The Laryngoscope

Total Intravenous Anesthesia Versus Inhaled Sevoflurane in Obstructive Sleep Apnea Surgery: A Randomized Controlled Trial

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Objective: Specific guidelines regarding an optimal general anesthesia (GA) approach to obstructive sleep apnea (OSA) patients remain undefined. Literature comparing the efficacy of total intravenous anesthesia (TIVA) and inhalational anesthesia in this population is sparse. We hypothesize that OSA patients receiving TIVA will experience reduced recovery times and other improved post-surgical outcomes.

Study Design: Randomized controlled trial.

Methods: Adult OSA patients undergoing upper airway surgery (hypoglossal nerve stimulation [HNS], nasal, or palate surgery) from February 2020–December 2020 were included. A post-anesthesia care unit (PACU) nursing survey documented patients' alertness, pain, oxygen supplementation, and postoperative nausea and vomiting from PACU arrival to 2 hours. Perioperative timepoints from the electronic medical record (EMR) and a nurse-estimated Phase I recovery time were collected.

Results: One hundred eleven patients were included (46 TIVA and 65 inhalational anesthesia). Per EMR-recorded timepoints, TIVA patients undergoing HNS and palate surgery experienced Phase I Time reductions of 12.5 min ($p = 0.042$) and 27.5 min ($p = 0.016$), respectively. Per the PACU survey, TIVA patients undergoing any surgery, HNS, or palate surgery experienced nurse-estimated Phase I Time reductions of 16.5 min ($p = 0.004$), 12.5 min ($p = 0.031$), and 38.5 min ($p = 0.024$), respectively. Overall, TIVA patients experienced higher alertness and pain ratings, and lower oxygen supplementation requirements from PACU arrival to 30 min ($p < 0.05$).

Conclusion: Patients with OSA receiving TIVA for GA maintenance during upper airway procedures experienced reduced recovery times and oxygen supplementation requirements, and a more rapid return to alertness. Future work toward developing optimized anesthetic guidelines for OSA patients is merited.

Key Words: inhalational anesthesia, hypoglossal nerve stimulation, obstructive sleep apnea, recovery time, total intravenous anesthesia.

Level of Evidence: 3

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INTRODUCTION

Obstructive sleep apnea (OSA) is a condition of sleep-disordered breathing that involves nighttime airway collapse leading to complete (apnea) or partial (hypopnea) disruptions of airflow. Patients with OSA experience an increased risk of stroke, cardiac arrhythmias, metabolic dysregulation, cognitive dysfunction, and depression.[1] Therefore, OSA represents a significant contribution to medical morbidity and mortality. The prevalence of OSA in the United States continues to increase, with greater than 26% of men and 8% of women aged 30–49 years, and greater than 43% of men and 27% of women aged 50–70 years exhibiting the disease.[2] Continuous positive airway pressure (CPAP) remains the first-line treatment of OSA, however, despite its known efficacy, adherence is challenging for many patients.[3] Upper airway surgery and hypoglossal nerve stimulation (HNS) are effective alternative options to improve airway patency in the setting of CPAP intolerance.[4] OSA represents a complicating perioperative factor for surgeons, anesthesiologists, and recovery teams providing surgical care. Specific guidelines for perioperative management of OSA patients are greatly important, yet are limited.[5] Regarding intraoperative management, an optimal general anesthesia (GA) approach to OSA patients is poorly defined.[6] Two commonly utilized GA approaches include total intravenous anesthesia (TIVA) often involving propofol paired with opioid analgesics (e.g., remifentanil) and inhalational anesthesia with volatile fluorinated agents (e.g., sevoflurane, desflurane). Comparatively, inhalational regimens have been cited as more frequently administered. Tolerability, however, is generally considered to be better with TIVA in adult patients with adequate intravenous access.[7] Of note, previous studies have

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suggested that TIVA regimens are more costly when compared with inhaled anesthetics, which is an important factor to consider.[8] Several advantages of TIVA administration in the general population have been proposed including increased patient satisfaction, and reduced emergence agitation, postoperative pain and nausea, and duration in hospital facilities.[9–11] Further, our group has retrospectively shown that OSA patients undergoing upper airway surgery experience reduced postoperative recovery time following TIVA compared to inhaled sevoflurane.[12] We believe that, to date, no prospective randomized controlled trial has examined time of recovery care or other outcome metrics for surgical OSA patients dependent on the GA regimen received. Based on surgical literature and our prior findings, we hypothesize that the perioperative advantage of reduced recovery time for OSA patients receiving TIVA will be redemonstrated in a single-center prospective controlled trial. In addition, the present study will assess outcome metrics based on anesthetics received including surgical or anesthetic complications, as well as recovery room alertness, pain levels, pain medication requirements, supplemental oxygen requirements, and postoperative nausea and vomiting (PONV).

METHODS

Patient Inclusion and Data Collection

This study was approved by the Thomas Jefferson University Hospital Institutional Review Board. A prospective randomized controlled trial of patients undergoing OSA surgery by board-certified sleep medicine surgeons (certified in Otolaryngology & Sleep Medicine) and anesthesiologists at a single tertiary care center from February 2020 to December 2020 was conducted. Patients with diagnosed OSA receiving nasal, palate, or HNS implantation surgery were included. All surgical cases included in this study were performed at a single surgery center, and all patients were discharged on the day of surgery. Nasal surgery included septoplasty, turbinectomy, open reduction and internal fixation, nasal valve repair, and pyriform aperture reduction. Palate surgery included expansion sphincter pharyngoplasty (ESP) and tonsillectomy. OSA diagnoses were supported by preoperative polysomnography or home sleep study results. Exclusion criteria included a history of adverse effects to anesthesia, chronic pain syndromes, chronic narcotic use, current pregnancy, and mixed GA regimens of TIVA and sevoflurane.

Initially, patients were randomized into anesthesia groups by simple randomization. However, due to institutional policies aimed at decreasing expenses during the COVID-19 pandemic, we were forced to initiate block randomization with sevoflurane until hospital policies permitted TIVA use. Following this point, cases were carried out as part of the TIVA block to achieve approximately equal cohorts. This was performed as a single-blinded study design as the anesthesia team could not be blinded to anesthesia administered.

Data collected, in addition to surgery and anesthesia received, included patient age, race, sex, body mass index (BMI), preoperative apnea-hypopnea index (AHI) or respiratory event index (REI), OSA severity, perioperative timepoints, recovery data, complications, and emergency department presentations or hospital readmissions.

Anesthesia Protocol

All study patients underwent induction of GA with propofol, rocuronium, and fentanyl. Following induction, each patient was intubated endotracheally with subsequent ventilation control. Maintenance of GA in the inhalation cohort was performed using sevoflurane, while the TIVA cohort received remifentanil and propofol via titrated continuous infusion. The following intraoperative medications were utilized when clinically indicated and respective amounts were documented: midazolam, ketorolac, hydromorphone, lidocaine, succinylcholine, neostigmine, ondansetron, dexamethasone. Anesthesia care for patients were provided either directly or through certified registered nurse anesthetist (CRNA) oversight by board-certified attending anesthesiologists. The two anesthesiologists listed as authors of this manuscript, who combined share over 40 years of experience in practice, were responsible for 94 of 111 cases (84.6%). The remaining procedures were carried out by additional anesthesiologists from the department, with study goals and consistency being maintained for all included cases.

Perioperative Timepoints

Phase I of PACU recovery immediately follows surgery, during which patients are monitored for recovery from anesthesia and vital sign stabilization. During Phase II, patients are prepared for discharge and given postoperative instructions. The institution's protocol for progression from Phase I to Phase II involves a modified version of the Aldrete and Post-Anesthesia Discharge Scoring Systems (PADSS).[13] A score of ≥9 is required to move from Phase I to Phase II. The time at which each patient scored a maximum score of 10 (Time to Maximum Aldrete Score) was recorded.

Anesthesia reports within the electronic medical record (EMR) were reviewed for the following perioperative timepoints: induction, surgery start, surgery end, emergence, time in PACU, time out of PACU, time in Phase II, time out of Phase II (discharge). Time intervals were defined as follows: Total anesthesia time (Δ[emergence – induction]), Total surgery time (Δ[surgery end – surgery start]), PACU Phase I (Δ[time out of PACU – time in PACU]), PACU Phase II (Δ[time out of Phase II – time in Phase II]), Total recovery time (Phase I + Phase II times). The corresponding timepoints and time intervals are present in Figure 1.

PACU Survey

We developed a bedside patient assessment survey for PACU nurses to document various recovery metrics including alertness, pain, supplemental oxygen needs, and PONV. Patients were assessed in 15 min increments from PACU arrival to 2 h post-surgery. Alertness was rated on a 4-point scale (A-D): A (awake and alert), B (slightly drowsy, but easily aroused), C (frequently drowsy, but arousable), D (somnolent, minimal response to stimulation). Pain was assessed on a visual analog scale from 0 (lowest pain) to 10 (highest pain), and pain medication was documented if given. Requirement of supplemental oxygen and incidence of PONV in the recovery room were recorded. Oxygen supplementation requirements were determined through close pulse oximetry monitoring performed by PACU nurses. A nurse-estimated PACU Phase I completion time was documented on the survey for subsequent analysis. The PACU survey is displayed in Figure 2.

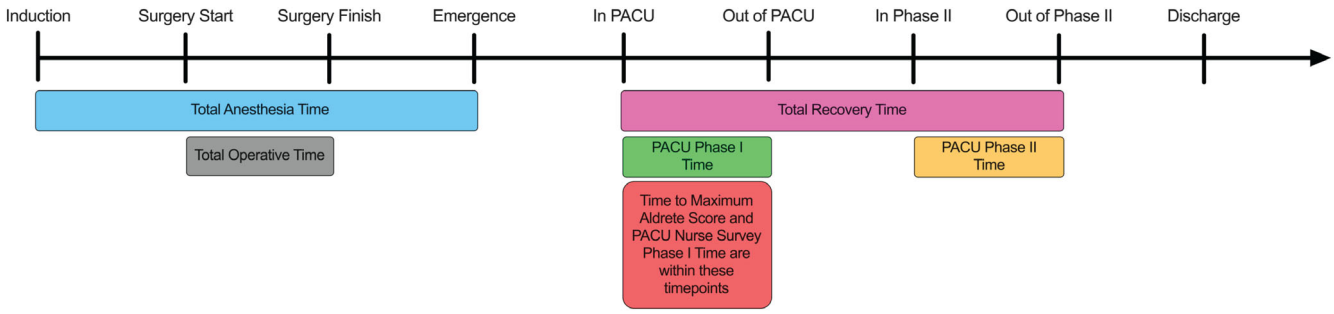

Fig. 1. Day of surgery timepoints and intervals. Time interval box sizes are not drawn to scale. Abbreviations: PACU, Post-Anesthesia Care Unit. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Statistical Analysis

Summary statistics including means, standard deviations and percentages are provided in Table I. Comparisons using two-sample t-tests, Wilcoxon sum rank tests, chi-squared tests and Fisher's exact tests are provided in the remaining tables. Statistical analyses were performed using

RANDOMIZED ANESTHESIA STUDY: PACU ASSESSMENT

	Alertness *(Use A-D, below)*	**Pain 1-10** *(Use VAS, note if requested pain meds)*	**Require supplemental O_2?** *(Include **liters** and whether nasal airway, nasal cannula, face mask, etc)*	**PONV (Y/N)**
Upon receiving patient				
15 min				
30 min				
45 min				
1 hr				
1 hr 15 min				
1 hr 30 min				
1 hr 45 min				
2 hr				

Time RN thinks the patient is ready for discharge to Phase II: _____

*Note, this is when **the nurse** thinks the patient is ready, not when the anesthesiologist officially signs off

Alertness

A. Awake and alert
B. Slightly drowsy, but easily aroused
C. Frequently drowsy, but arousable
D. Somnolent, minimal response to stimulation

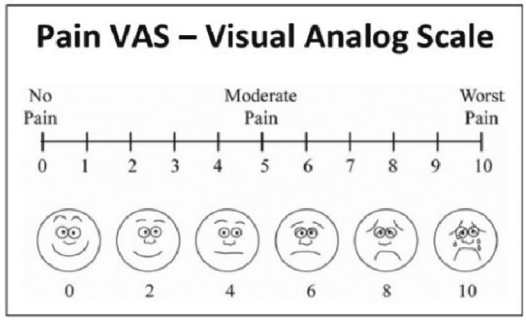

Fig. 2. PACU survey completed by trained recovery nurses at outpatient surgery center. Abbreviations: O_2, oxygen; PACU, Post-Anesthesia Care Unit; PONV, postoperative nausea and vomiting; RN, registered nurse; VAS, visual analog scale.

TABLE I.
Patient Demographics and Clinical Characteristics.

N (%) or Mean (SD)	All patients ($n = 111$)	TIVA ($n = 46$)	Inhalation ($n = 65$)	*p*-value
Demographics				
Age (years)	55.6 (13.0)	56.2 (12.4)	55.1 (13.5)	0.677*
Male:Female	78:33	32:14	46:19	1.000†
Race				
Caucasian	94 (84.7%)	38 (82.6%)	56 (86.2%)	0.141†
Black or African American	12 (10.8%)	5 (10.9%)	7 (10.8%)	
Hispanic	3 (2.7%)	3 (6.5%)	0 (0%)	
Other	2 (1.8%)	0 (0%)	2 (3.1%)	
BMI	29.9 (4.5)	29.7 (4.3)	30.1 (4.7)	0.624*
AHI	32.9 (19.1)	32.5 (19.2)	33.2 (19.1)	0.863*
OSA severity‡	$N = 106$	$N = 43$	$N = 63$	
Mild OSA	12 (11.3%)	5 (11.6%)	7 (11.1%)	0.884†
Moderate OSA	39 (36.8%)	17 (39.5%)	22 (34.9%)	
Severe OSA	55 (51.9%)	21 (48.8%)	34 (54.0%)	
Surgery received	$N = 111$	$N = 46$	$N = 65$	
Nasal surgery§	47 (42.3%)	19 (41.3%)	28 (43.1%)	0.500†
HNS	43 (38.7%)	16 (34.8%)	27 (41.5%)	
Palate surgery§	21 (18.9%)	11 (23.9%)	10 (15.4%)	

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; ESP, expansion sphincter pharyngoplasty; HNS, hypoglossal nerve stimulation; OSA, obstructive sleep apnea; SD, standard deviation; TIVA, total intravenous anesthesia.

*Two-sample *t*-test.

†Fisher's Exact test.

‡OSA Severity was not determined for all patients. Total per group is denoted in the table.

§Nasal surgery includes turbinectomy, septoplasty, open reduction and internal fixation, nasal valve repair, and functional endoscopic sinus surgery (FESS). Palate surgery includes ESP and tonsillectomy.

GraphPad Prism 9 or R 4.1.3, with significance defined as $p < 0.05$.[14,15]

RESULTS

Demographics and Clinical Characteristics

Our cohort included 111 total patients: 47 underwent nasal surgery, 43 underwent HNS implantation, and 21 underwent ESP or tonsillectomy. Forty-six patients (41.4%) received TIVA and 65 patients (58.6%) received sevoflurane. The average age was 55.6 (±13.0) years with an average BMI of 29.9 (±4.5) and AHI of 32.9 (±19.1). Patients were predominantly male (70.3%) and Caucasian (84.7%). Of patients with preoperative sleep studies available ($n = 106$), most carried a diagnosis of severe OSA (52%), as compared to moderate (37%) and mild (11%) disease. Cohort characteristics of the TIVA and sevoflurane subsets were comparable with respect to age, sex, race, BMI, AHI, OSA severity, and surgery received ($p > 0.05$). Cohort demographic data and clinical characteristics are displayed in Table I.

Perioperative Time Intervals

Patients undergoing HNS that received TIVA as compared to inhalational anesthesia experienced significant reductions in median Phase I Time (86.5 vs. 99 min, $p = 0.042$), Time to Maximum Aldrete Score (28 vs. 44.5 min, $p = 0.043$), and estimated Phase I Time based on the PACU Survey (75 vs. 87.5 min, $p = 0.031$). Likewise, TIVA patients undergoing palate surgery experienced reductions in median Phase I Time (91 vs. 118.5 min, $p = 0.016$), Time to Maximum Aldrete Score (32 vs. 54 min, $p = 0.039$), and Phase I Time based on the PACU survey (80 vs. 118.5 min, $p = 0.024$). When assessing all patients combined, those receiving TIVA experienced a median 10.5 min reduction in Phase I Time and 13 min reduction in Time to Maximum Aldrete Score, however, neither of these were statistically significant. For this comprehensive TIVA group, the Phase I Time estimated by the PACU survey demonstrated a significant reduction as compared to the inhalational group (83 vs. 99.5 min, $p = 0.004$). Nurse-estimated Phase I duration was 15.6 min shorter on average for all patients regardless of anesthesia or surgery received than Phase I duration based on EMR-recorded timepoints ($p < 0.0001$). No nasal surgery time intervals or remaining intervals (Total Operative Time, Total Anesthesia Time, Total Recovery Time, or PACU Phase II Time) for any cohort stratifications differed based on anesthesia received. Time intervals are summarized in Table II.

Complications

No intraoperative surgical or anesthesia complications occurred in either cohort. There was no significant difference in postoperative complications, ED visits, or hospital readmissions between groups ($p > 0.05$).

TABLE II.
Median Time Interval Analysis Between Anesthetic Methods by Type of Surgery.

Median (min)	TIVA ($n = 46$)	Inhalation ($n = 65$)	Δ (TIVA–Inhalation)	p-value
All patients ($n = 111$)	$N = 46$	$N = 65$		
Total operative time	110 min	121 min	−11 min	0.970*
Total anesthesia time	140 min	150 min	−10 min	0.993*
Total recovery time	158 min	166 min	−8 min	0.274*
PACU phase I time	101.5 min	112 min	−10.5 min	0.135*
PACU phase II time	53 min	53 min	0 min	0.397*
Time to maximum aldrete score	42.5 min	55.5 min	−13 min	0.184*
PACU nurse survey phase I time	83 min	99.5 min	−16.5 min	**0.004***
Nasal surgery (n = 47)	$N = 19$	$N = 28$		
Total operative time	125 min	136.5 min	−11.5 min	0.519*
Total anesthesia time	140 min	145 min	−5 min	0.457*
Total recovery time	179.5 min	174.5 min	5 min	0.327†
PACU phase I time	129 min	123 min	6 min	0.501*
PACU phase II time	63 min	53.5 min	9.5 min	0.278*
Time to maximum aldrete score	74.5 min	59 min	15.5 min	0.492*
PACU nurse survey phase I time	100 min	110 min	−10 min	0.443*
HNS ($n = 43$)	$N = 16$	$N = 27$		
Total operative time	138 min	129 min	9 min	0.716*
Total anesthesia time	186 min	170 min	16 min	0.221*
Total recovery time	138 min	162 min	−24 min	0.090*
PACU phase I time	86.5 min	99 min	−12.5 min	**0.042†**
PACU phase II time	51.5 min	53 min	−1.5 min	0.931*
Time to maximum aldrete score	28 min	44.5 min	−16.5 min	**0.043†**
PACU nurse survey phase I time	75 min	87.5 min	−12.5 min	**0.031†**
Palate surgery ($n = 21$)	$N = 11$	$N = 10$		
Total operative time	73 min	67.5 min	5.5 min	0.857*
Total anesthesia time	84 min	80 min	4 min	0.514*
Total recovery time	144 min	171.5 min	−27.5 min	0.101*
PACU phase I time	91 min	118.5 min	−27.5 min	**0.016†**
PACU phase II time	52 min	48.5 min	3.5 min	0.486*
Time to maximum aldrete score	32 min	54 min	−22 min	**0.039†**
PACU nurse survey phase I time	80 min	118.5 min	−38.5 min	**0.024***

Note: Time intervals listed are medians; therefore, the sum of PACU Phase I and Phase II Time will not add up to Total Recovery Time listed. Significant findings are in boldface ($p < 0.05$).

Abbreviations: HNS, hypoglossal nerve stimulation; PACU, post-anesthesia care unit; TIVA, total intravenous anesthesia.

*Two-sample *t*-test.

†Wilcoxon rank sum test.

Perioperative Medications

Dosages and proportions of patients receiving the previously listed intraoperative medications and recovery room pain, antiemetic, and anti-inflammatory medications were analyzed. There were no significant differences between study groups for proportions or dosages of any of the medications listed ($p > 0.05$).

PACU Alertness

Patients undergoing any surgery that received TIVA had a higher proportion of full alertness ratings on our PACU survey scale as compared to inhalational anesthesia patients at arrival (28% vs. 3%, $p = 0.001$), 15 min (36% vs. 17%, $p = 0.045$), and 30 min (60% vs. 34%, $p = 0.012$). Patients receiving TIVA while undergoing HNS were proportionately more alert at PACU arrival (31% vs. 4%, $p = 0.021$). No other comparisons reached statistical significance, and alertness ratings are summarized in Table III.

PACU Pain Levels and Medications

For all surgeries combined, TIVA patients had higher mean pain scores at PACU arrival (3.0 vs. 1.6, $p = 0.026$), 15 min (4.0 vs. 2.6, $p = 0.039$), and 30 min (4.9 vs. 3.5, $p = 0.029$) as compared to inhalational anesthesia patients. Nasal surgery patients receiving TIVA had increased pain scores at PACU arrival (3.4 vs. 1.3, $p = 0.017$) and 30 min (5.7 vs. 3.7, $p = 0.025$). Patient

TABLE III.
Summary of PACU Survey Documentation of Full Alertness Rating (A) Over Time.

	All surgeries ($n = 111$)			Nasal ($n = 47$)			HNS ($n = 43$)			Palate ($n = 21$)		
N/total (%)	TIVA ($n = 46$)	Inhalation ($n = 65$)	p-value	TIVA ($n = 19$)	Inhalation ($n = 28$)	p-value	TIVA ($n = 16$)	Inhalation ($n = 27$)	p-value	TIVA ($n = 11$)	Inhalation ($n = 10$)	p-value
Alertness												
Arrival	12/43 (28)	2/65 (3)	**0.001***	3/16 (19)	0/28 (0)	–	5/16 (31)	1/27 (4)	**0.021**†	4/11 (36)	1/10 (10)	0.311†
15 min	16/45 (36)	11/65 (17)	**0.045***	5/18 (28)	3/28 (11)	0.232†	7/16 (44)	6/27 (22)	0.178†	4/11 (36)	2/10 (20)	0.635†
30 min	27/45 (60)	22/65 (34)	**0.012***	7/18 (39)	5/28 (18)	0.170†	11/16 (69)	12/27 (44)	0.219*	9/11 (82)	5/10 (50)	0.183†
45 min	27/43 (63)	33/65 (51)	0.302*	6/17 (35)	11/28 (39)	1.000*	12/15 (80)	18/27 (68)	0.485†	9/11 (82)	4/10 (40)	0.080†
60 min	31/42 (74)	39/64 (61)	0.246*	10/17 (59)	14/27 (52)	0.888*	12/14 (86)	19/27 (70)	0.447†	9/11 (82)	6/10 (60)	0.361†
75 min	28/34 (82)	42/57 (74)	0.489*	11/16 (69)	15/23 (65)	1.000*	9/9 (100)	21/25 (84)	–	8/9 (89)	6/9 (67)	0.576†
90 min	23/29 (79)	34/43 (79)	1.000*	9/14 (64)	14/19 (74)	0.707†	8/8 (100)	15/17 (88)	–	6/7 (86)	5/7 (71)	1.000†
105 min	10/14 (71)	23/32 (72)	1.000†	5/9 (56)	10/16 (63)	1.000†	3/3 (100)	9/10 (90)	–	2/2 (100)	4/6 (67)	–
120 min	11/13 (85)	16/22 (73)	0.680†	6/8 (75)	7/10 (70)	1.000†	3/3 (100)	6/7 (86)	–	2/2 (100)	3/5 (60	–

Note: Data are number of patients receiving a rating of A (awake and alert) / total number of patients remaining in the PACU (%). Significant findings are in boldface ($p < 0.05$).

Abbreviations: HNS, hypoglossal nerve stimulation; PACU, post-anesthesia care unit; TIVA, total intravenous anesthesia.

*Chi-squared test.

†Fisher's Exact test.

pain for the HNS cohort receiving TIVA also experienced increased pain at PACU arrival (2.1 vs. 0.3, $p = 0.032$) and 15 min (2.5 vs. 0.9, $p = 0.023$). Pain scores did not differ for any other recorded timepoints for the above surgery distinctions, or for any timepoint in patients undergoing palate surgery ($p > 0.05$). In addition to pain scores, whether patients received a pain medication at each timepoint was analyzed. For all patients combined, in addition to stratifications by surgery, there were no differences in number of patients receiving pain medication in the PACU at any timepoint ($p > 0.05$). A summary of mean pain scores is detailed in Table IV.

PACU Supplemental Oxygen

Recovery room supplemental oxygen requirements for the TIVA and inhalational cohorts were assessed using our PACU survey. When comparing all surgeries combined, significantly lower proportions of TIVA versus inhalational patients required oxygen (O_2) supplementation at PACU arrival (26% vs 49%, $p = 0.029$), 15 min (24% vs. 47%, $p = 0.023$), and 30 min (20% vs. 41%, $p = 0.031$). Similarly, lower proportions of TIVA patients at these timepoints required supplemental O_2 when stratified by each surgery distinction, however, these comparisons were not statistically significant ($p > 0.05$). There were no differences in O_2 supplementation requirements between cohorts at the remaining timepoints (45–120 min) for any surgical comparison. Supplemental O_2 data are present in Table IV.

PACU Postoperative Nausea and Vomiting

Four TIVA (8.7%) and 2 inhalational (3.1%) patients experienced PONV in the PACU. This did not differ based on anesthesia received either when comparing all surgeries or following stratification by surgery at any timepoint ($p > 0.05$).

DISCUSSION

Considerations in the perioperative management of patients with OSA include alterations to airway anatomy, cardiopulmonary effects, use of opioid analgesia, and challenges regarding overall airway management.[5] In the general population, practices for the effective use of TIVA are safe and well-described.[16] However, to date, literature describing optimal anesthetic regimens for OSA patients is sparse, even more so for OSA patients undergoing otolaryngology-based procedures.[6] Development of evidence-based guidelines detailing the ideal anesthetic approach to OSA patients is an important area of clinical practice that is currently lacking. In this prospective study, we describe several benefits to patients with OSA undergoing TIVA for ambulatory upper airway procedures. As previously reported, patients undergoing HNS and palate surgery experienced significant reductions in median Phase I recovery time. Furthermore, through our PACU recovery survey, we have demonstrated that these subsets, as well as all combined patients, had significantly lower estimated Phase I duration after receiving TIVA. All patients receiving TIVA required less O_2 supplementation and were rated as more alert by PACU nurses early in the recovery process as compared to inhalational anesthesia patients.

Advantages for patients receiving TIVA have been consistently reported across surgical disciplines, namely regarding recovery time and PONV. In a systematic review and meta-analysis of 18 ambulatory surgical trials collectively totaling 1621 patients, Kumar et al. described a 14 min reduction in hospital duration for patients receiving propofol versus any inhalational anesthesia, as well as a 14 min reduction in hospital duration for

TABLE IV.
Summary of PACU Survey Pain Scores (0–10) and Supplemental O_2 Requirements Over Time.

	All surgeries ($n = 111$)			Nasal ($n = 47$)			HNS ($n = 43$)			Palate ($n = 21$)		
Mean (SD)	TIVA ($n = 46$)	Inhalation ($n = 65$)	*p*-value	TIVA ($n = 19$)	Inhalation ($n = 28$)	*p*-value	TIVA ($n = 16$)	Inhalation ($n = 27$)	*p*-value	TIVA ($n = 11$)	Inhalation ($n = 10$)	*p*-value
Pain score												
Arrival	3.0 (3.4) ($n = 42$)	1.6 (2.9) (n = 61)	**0.026**[*]	3.4 (3.1) ($n = 16$)	1.3 (2.3) ($n = 25$)	**0.017**[†]	2.1 (3.3) ($n = 16$)	0.3 (1.2) ($n = 27$)	**0.032**[†]	4.0 (4.1) ($n = 10$)	5.9 (4.0) ($n = 9$)	0.316[†]
15 min	4.0 (3.4) ($n = 45$)	2.6 (3.5) (n = 63)	**0.039**[*]	4.4 (3.3) ($n = 18$)	2.8 (3.1) ($n = 26$)	0.089[†]	2.5 (3.0) ($n = 16$)	0.9 (2.5) ($n = 27$)	**0.023**[†]	5.6 (3.7) ($n = 10$)	6.8 (3.2) ($n = 9$)	0.372[†]
30 min	4.9 (3.0) ($n = 45$)	3.5 (3.2) (n = 64)	**0.029**[*]	5.7 (2.8) ($n = 18$)	3.7 (2.9) ($n = 27$)	**0.025**[†]	3.1 (3.1) ($n = 16$)	2.1 (2.9) ($n = 27$)	0.244[†]	6.0 (2.4) ($n = 10$)	6.9 (2.1) ($n = 9$)	0.374[*]
45 min	4.4 (2.5) ($n = 43$)	3.9 (2.8) (n = 64)	0.373[*]	5.0 (2.1) ($n = 17$)	4.5 (2.8) ($n = 27$)	0.480[*]	2.7 (2.6) ($n = 15$)	2.5 (2.3) ($n = 27$)	0.764[†]	5.6 (2.1) ($n = 10$)	6.2 (2.1) ($n = 9$)	0.543[*]
60 min	4.1 (2.4) ($n = 42$)	3.9 (2.5) (n = 64)	0.673[*]	4.8 (2.4) ($n = 17$)	4.1 (2.5) ($n = 27$)	0.326[*]	2.6 (2.3) ($n = 14$)	3.1 (2.1) ($n = 27$)	0.455[†]	4.9 (1.8) ($n = 10$)	5.6 (2.3) ($n = 9$)	0.543[†]
75 min	3.7 (2.2) ($n = 35$)	3.9 (2.5) (n = 55)	0.607[*]	3.9 (2.4) ($n = 17$)	4.4 (2.4) ($n = 23$)	0.560[*]	2.8 (1.9) ($n = 9$)	2.9 (2.2) ($n = 24$)	0.917[†]	4.1 (2.1) ($n = 9$)	5.8 (2.5) ($n = 8$)	0.108[†]
90 min	4.1 (2.5) ($n = 29$)	4.0 (2.4) (n = 42)	0.864[*]	5.0 (2.7) ($n = 14$)	4.2 (2.0) ($n = 19$)	0.374[*]	2.5 (1.9) ($n = 8$)	2.9 (2.4) ($n = 17$)	0.626[*]	4.1 (2.0) ($n = 7$)	6.3 (2.2) ($n = 6$)	0.085[*]
105 min	4.6 (2.9) ($n = 15$)	4.0 (2.2) (n = 31)	0.481[*]	4.9 (3.3) ($n = 9$)	4.0 (2.0) ($n = 16$)	0.476[*]	3.8 (2.6) ($n = 4$)	3.8 (2.3) ($n = 10$)	0.975[*]	5.2 (1.8) ($n = 2$)	4.6 (2.8) ($n = 5$)	1.000[†]
120 min	3.8 (3.0) ($n = 14$)	3.9 (2.3) (n = 21)	0.905[†]	4.2 (3.4) ($n = 8$)	4.1 (2.3) ($n = 10$)	0.892[†]	2.2 (2.6) ($n = 4$)	3.3 (2.1) ($n = 7$)	0.527[*]	5.2 (1.8) ($n = 2$)	5.2 (1.8) ($n = 2$)	0.814[†]
N/total (%)	TIVA ($n = 46$)	Inhalation ($n = 65$)	*p*-value	TIVA ($n = 19$)	Inhalation ($n = 28$)	*p*-value	TIVA ($n = 16$)	Inhalation ($n = 27$)	*p*-value	TIVA ($n = 11$)	Inhalation ($n = 10$)	*p*-value
Supplemental O_2												
Arrival	12/45 (26)	32/65 (49)	**0.029**[‡]	4/18 (22)	14/28 (50)	0.115[‡]	4/16 (25)	13/27 (48)	0.239[‡]	4/11 (36)	5/10 (50)	0.670[§]
15 min	11/45 (24)	31/65 (47)	**0.023**[‡]	4/18 (22)	15/28 (53)	0.072[‡]	3/16 (18)	11/27 (40)	0.250[‡]	4/11 (36)	5/10 (50)	0.670[§]
30 min	9/45 (20)	27/65 (41)	**0.031**[‡]	4/18 (22)	12/28 (43)	0.264[‡]	2/16 (12)	9/27 (33)	0.166[§]	3/11 (27)	6/10 (60)	0.198[§]
45 min	6/43 (14)	15/65 (23)	0.355[§]	4/17 (23)	6/28 (21)	1.000[§]	1/15 (6)	7/27 (26)	0.222[§]	1/11 (9)	2/10 (20)	0.586[§]
60 min	3/42 (7)	6/64 (9)	1.000[§]	3/17 (17)	2/27 (7)	1.000[§]	0/14 (0)	3/27 (11)	–	0/11 (0)	1/10 (10)	–
75 min	1/34 (3)	5/57 (8)	0.405[§]	1/16 (6)	1/23 (4)	0.359[§]	0/9 (0)	3/25 (12)	–	0/9 (0)	1/9 (11)	–
90 min	1/29 (3)	3/43 (7)	0.644[§]	1/14 (7)	1/19 (5)	1.000[§]	0/8 (0)	2/17 (11)	–	0/7 (0)	0/7 (0)	–
105 min	1/14 (7)	2/32 (6)	1.000[§]	1/9 (11)	1/16 (6)	1.000[§]	0/3 (0)	1/10 (10)	–	0/2 (0)	0/6 (0)	–
120 min	2/14 (14)	1/22 (4)	0.547[§]	2/9 (22)	0/10 (0)	–	0/3 (0)	1/7 (14)	–	0/2 (0)	0/5 (0)	–

Note: Pain scores are mean (SD). Supplemental oxygen data are number of patients requiring supplementation/total patients remaining in PACU (%). Significant findings are in boldface ($p < 0.05$).
Abbreviations: HNS, hypoglossal nerve stimulation; O_2, oxygen; PACU, post-anesthesia care unit; TIVA, total intravenous anesthesia.
[*]Two-sample *t*-test.
[†]Wilcoxon rank sum test.
[‡]Chi-squared test.
[§]Fisher's Exact test.

propofol versus sevoflurane patients. In addition, patients receiving propofol experienced less PONV before discharge as compared to inhalational anesthesia patients (13.8% vs. 29.2%).[10] In a separate meta-analysis, Schraag et al. reviewed 229 trials comprised of 20,991 patients undergoing ambulatory or inpatient procedures and reported a reduced relative risk of 0.61 for PONV in patients receiving propofol as compared to inhalational agents.[9] Visser et al. performed a prospective control trial including 2010 patients undergoing various elective surgical procedures that were randomized to receive TIVA with propofol or inhalational anesthesia with isoflurane-nitrous oxide. Results were organized based on inpatient (n = 1447) or outpatient (n = 563) status, and they reported absolute risk reductions of PONV for TIVA patients of 15%–18% for inpatients and outpatients, respectively. Median PACU recovery time was significantly reduced for TIVA inpatients by 20 min and outpatients by 10 min.[17] We found that TIVA patients experienced reductions in median Phase I recovery time which is consistent with previous literature, however, no difference in PONV was evident in our study.

In addition to decreased recovery time, our TIVA patients experienced improved alertness ratings early in recovery. Studies assessing recovery alertness dependent on anesthesia received are limited, however, several evaluated delirium or agitation following emergence. Anesthesia emergence with TIVA is generally considered rapid and uneventful.[11] A TIVA regimen including an opioid medication requires approximately 50% less propofol to maintain GA. Remifentanil, as compared to sufentanil, fentanyl, or alfentanil, prompts a more rapid return to consciousness.[18] Jo et al. evaluated emergence agitation (ED) using two distinct agitation scales following various nasal procedures in 80 patients randomized to receive either TIVA with propofol and remifentanil or volatile anesthesia with sevoflurane and nitrous oxide. Emergence agitation occurred in 20% (Richmond Agitation Sedation Scale) and 25% (Riker Sedation-Agitation Scale) of volatile anesthesia patients compared to 2.5% (both scales) of TIVA patients.[19] In addition to recovery room alertness, postoperative pain was a valuable metric we quantified in the context of anesthesia received.

Postoperative pain may occur in greater than 80% of completed surgical cases, and is a factor important to both the patient and healthcare team.[20] Studies reporting postoperative pain levels following TIVA versus inhalational anesthesia have shown mixed results. In our cohort, TIVA patients had higher mean pain scores for all procedures combined, as well as following nasal and HNS cases before the 30 min mark. There was, however, no difference in pain medications provided. We believe improved alertness in the TIVA cohort may have contributed to heightened awareness of pain early in recovery. Jo et al. performed a randomized trial including 72 patients undergoing total thyroidectomy that received either TIVA with propofol or desflurane-nitrous oxide. A postoperative pain numerical rating scale showed a significantly higher mean score for TIVA patients (5.7) versus inhalational patients (4.7). Further, their TIVA patients required higher morphine equivalent doses in the PACU (16.7 vs. 14.1 mg).[21] In a double-blind randomized study of middle ear surgery patients, Mukherjee et al. assessed 100 individuals receiving either TIVA with propofol-remifentanil or a balanced anesthesia approach with fentanyl, propofol, and isoflurane. In the PACU, TIVA patients had elevated pain scores, and required significantly more morphine.[22] In the aforementioned large-scale systematic reviews and meta-analyses, Kumar et al. and Schraag et al. reported no difference in postoperative pain for TIVA versus inhalational methods, and reduced postoperative pain for patients receiving propofol for GA, respectively.[9,10]

Required supplemental oxygen was the final measurement addressed by our PACU survey. A significantly lower proportion of our comprehensive TIVA cohort required supplemental O_2 support compared to our inhalational cohort from PACU arrival to 30 minutes. Previous literature has described less respiratory irritation and improved lung blood flow for patients receiving TIVA, potentially contributing to a reduced need of oxygen supplementation.[23] Hohlreider et al. studied 50 adults undergoing lumbar disk surgery that received either propofol-remifentanil or a balanced mixture of fentanyl-nitrous oxide-sevoflurane to ultimately assess cough at anesthesia emergence. The median number of coughs for intravenous anesthesia patients (1, range 0–9) was significantly less than the balanced regimen (4, range 0–20), indicating a potentially improved state of the respiratory system following TIVA.[24] Anesthesia-dependent pulmonary complications have also been previously studied. Chang et al. retrospectively reviewed 156 patients undergoing free flap reconstruction for head and neck cancer after receiving TIVA or inhaled anesthesia. Their TIVA cohort developed fewer subsequent pulmonary complications than their inhalational cohort (18 vs. 47), and they concluded that TIVA patients experienced a significantly reduced risk of pulmonary complication using multivariate regression.[25] Given that OSA patients can demonstrate worsened airway reactivity, pulmonary effects of different anesthetic regimens are highly important.

Implications of anesthetic agents outside of direct patient care, such as economic impacts should also be considered. Historically, TIVA regimens have been regarded as more costly than inhalational methods.[26] Cost implications, at least in part, drove institutional decisions to preferentially use sevoflurane during our hospital response to COVID-19. Recently, however, studies have shown a declining economic burden of the propofol-remifentanil combination, and more emphasis should be placed on considering costs of TIVA based on the operative setting and individual patient scenario, as opposed to considering the TIVA concept overall as more expensive.[11] In a recent retrospective review, our group studied whether reduced recovery times for surgical OSA patients that received TIVA may be cost-effective. We ultimately concluded that the use of TIVA in our cohort did lead to increased medication and operating room costs, but these were offset by lower costs accrued through supply, anesthesia, and the recovery room.[27] In all, non-clinical implications of anesthetic regimens such as cost should

contribute to provider decision-making and merit further study.

We acknowledge a few limitations of this study. Our original simple randomization schedule was interrupted due to institutional policies instituted in response to the COVID-19 pandemic. Therefore, our entire cohort did not undergo an identical randomization protocol. Our study was single-blinded, as patients were unaware of the anesthesia received, however administering anesthesiologists were unable to be blinded. Recovery personnel were supposed to be unaware of anesthesia received by study design, however due to COVID-19 policies, use of sevoflurane only for the aforementioned period may have been known. We believe the clear definitions of the PACU survey measurements adequately reduce any potential observer bias. Assessment of anesthesia depth through methods such as Bispectral Index monitoring was not performed during this study, as depth of anesthesia was primarily assessed through standard vital sign monitoring. Future studies of this topic may benefit from increased information provided by supplemented monitoring techniques of anesthesia depth.[28] In addition, this is a single-center prospective study, and a future multicenter approach could strengthen our findings. Although our sample size provided enough statistical power to make significant conclusions, increased patient involvement in future studies would likely enhance our ability to arrive at data-driven conclusions regarding our study topic. We believe this is the first prospective trial assessing anesthetic modalities in OSA patients undergoing upper airway surgery, however, generalizability to any surgical procedure in OSA patients may be limited.

CONCLUSION

This prospective study suggests that administration of TIVA, as opposed to inhaled anesthesia, leads to reduced postoperative recovery times, decreased need for supplemental oxygenation, and a more rapid return of alertness in patients undergoing OSA surgery. Future work should focus on the development of clinical practice guidelines for safe and effective anesthesia protocols in this specific patient population.

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