ORIGINAL CLINICAL RESEARCH REPORT

Postoperative Critical Events Associated With Obstructive Sleep Apnea: Results From the Society of Anesthesia and Sleep Medicine Obstructive Sleep Apnea Registry

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BACKGROUND: Obstructive sleep apnea (OSA) patients are at increased risk for pulmonary and cardiovascular complications; perioperative mortality risk is unclear. This report analyzes cases submitted to the OSA Death and Near Miss Registry, focusing on factors associated with poor outcomes after an OSA-related event. We hypothesized that more severe outcomes would be associated with OSA severity, less intense monitoring, and higher cumulative opioid doses.

METHODS: Inclusion criteria were age ≥18 years, OSA diagnosed or suspected, event related to OSA, and event occurrence 1992 or later and <30 days postoperatively. Factors associated with death or brain damage versus other critical events were analyzed by tests of association and odds ratios (OR; 95% confidence intervals [CIs]).

RESULTS: Sixty-six cases met inclusion criteria with known OSA diagnosed in 55 (83%). Patients were middle aged (mean = 53, standard deviation [SD] = 15 years), American Society of Anesthesiologists (ASA) III (59%, n = 38), and obese (mean body mass index [BMI] = 38, SD = 9 kg/m^2); most had inpatient (80%, n = 51) and elective (90%, n = 56) procedures with general anesthesia (88%, n = 58). Most events occurred on the ward (56%, n = 37), and 14 (21%) occurred at home. Most events (76%, n = 50) occurred within 24 hours of anesthesia end. Ninety-seven percent (n = 64) received opioids within the 24 hours before the event, and two-thirds (41 of 62) also received sedatives. Positive airway pressure devices and/or supplemental oxygen were in use at the time of critical events in 7.5% and 52% of cases, respectively. Sixty-five percent (n = 43) of patients died or had brain damage; 35% (n = 23) experienced other critical events. Continuous central respiratory monitoring was in use for 3 of 43 (7%) of cases where death or brain damage resulted. Death or brain damage was (1) less common when the event was witnessed than unwitnessed (OR = 0.036; 95% CI, 0.007–0.181; $P < .001$); (2) less common with supplemental oxygen in place (OR = 0.227; 95% CI, 0.070–0.740; $P = .011$); (3) less common with respiratory monitoring versus no monitoring (OR = 0.109; 95% CI, 0.031–0.384; $P < .001$); and (4) more common in patients who received both opioids and sedatives than opioids alone (OR = 4.133; 95% CI, 1.348–12.672; $P = .011$). No evidence for an association was observed between outcomes and OSA severity or cumulative opioid dose.

CONCLUSIONS: Death and brain damage were more likely to occur with unwitnessed events, no supplemental oxygen, lack of respiratory monitoring, and coadministration of opioids and sedatives. It is important that efforts be directed at providing more effective monitoring for OSA patients following surgery, and clinicians consider the potentially dangerous effects of opioids and sedatives—especially when combined—when managing OSA patients postoperatively. (Anesth Analg XXX;XXX:00–00)

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Conflicts of Interest: See Disclosures at the end of the article.

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KEY POINTS

- **Question:** Are worse outcomes following a postoperative obstructive sleep apnea (OSA)–related critical event associated with more severe OSA, less intense monitoring, and higher cumulative dose of opioids?
- **Findings:** Respiratory monitoring, personnel closely observing the patient, and supplemental oxygen were associated with better outcomes, while combinations of opioids plus sedatives were associated with worse outcomes sustained by OSA patients after a critical event.
- **Meaning:** It is important that efforts be directed at providing more effective postoperative monitoring of OSA patients following surgery, and clinicians consider the potentially dangerous effects of opioids combined with sedative agents when managing pain in OSA patients.

GLOSSARY

AHI = apnea–hypopnea index; **ASA** = American Society of Anesthesiologists; **BMI** = body mass index; **BPAP** = bilevel positive airway pressure; **CCP** = Anesthesia Closed Claims Project and its Registries; **CI** = confidence interval; **CONSORT** = Consolidated Standards of Reporting Trials; **COPD** = chronic obstructive pulmonary disease; **CPAP** = continuous positive airway pressure; **ICU** = intensive care unit; **IQR** = interquartile range; **MME** = morphine milligram equivalent; **OR** = odds ratio; **OSA** = obstructive sleep apnea; **OSA Registry** = OSA Death and Near Miss Registry; **PACU** = postanesthesia care unit; **PAP** = positive airway pressure; **SASM** = Society of Anesthesia and Sleep Medicine; **SD** = standard deviation; **Spo_2** = pulse oximetry monitoring; **STOP** = STOP Questionnaire; **STOP-Bang** = STOP-Bang Questionnaire; **STROBE** = Strengthening the Reporting of Observational Studies in Epidemiology

Obstructive sleep apnea (OSA) is a sleep disorder that is estimated to affect 26% of the adult population in the United States (ages 30–70) with 13% of men and 6% of women having OSA of a moderate to severe degree.[1] The majority of patients with clinical OSA are currently undiagnosed.[2] Various studies have found that patients with OSA are at increased risk for pulmonary and cardiovascular complications following surgery.[3–5] Additionally, there have been very concerning reports of unexpected deaths and anoxic brain injuries in patients with OSA receiving opioids in the postoperative period.[6–11]

The Society of Anesthesia and Sleep Medicine (SASM) appointed a committee (The OSA Death and Near Miss Registry Committee) to collate and critically review reports of cases where patients were found "dead in bed" following surgery. With OSA-related critical events at any single institution being relatively rare, it was believed that creating a database of OSA critical events would facilitate a more meaningful root cause analysis of OSA critical events. The SASM committee partnered with the Anesthesia Closed Claims Project and its Registries (CCP)—affiliated with the Anesthesia Quality Institute of the American Society of Anesthesiologists (ASA)—to create an international registry of unexpected critical events occurring in patients with OSA. The goals of this "OSA Death and Near Miss Registry" were to provide a better understanding of why adverse events occurred, identify the level of monitoring in use when deaths or "other critical events" occurred, determine areas where interventions could potentially limit the events, and provide insight regarding how best to construct future studies to elucidate best practices for perioperative care of OSA patients. This report provides a comprehensive analysis of 66 cases submitted to the OSA Death and Near Miss Registry with a focus on factors associated with poor outcomes after an OSA-related event. It was our hypothesis that more severe outcomes would be associated with OSA severity, less intense monitoring, and higher cumulative dose of opioids.

METHODS

This study was approved by the University of Washington Human Subjects Committee (Applications No. 47317 and 43939), which waived the requirement for written informed consent. This article adheres to the Consolidated Standards of Reporting Trials (CONSORT), adhering to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for observational studies.[12] The project was initiated by the SASM Death and Near Miss Registry (OSA Registry) Committee, which developed the case report form. Case report forms were publicly available on the CCP website from 2014 to 2016, and cases were solicited through newsletter articles[13–17] and public presentations. Cases were also collected via the CCP. Full details on case solicitation and other methods are included in Supplemental Digital Content, File 1, http://links.lww.com/AA/D118. Cases were collected without patient, physician, or hospital identifiers. Case submission was permanently closed at the end of 2016.

There were 3 sets of registry case submission criteria related to patients, events, and outcomes. Patient inclusion criteria were age ≥18 years at the time of the

event and diagnosed or screened as high risk of OSA. Inclusion criteria for events were occurrence in 1993 or later, within 30 days of surgery, and deemed to be related to OSA. Outcome inclusion criteria were unanticipated death, brain damage diagnosed by a neurologist, or other critical events (eg, urgent or emergent transfer to an intensive care unit [ICU], respiratory arrest, Code Blue or Advanced Cardiac Life Support protocol) that occurred within 30 days of surgery and were determined to be related to OSA. Cases were required to meet all patient, event, and outcome criteria for inclusion in the registry. There were no exclusion criteria. The current analysis includes events that occurred during recovery from anesthesia, after end of anesthesia care, or later. Events that occurred during emergence from general anesthesia before transfer of the patient to recovery (n = 6) or during sedation or monitored anesthesia care (n = 3) were not included. A copy of the case report packet is included as Supplemental Digital Content, File 2, http://links.lww.com/AA/D118.

Definition of Variables

The primary outcomes were defined before data analysis as (1) death or brain damage versus (2) other critical events (Code Blue, respiratory arrest, urgent transfer to ICU). OSA diagnosis was defined as diagnosis by polysomnogram. High risk of OSA was defined as results from screening tools such as the STOP Questionnaire (STOP), STOP-Bang Questionnaire (STOP-Bang), or Berlin Questionnaire[18,19] or identification as high risk of OSA from patient history. Mild OSA was defined as apnea–hypopnea index (AHI) 5–<15, moderate OSA as AHI 15–30, and severe OSA as AHI >30 events per hour.[20] Comorbidities were grouped as cardiovascular, pulmonary, or other (see Supplemental Digital Content, File 1, http://links.lww.com/AA/D118, for full list of comorbidities). Cardiovascular and pulmonary comorbidities were combined for analysis.

Opioids taken by the patient or administered within 24 hours of the event were calculated in oral morphine milligram equivalents (MMEs).[21–24] For cases with missing data, a range was calculated based on available data, infusion settings, and timing. Total MME for each case was recorded as known values if all opioid administrations were reported and ranges when data were partially unknown. Ranges were converted to estimates using 3 methods: (1) minimum using the lowest estimated MME; (2) maximum using highest estimated MME; and (3) average using the arithmetic mean of estimated MME values.

Nonopioids with the potential to suppress ventilatory drive (referred to as "sedatives") were tabulated by drug class: benzodiazepines, antihistamines, other drugs with sedating properties (ie, nonbenzodiazepine sedatives, pain adjuvants, anticonvulsants, adrenergic drugs, dopamine and serotonin receptor antagonists, and other antinausea drugs), and nonopioid pain medications. Inhalational anesthetics, propofol, and N_2O administered during the procedure were not included. Alcohol and marijuana use were also tabulated. Only drugs within 24 hours of the event were included.

An event was classified as monitored if any intermittent or continuous respiratory monitoring (eg, pulse oximetry, chest impedance, and/or end-tidal carbon dioxide) was reported as in place at the time of the event. The OSA-related event was classified as witnessed if this was explicitly reported on the case report form. In the case of missing data, cases with an outcome of urgent or emergent transfer to an ICU after naloxone administration in the absence of respiratory arrest were classified as witnessed.

OSA Event Contribution Assessment

All cases were adjudicated by 3 of the physician-authors (N.B., F.C., and K.B.D.) for inclusion criteria. Each of these authors independently assessed the contribution of OSA to the event using "more likely than not (>50:50 but close call)" as the criterion for inclusion. Agreement by 2 of the 3 authors was required for classification.

Statistical Analysis

Factors associated with outcomes were compared by χ^2, Fisher exact test (for 2 × 2 tables or larger tables with expected cell counts <5 for 25% or more cells), 2-sample unpaired *t* test, and Mann–Whitney *U* test (for variables with non-normal distributions) with $P < .05$ the criterion for statistical significance. For tables greater than 2 × 2 but expected cell counts of <5 in >25% of cells, Fisher exact test with Monte Carlo significance was calculated based on 10,000 randomly sampled tables. Odds ratios (OR) and their 95% confidence intervals (CIs) were calculated by logistic regression. All statistical analysis used IBM SPSS Statistics 26 (International Business Machines Corporation, Armonk, NY). The sample size was based on available data; no a priori power analysis was conducted.

RESULTS

Seventy-seven case reports were evaluated by the authors. Two cases were not included in the final analysis based on author assessment and 100% agreement that OSA was noncontributory (Figure 1). Nine cases were not included in the analysis because the event occurred before end of anesthesia time, leaving 66 cases with OSA-related postoperative events for analysis (Figure 1). Event dates for the final 66 cases ranged from 1997 to 2016, with 77% (n = 51) reported from 2005 to 2016.

Patient and case characteristics are summarized in Table 1. Most of the procedures were conducted

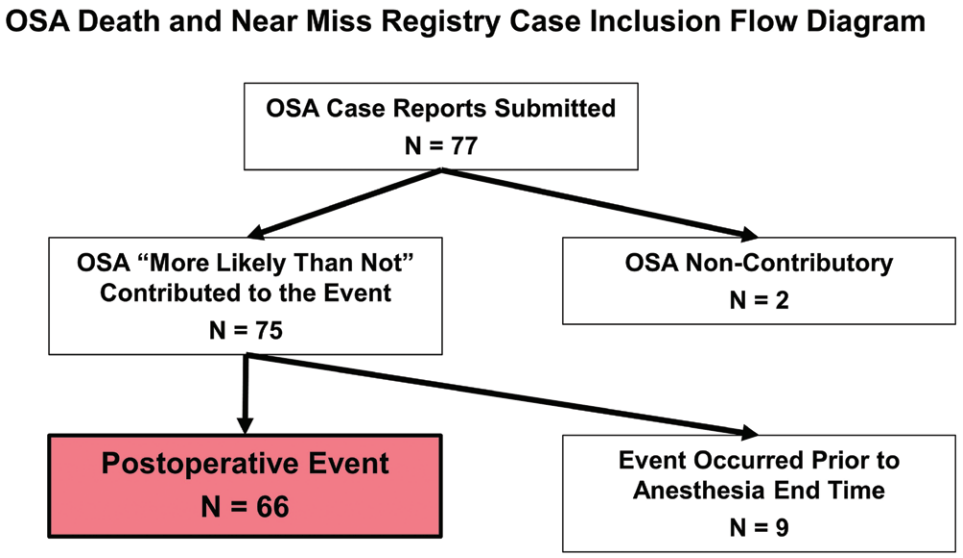

Figure 1. Among the 77 cases submitted to the OSA Death and Near Miss Registry, 66 cases with OSA-related postoperative events were included in the final analysis. OSA indicates obstructive sleep apnea.

under general anesthesia or combined general plus regional anesthesia (94%). Most patients (n = 55, 83%) had a diagnosis of OSA, with the remainder having been screened as high risk for OSA. Of those with a diagnosis, sleep study results were available in 37 patients: 24 met criteria for severe OSA, 6 moderate OSA, and 7 mild OSA (Table 1). Continuous positive airway pressure (CPAP) had been prescribed for 37 patients with 15 using it as prescribed most of the time, 2 sometimes, 9 rarely or not at all, and 11 unknown (Supplemental Digital Content, File 3, Table 1, http://links.lww.com/AA/D118). Only one patient had been prescribed bilevel positive airway pressure (BPAP, usage unknown). Two patients had home oxygen therapy prescribed; no patients had been prescribed oral appliance devices.

Location and timing of events are shown in Figure 2. Fifty-six percent (n = 37) of events occurred on the hospital ward, and 21% (n = 14) occurred at home after discharge. Most events in each location occurred within 24 hours of the end of anesthesia time (Figure 2).

Of the 14 events that occurred at home, half (n = 7, 50%) occurred within 24 hours of procedure end. These patients were ASA physical status III (n = 6) or IV (n = 7). They had all received opioids within 24 hours of the event, with 8 having complete opioid data indicating median MME 64 (interquartile range [IQR] = 18–117). Estimated median MME in 12 of these 14 patients was 60 (IQR = 11–109) minimum, average 60 (standard deviation [SD] = 15–113), and maximum 60 (IQR = 19–117). The event was witnessed in 4 cases, and death or severe brain damage occurred in 12. One of the 2 cases with no injury was witnessed, the other not.

Table 2 shows event details by location. Monitoring differed by location with all patients in the postanesthesia care unit (PACU) and most (88%) in the step-down or ICU being monitored, compared to only 57% on the ward and none at home ($P < .001$, Table 2). Monitoring consisted of intermittent or continuous pulse oximetry; there were no reports of chest impedance or end-tidal carbon dioxide monitoring. Nearly all PACU or ICU/step-down unit events were witnessed, with most ward or at-home cases not witnessed ($P = .006$, Table 2).

Half (52%, n = 34) of the patients were receiving supplemental oxygen at the time of the event. Five patients (7.5%) had a positive airway pressure (PAP) device at the time of the event (4 CPAP, 1 BPAP), with 3 of these also receiving supplemental oxygen. Events that occurred in the presence of PAP took place on the ward (n = 4, CPAP) and ICU (n = 1, BPAP). Two patients with PAP but without respiratory monitoring died; the remaining 3 patients with PAP plus respiratory monitoring sustained respiratory arrest but recovered without brain injury.

Ninety-seven percent (n = 64) received opioids within 24 hours before the event; only one received no opioids (1 unknown). The amount of opioids was reported for 36 patients; another 27 had information to estimate a range but not a definitive MME. Among the 36 patients with full opioid data, the amount administered within 24 hours of the event ranged from 0 to 423 MME (median = 122, IQR = 72–191 mg). Adding data from those with estimated MME, the amount was similar using the minimum estimate (median = 126, IQR = 66–198 mg) and slightly higher using the average estimate (median = 135, IQR = 86–218) or the maximum estimate (median = 147, IQR = 90–218 mg).

Sedative medications were coadministered with opioids in 41 patients (62%). One patient used marijuana (plus a benzodiazepine not provided as a discharge prescription) within 24 hours of the event.

Table 1. Patient and Case Characteristics

Characteristic	Descriptive Statistics
Sex: male	43 (65%)
Age: y: mean (SD) [range]	53 (15) [27–88]
BMI (kg/m^2): mean (SD) [interquartile range]	38 (9) [32–44]
ASA physical status (n = 64)	
I–II	22 (34%)
III	38 (59%)
IV	4 (6%)
OSA severity (n = 37)	
Mild	7 (19%)
Moderate	6 (16%)
Severe	24 (65%)
Comorbidities: any cardiovascular	34 (52%)
Hypertension	25 (38%)
Coronary artery disease	15 (23%)
Congestive heart failure	3 (5%)
Other cardiovascular disease	5 (8%)
Any pulmonary	17 (26%)
COPD/asthma	14 (21%)
Airway disease	2 (3%)
Current smoker	1 (2%)
Other severe pulmonary disease	2 (3%)
Other comorbidities	
Diabetes mellitus	21 (32%)
Renal disease	6 (9%)
Cerebrovascular disease	4 (6%)
Peripheral vascular disease	4 (6%)
Substance abuse[a]	3 (5%)
Anesthetic technique	
General anesthesia	58 (88%)
General plus regional anesthesia	4 (6%)
Sedation or monitored anesthesia care	4 (6%)
Schedule type	
Elective (n = 62)	56 (90%)
Inpatient (n = 64)	51 (80%)
Surgical procedure	
General surgery	19 (29%)
Orthopedic	16 (24%)
Ear, nose, throat	8 (12%)
Gynecologic	5 (8%)
Urology	5 (8%)
Spine	4 (6%)
Thoracic	3 (5%)
Endoscopy	2 (3%)
Interventional radiology	2 (3%)
Dental extractions	1 (2%)
Unknown	1 (2%)

Descriptive statistics = number and column % unless otherwise stated. Statistics based on n = 66 cases unless otherwise indicated. Cases with missing data excluded from calculation of statistics. Percentages may sum to >100% or <100% due to rounding. Listed pulmonary and cardiovascular comorbidities may sum to larger than total due to multiple comorbidities in some cases. Other comorbidity total not tabulated; only comorbidities with frequency of ≥3 listed.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; SD, standard deviation.

[a]Alcohol, marijuana, and prescription narcotics (1 case each).

Outcomes

Sixty-five percent (43 of 66) of patients died or had brain damage; the remaining 35% (23 of 66) experienced other critical events. Tables 3 and 4 and Supplemental Digital Content, File 3: Table 2, http://links.lww.com/AA/D118, show associations between patient and case factors with outcomes. Outcomes were associated with whether the event was witnessed or not, supplemental oxygen use, and respiratory monitoring. Death or brain damage was less common when the event was witnessed (37%, OR = 0.036; 95% CI, 0.007–0.181) than not witnessed (94%, $P < .001$, Table 3). Death or brain damage was less common when patients were receiving supplemental oxygen (OR = 0.227; 95% CI, 0.070–0.740) than when not ($P = .011$, Table 4). Death or brain damage was also less common in patients with respiratory monitoring (OR = 0.109; 95% CI, 0.031–0.384; $P < .001$; Table 4). Among 43 cases with death or brain damage, there were 14 cases with respiratory monitoring in place at the time of the event; 3 (7%) had continuous central monitoring (Table 4). Two patients wearing PAP on the wards (unwitnessed) suffered death/brain damage.

There was no evidence for an association between the outcome and sex, age, body mass index (BMI), ASA physical status, OSA diagnosed versus suspected, presence of cardiovascular or pulmonary comorbidities, or hours between anesthesia end and the event (Supplemental Digital Content, File 3: Table 2, http://links.lww.com/AA/D118). Among the 37 patients with known severity of OSA, there was no evidence for an association between severity of OSA and outcome (Table 3).

Death or brain damage was more common in patients receiving sedatives in addition to opioids compared to patients receiving opioids without sedatives (OR = 4.133; 95% CI, 1.348–12.672; $P = .011$; Table 4). Among 41 patients receiving sedatives in addition to opioids, 31 (76%) died or had brain damage; death or brain damage occurred in only 9 (43%) of 21 patients who received opioids only. There was no evidence for an association between MME and outcome (Table 4).

DISCUSSION

There are several important observations from our analysis of the OSA Registry's postoperative critical events. The majority of events occurred within the first 24 postoperative hours. Inadequate respiratory monitoring, no supplemental oxygen, lack of personnel closely observing the patient, and coadministration of sedatives and opioids were all associated with worse outcomes.

Our observation that the majority of events occurred within the first 24 hours is consistent with previous studies.[8,25,26] Some OSA protocols include additional monitoring for the first 24 hours postoperatively, with extension if concerning events were observed during this period.[7,27]

Better outcomes were associated with higher levels of monitoring and whether the event was witnessed. Clinically, these factors are related. Patients identified as high risk are routinely triaged to areas

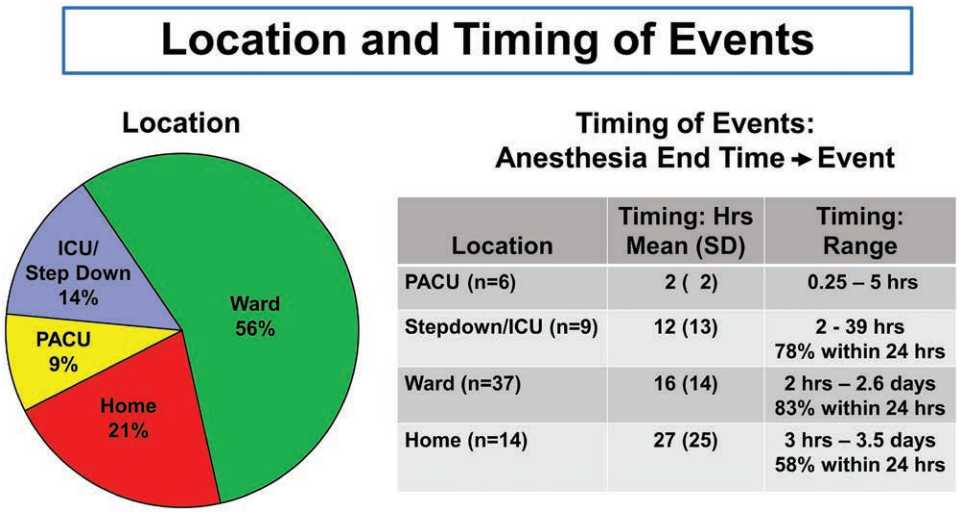

Figure 2. Greater than half of the events occurred on the ward. Most events occurred within 24 h of anesthesia end time. Cases with missing data on exact time of event (n = 3: n = 1 ward and n = 2 home events) were excluded from timing statistics. ICU indicates intensive care unit; PACU, postanesthesia recovery unit; SD, standard deviation.

Table 2. Event Details by Location

	All Cases N = 66	PACU N = 6	Step Down/ICU N = 9	Ward N = 37	Home N = 14	*P* Value
Respiratory monitoring in place? (n = 64)						<.001
Yes	33 (52%)	5 (100%)	7 (88%)	21 (57%)	0 (0%)	
No	31 (48%)	0 (0%)	1 (13%)	16 (43%)	14 (100%)	
Type of monitoring (n = 64)						<.001
None	31 (48%)	0 (0%)	1 (13%)	16 (43%)	14 (100%)	
Intermittent (spot) Spo_2	13 (20%)	0 (0%)	0 (0%)	13 (35%)	0 (0%)	
Continuous Spo_2—no central monitoring	9 (14%)	2 (40%)	1 (13%)	6 (16%)	0 (0%)	
Continuous Spo_2 with central monitoring	11 (17%)	3 (60%)	6 (75%)	2 (5%)	0 (0%)	
Event witnessed (n = 64)						.016
Yes	30 (47%)	5 (83%)	6 (86%)	15 (41%)	4 (29%)	
No	34 (53%)	1 (17%)	1 (14%)	22 (59%)	10 (71%)	

N = 66 cases unless otherwise specified. Percentages are based on column totals; cases with missing data excluded. Percentages may sum to <100% or > 100% due to rounding. Respiratory monitoring included intermittent pulse oximetry, continuous pulse oximetry with or without central monitoring, and continuous pulse oximetry with central monitoring. No cases reported chest impedance or end-tidal carbon dioxide monitoring. *P* value by Fishers exact test with Monte Carlo significance based on 10,000 randomly sampled tables. *P* values are reported to 3 decimals; *P* values <.001 are reported as *P* <.001.

Abbreviations: ICU, intensive care unit; PACU, postanesthesia care unit/recovery room; Spo_2, pulse oximetry monitoring.

Table 3. Association Between Patient and Case Factors With Outcomes

	Death or Brain Damage (N = 43) n (row %)	Other Critical Events (N = 23) n (row %)	Odds Ratio (95% CI)	*P* Value
OSA severity (n = 37)				.259[a]
Mild	3 (43)	4 (57)	Reference	
Moderate	4 (67)	2 (33)	2.667 (0.277–25.636)	
Severe	18 (75)	6 (25)	4.000 (0.689–23.229)	
Event location				.060[a]
Ward (n = 37)	25 (68)	12 (32)	Reference	
PACU (n = 6)	3 (50)	3 (50)	0.480 (0.084–2.740)	
Step down or ICU (n = 9)	3 (33)	6 (67)	0.240 (0.051–1.128)	
Home (n = 14)	12 (86)	2 (14)	2.880 (0.554–14.960)	
Event witnessed				<.001
Witnessed (n = 30)	11 (37)	19 (63)	0.036 (0.007–0.181)	
Not witnessed (n = 34)	32 (94)	2 (6)	Reference	

N = 66 unless otherwise specified. Percentages based on row totals. Cases with missing data excluded. Odds ratio for death or brain damage compared to other critical events (reference). Mild OSA: apnea–hypopnea index, 5–<15; moderate–severe: apnea–hypopnea index ≥15.

Abbreviations: CI, confidence interval; ICU, intensive care unit; OSA, obstructive sleep apnea; PACU, post anesthesia care unit/recovery room.

[a]Fisher exact test with Monte Carlo significance due to cells with <5 expected counts; all other tests of differences in proportions by χ^2 test. *P* values are reported to 3 decimals; *P* values <.001 are reported as *P* <.001.

of the hospital with advanced monitoring and higher nurse to patient ratios, allowing earlier detection of, and intervention for, clinical deterioration. Subramani et al[8] also found that the level of monitoring was a risk factor for death/near-death events. Taenzer et al[28] demonstrated that continuous pulse oximetry for hospitalized patients receiving opioids decreased adverse events. Effective monitoring strategies should

Table 4. Association Between Supplemental Oxygen, Monitoring, Opioid Dose, and Opioids With or Without Sedatives With Outcomes

	Death or Brain Damage (N = 43) n (row %)	Other Critical Events (N = 23) n (row %)	Odds Ratio (95% CI)	*P* Value
Supplemental oxygen (n = 61)				.011
Yes (n = 34)	17 (50)	17 (50)	0.227 (0.070–0.740)	
No (n = 27)	22 (81)	5 (19)	Reference	
Any respiratory monitoring in place (n = 64)				<.001
Yes (n = 33)	14 (42)	19 (58)	0.109 (0.031–0.384)	
No (n = 31)	27 (87)	4 (13)	Reference	
Type of respiratory monitoring (n = 64)				<.001[a]
None (n = 31)	27 (87)	4 (13)	Reference	
Intermittent (spot) Spo_2 (n = 13)	4 (31)	9 (69)	0.066 (0.014–0.319)	
Continuous Spo_2—no central monitoring (n = 9)	7 (78)	2 (22)	0.519 (0.078–3.432)	
Continuous Spo_2 with central monitoring (n = 11)	3 (27)	8 (73)	0.056 (0.010–0.302)	
Opioids versus opioids + sedatives (n = 62)				.011
Opioids + sedatives (n = 41)	31 (76)	10 (24)	4.133 (1.348–12.672)	
Opioids only (n = 21)	9 (43)	12 (57)	Reference	
MME Within 24 h of Event	**Median (IQR)**	**Median (IQR)**	**Odds Ratio (95% CI)[b]**	***P* Value[c]**
MME (n = 36)	120 (60–190)	145 (86–272)	0.965 (0.906–1.029)	.548
MME minimum (n = 63)	120 (60–195)	146 (87–272)	0.967 (0.924–1.013)	.231
MME average (n = 63)	126 (68–198)	149 (95–276)	0.965 (0.920–1.011)	.175
MME maximum (n = 63)	134 (90–198)	150 (95–327)	0.971 (0.931–1.013)	.341

N = 66 unless otherwise specified. Percentages based on row totals. Cases with missing data excluded. Odds ratio for death or brain damage compared to other critical events (reference). Respiratory monitoring included intermittent pulse oximetry, continuous pulse oximetry with or without central monitoring, and continuous pulse oximetry with central monitoring. Sedatives: nonopioids with potential to suppress ventilatory drive included benzodiazepines, antihistamines, other drugs with sedating properties (including nonbenzodiazepine sedatives, pain adjuvants, anticonvulsants, adrenergic drugs, dopamine and serotonin receptor antagonists, and other antinausea drugs), and nonopioid pain medications. MME for each case was recorded as known values if all opioid administrations were reported. For cases with some MME data missing, MME minimum was estimated using the lowest estimated MME based on the available data. Maximum estimates used the maximum MME that might have been administered based on device settings or orders. Average took the arithmetic mean between minimum and maximum estimates. More details on MME calculations are given Methods. *P* values are reported to 3 decimals; *P* values <.001 are reported as *P* <.001.

Abbreviations: CI, confidence interval; IQR, interquartile range; MME, morphine milligram equivalent; Spo_2, pulse oximetry monitoring.

[a]Fisher exact test with Monte Carlo significance due to cells with <5 expected counts; all other tests of differences in proportions by χ^2 test.

[b]Per 10 MME.

[c]*P* values by Mann–Whitney *U* test.

be explored for OSA surgical patients to reduce these catastrophic events.

While the most common location for OSA-related events was the hospital ward, it is striking that 21% occurred at home. With the trend toward ambulatory rather than inpatient surgery,[29,30] OSA patients will increasingly have ambulatory surgery and potentially be at risk for catastrophic outcomes after discharge. Our data should stimulate reassessment of discharge criteria for OSA patients and research to identify OSA patients most at risk for adverse events. Protocols should be explored where high-risk OSA patients can be monitored post discharge with home monitoring systems to improve their safety.

Five patients were wearing PAP devices at the time of their critical event, with 2 deaths and 3 other critical events. The 2 patients who died had unwitnessed events while on the ward without monitoring. We had insufficient data to explore preoperative PAP compliance and outcomes. PAP devices can improve postoperative oxygenation and mitigate opioid-induced worsening of OSA.[31] Despite use of CPAP, patients may still experience postoperative hypoxic events. Preoperative CPAP settings may be insufficient to overcome postoperative physiological cardiorespiratory changes.[32] Our data highlight the fact that PAP devices are not 100% protective, and OSA patients on PAP therapy postoperatively may still require careful monitoring.

Death and brain damage were more likely to occur with no supplemental oxygen in our series. Chan et al[3] found that OSA patients with postoperative cardiovascular events had longer duration of severe oxygen desaturation. Given that 52% of patients in our series had supplemental oxygen at the time of their critical event, oxygen therapy should not be considered completely protective against catastrophic outcomes. While there may be concern that supplemental oxygen could be detrimental due to alarm delays, we did not collect data on alarm settings or response times so we cannot address that concern with these data.

We found no statistically significant association between severity of OSA and outcome. This negative finding may be due to the small sample size and must not be interpreted as evidence for the lack of an association. Two large studies demonstrated that patients with severe OSA had higher risk for postoperative adverse outcomes. Chan et al[3] found an association between higher risk for postoperative cardiovascular events and OSA among patients with severe OSA. Mutter et al[33] found that patients with severe or undiagnosed OSA had significantly increased risk of respiratory and cardiovascular complications, respectively.

The coadministration of opioids and sedatives was associated with worse outcomes. Medications with sedative properties potentiate opioid-induced respiratory depression. Receiving both classes of

medications has been shown to increase risk of cardiopulmonary and respiratory arrests in hospitalized patients.[34] Based on the propensity for antihistamines to cause sedation and reports of ventilatory depression with their use,[35–37] we included antihistamines among the sedatives in our study with potential to suppress ventilatory drive. However, previous studies in young healthy volunteers found that diphenhydramine stimulated ventilatory drive.[38,39] It is plausible that the effect may depend on patient disease such as OSA and drug levels, which may be unpredictable in the postoperative setting.

We did not find an association between MME and outcome, though others have.[6,8,26] Our findings should be interpreted with caution given the small sample size and estimated MME. A recent meta-analysis on opioid-induced respiratory depression found 40% higher risk in OSA versus non-OSA patients.[6] Subramani et al[8] reported a clear dose–response pattern on death/near-death with increasing opioid doses. While Rowsell et al[40] did not find 40 mg oral controlled-release morphine worsened OSA, this dose is low compared to doses often used postoperatively. The complex combination of interindividual variability to opioid sensitivity,[40] coupled with differences in OSA endotypes and phenotypes, may contribute to critical complications.[41]

Continuous respiratory central monitoring was in use for 3 of 43 (7%) of cases with death or brain damage. Improved monitoring solutions could impact outcomes of OSA-related critical events but may not be completely protective, underscoring the importance of optimal preparation and management. Some have recommended nonopioid anesthesia/analgesia and multimodal pain management to prevent or reduce opioid-induced adverse events.[42,43] Preoperative identification of OSA, optimization before surgery, and careful perioperative management were highlighted in SASM perioperative OSA management guidelines to limit adverse perioperative outcomes in OSA patients.[44,45] These recommendations warrant attention.

Limitations of this analysis include opportunity sampling, voluntary case submission, and missing OSA severity and other data. Incomplete opioid data were addressed by estimation. There are no laboratory tests or autopsy findings that allow confirmation that critical events were related to OSA. The assessment of whether OSA "more likely than not" contributed to the event was subjective and based on information in the case report and not original medical records. However, there was a high level of agreement between the authors. The various clinical factors associated with poor outcomes overlap clinically, rendering it difficult to assess their relative contributions within the small and potentially biased sample. Confounding limits our conclusions. The associations identified between individual clinical factors and outcomes are suggestive, not conclusive evidence, with potentially inflated type 1 error. Despite these limitations, the data were sufficient to suggest important lessons.

In conclusion, the OSA Death and Near Miss Registry found that OSA patients are at risk for postoperative critical events, most within the first 24 hours. Death and brain damage were more likely to occur with unwitnessed events, no supplemental oxygen, lack of respiratory monitoring, and combination of opioids plus sedative agents. Postoperative PAP use, supplemental oxygen, and central respiratory monitoring were not completely protective against catastrophic events. It is important that efforts be directed at providing more effective monitoring for OSA patients following surgery, and clinicians consider the potentially dangerous effects of coadministration of opioids with sedative agents when managing pain in OSA patients. ■

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