was 1,250 [400, 2,050] μg. The estimated average change in the total dose of vasopressor was −3 (97.5% CI, −14 to 8) μg for each 1% absolute increase in the percentage of total sleep time spent at Sa_{O_2} less than 90% (P = 0.59), after adjusting for age, sex, and preoperative use of antihypertensive medications. The estimated change in the dose was 9 (−16, 34) μg for each 1% absolute decrease in the minimum nocturnal Sa_{O_2} (P = 0.41), after adjusting for age, sex, smoking, diabetes, and preoperative use of antihypertensive medications.

Exploratory Analyses

The median number of MAP measurements between endotracheal intubation and trocar insertion was 9 [6, 13], while between trocar insertion and end of case was 48 [37, 77]. Consistently with our primary analysis, we found that neither the percentage of total sleep time spent at Sa_{O_2} less than 90% nor the minimum nocturnal Sa_{O_2}, was associated with time-weighted average of MAP, during the period spanned from trocar insertion to end of case. However, the lower minimum

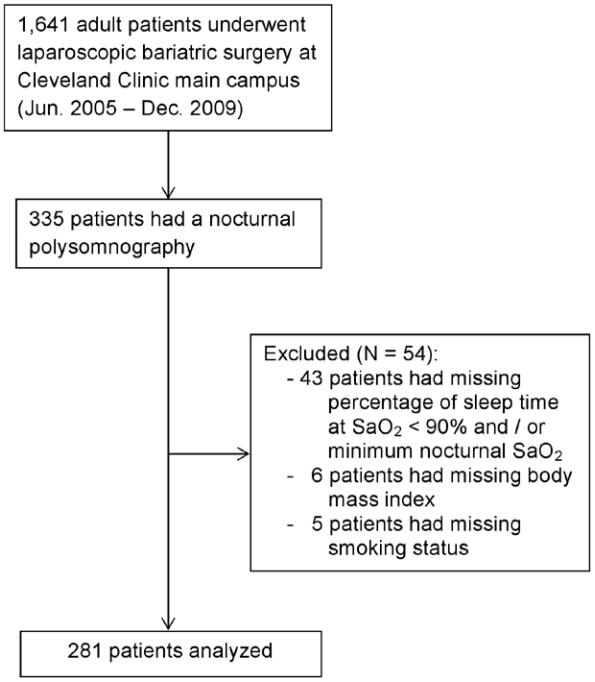

Fig. 1. Flow diagram for the selection of eligible patients. Sao_2 = oxyhemoglobin saturation.

nocturnal Sao_2 in the preoperative polysomnography was significantly associated with lower time-weighted average of MAP during the time period spanned from endotracheal intubation to trocar insertion ($P = 0.002$; table 2).

Discussion

After adjusting for prespecified potential confounders, intermittent nocturnal hypoxia (measured by the percentage of total sleep time spent at Sao_2 less than 90% and the minimum nocturnal Sao_2) was not significantly associated with intraoperative MAP during laparoscopic bariatric surgery in patients suffering from OSA.

Selection of chronic intermittent hypoxia indices as an explanatory variable for intraoperative hypotension was based on *a priori* information linking intermittent hypoxia to cardiovascular morbidity. The original clinical trials establishing the relationship between OSA, sympathetic overactivity[13,14,16,18] and cardiovascular morbidity[6,15] were based on the number of apnea/hypopnea events during sleep.[6,13,14,16,18,19] However, more recent research evidence has established recurrent nocturnal hypoxemia[17,20] as the putative causative component. Human[17] and animal[20] experiments show that intermittent hypoxia, through an enhancement of sympathetic adrenergic mechanisms, may reduce the cardiovascular system's ability to adequately compensate for acute hypotensive challenges. Both a depression of baroreceptor sensitivity[17,18] and the reduced vascular reactivity to adrenergic signals[19,20] may amount to the insufficiency of autonomic nervous control in counteracting hypotension during anesthesia.

Overnight preoperative polysomnography showed that approximately 60% of our bariatric patients had moderate-to-severe OSA with an apnea/hypopnea index ≥15 events per hour of sleep, which is consistent with the current epidemiological profile of the disease in the general population.[2] A median percentage of total sleep time spent at Sao_2 less than 90% of 8.1% and a median nocturnal minimum Sao_2 of 82% indicate clinically important hypoxemia, which compares with magnitudes of oxyhemoglobin desaturation in studies establishing OSA as an independent risk factor for stroke (median % of total sleep time at Sao_2 less than 90%: 0.4 *vs.* 0.1, with and without ischemic stroke)[36]; cardiovascular disease (hypopneas with a 4% or more decrease in Sao_2 were predictive *vs.* those with less 4%)[11]; atrial fibrillation (each 1% absolute decrease in the mean nocturnal Sao_2 tripled the risk for atrial fibrillation)[37]; insulin resistance (average nocturnal Sao_2 less than 94% and more than 2.2% of total sleep time at Sao_2 less than 90% predicted insulin resistance)[38]; and sleep-related pain (a decrease in the minimum nocturnal Sao_2 from 92 to 75% approximately doubled the odds for reporting pain).[39]

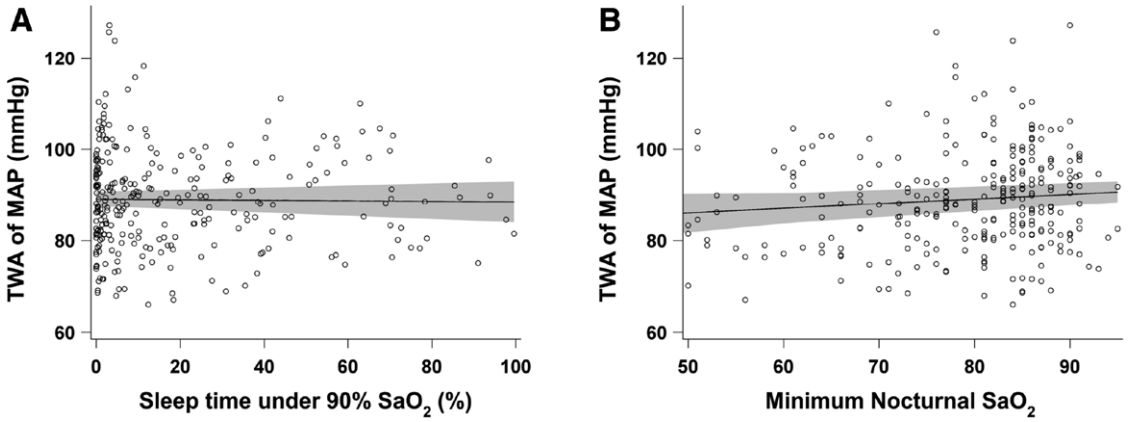

Fig. 2. Scatter plots presenting the unadjusted associations between the time-weighted average (TWA) of mean arterial pressure (MAP) during surgery, and the percentage of total sleep time spent at Sao_2 <90% (*A*) and minimum nocturnal Sao_2 (*B*), for the 281 patients included in the analysis. The *solid lines* are the fit regression lines; and the *shaded regions* are the 95% confidence bands. Sao_2 = oxyhemoglobin saturation.

Table 2. Association between Time-weighted Average of MAP and Percentage of Total Sleep Time Spent at Sa_{O_2} <90% and Minimum Nocturnal Sa_{O_2} (N = 281)

Exposure Variable	Estimated of Slope* (97.5% CI)†	*P* Value†
Primary analysis—intraoperative TWA of MAP		
% of TST spent at Sa_{O_2} < 90% (for each 1% absolute increase)	−0.02 (−0.08 to 0.04)	0.50
Minimum nocturnal Sa_{O_2} (for each 1% absolute decrease)	−0.13 (−0.27 to 0.01)	0.04
	Estimated of slope* (98.75% CI)†	*P* Value†
Exploratory analysis 1: TWA of MAP from ET intubation to trocar insertion		
% of TST spent at Sa_{O_2} < 90% (for each 1% absolute increase)	−0.04 (−0.12 to 0.03)	0.14
Minimum nocturnal Sa_{O_2} (for each 1% absolute decrease)	−0.22 (−0.39 to −0.04)	0.002‡
Exploratory analysis 2: TWA of MAP from trocar insertion to end of case		
% of TST spent at Sa_{O_2} < 90% (for each 1% absolute increase)	−0.02 (−0.09 to 0.06)	0.58
Minimum nocturnal Sa_{O_2} (for each 1% absolute decrease)	−0.14 (−0.30 to 0.03)	0.04

* All the prespecified potential confounders were considered for including in each model through the use of a backward selection procedure (alpha-to-stay = 0.20), including age, sex, race, body mass index, smoking status, diabetes mellitus, hypertension, coronary artery disease, preoperative usage of antihypertensive medications, continuous positive airway pressure therapy, and type of bariatric surgery (*i.e.*, laparoscopic gastroenterostomy *vs*. others). Smoking and coronary artery disease were retained in both primary analyses and two analyses for TWA of MAP from surgical incision to end of case. Age, sex, race and type of surgery were adjusted for two analyses for TWA of MAP from endotracheal intubation to surgical incision. † Bonferroni correction: The significance criterion of 0.025 for the two primary analyses and the criterion of 0.0125 for the four exploratory analyses. ‡ Statistically significant.

ET = endotracheal; MAP = mean arterial pressure; Sa_{O_2} = oxyhemoglobin saturation; TST = total sleep time; TWA = time-weighted average.

Intraoperative hypotension, as traditionally defined, is common[24,40] and as we[22,41] and others[42–44] have shown, low intraoperative MAP may increase morbidity and mortality after noncardiac surgery. A recent large-scale analysis of noncardiac surgery patients found that intraoperative MAP less than 55 mmHg for 5 min or less was strongly associated with postoperative acute kidney injury (30% increase) and myocardial injury (50% increase).[22] If OSA patients are prone to develop intraoperative hypotension, they might also be at elevated risk for adverse postoperative outcomes related to their decreased ability to cope with low perfusion insults;[25,26] possibly rendering this patient population vulnerable to postoperative central nervous system[45,46] and cardiovascular[27–29] morbidities.

Our exploratory analyses was based on the possibility that pneumoperitoneum, with its profound cardiovascular effects resulting in hyperdynamic circulation,[47,48] may have obscured the smaller potential effects of nocturnal hypoxia. We observed that the minimum nocturnal Sa_{O_2} in preoperative polysomnography was significantly associated with time-weighted average MAP, during the period spanning from endotracheal intubation to trocar insertion. A minimum nocturnal Sa_{O_2} of 74%, common occurrence among OSA populations, was associated with a reduction in average MAP of approximately 4 mmHg (98.5% CI, 7.0 to 0.7). Although the average effect of nocturnal hypoxemia on intraoperative MAP appears to be small and was restricted to the period between endotracheal intubation and trocar insertion, it is at least consistent with the biological rationale underlying our hypothesis. Large observational cohorts in noncardiac surgery patients have shown that 50% of patients experience at least a minute with MAP 60 mmHg or less, and that 30% experience at least 5 min with MAP 60 mmHg or less.[24] Such hypotensive episodes may thus be aggravated by nocturnal hypoxia, and may place patients at risk.[22,44] However, we urge cautious interpretation of this finding since it was from an unplanned *post hoc* analysis and only barely statistically significant.

As in any retrospective analysis, residual confounding is likely and it is essentially impossible to estimate its magnitude and potential influence on our conclusions. Furthermore, certain factors, like fluid administration and the use of drugs, might be mediating variables that transmit the effect of chronic intermittent hypoxia on the mean intraoperative arterial pressure. However, in our analysis, we did not investigate the possible mediator effects. Finally, although most sleep studies were performed within one year preoperatively, our ability to identify associations between nocturnal hypoxia and intraoperative hypotension may have been degraded by changes in the severity of OSA between the time nocturnal hypoxemia was measured and the actual date of surgery.

In summary, chronic recurrent nocturnal hypoxemia resulting from OSA is not associated with intraoperative hypotension. An exploratory *post hoc* analysis reveals a weak association and a small effect of nocturnal hypoxemia on MAP, only a limited period intraoperatively. The significance and potential clinical implications of this finding remain to be tested.

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Competing Interests

The authors declare no competing interests.

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