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Surgical Field Visualization during Functional Endoscopic Sinus Surgery: Comparison of Propofol- vs Desflurane-Based Anesthesia

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Abstract

Objective. To assess if the type of general anesthetic affects bleeding and field visualization during endoscopic sinus surgery.

Study Design. Prospective, randomized, controlled trial.

Setting. Academic teaching hospital and Veterans Affairs hospital in the United States.

Subjects and Methods. Seventy patients were randomized to 1 of 3 anesthetic regimens: (1) the volatile anesthetic desflurane (n = 22), (2) intravenous anesthesia with propofol (n = 25), or (3) a combination of propofol and desflurane (n = 23). Intravenous remifentanil was titrated to decrease the mean arterial pressure to 60 to 70 mm Hg but not $\geq$30% from baseline. Surgical bleeding scores were recorded along with bleeding rates and hemodynamic parameters, including cardiac output and systemic vascular resistance through pulse contour analysis from a radial arterial line. Statistics: multiple comparison tests and regression analyses; α = .05.

Results. There were no differences in bleeding rate (median, 0.58, 0.85, 0.57 mL min^{-1}), bleeding score (2.1, 2.0, 2.0), surgery duration (79, 81, 86 minutes), extubation time (9, 7, 8 minutes), recovery room time (65, 61, 61 minutes), or any hemodynamic parameters among groups 1 through 3, respectively. Group 1 required lower remifentanil infusions than group 2 (0.11 vs 0.26 $\mu g\ kg^{-1}\ min^{-1}$; *P* = .01). The bleeding score correlated positively with height (*P* = .014) and the Lund-MacKay score (*P* = .013). Bilateral vs unilateral surgery led to longer surgery duration (*P* = .001) and recovery room time (*P* = .004).

Conclusion. When remifentanil is used for controlled hypotension, propofol has no advantage over desflurane to improve surgical field visualization during functional endoscopic sinus surgery.

Keywords

cardiac output, FloTrac, remifentanil, TIVA, volatile anesthetics

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Functional endoscopic sinus surgery (FESS) is the standard surgical procedure to treat chronic rhinosinusitis (CRS). Despite its low risk, complications may occur.[1] Due to the sinuses' location near the skull base, the orbits, the optic nerves, and carotid arteries, major complications occur in up to 1% of cases and include injury of the dura with a cerebrospinal fluid leak, injury of the lacrimal duct, severe bleeding, intracerebral hemorrhage, meningitis, blindness, and brain death, while minor complications (<4%) encompass minor bleeding, perforation of the lamina papyracea, and periorbital ecchymosis.[1]

Thus, adequate surgical field visualization is utmost important. A bloodless field allows optimal exposure and identification of vital neurovascular structures. Even small bleeding, inconsequential for the patient's volume status, can create great technical difficulty in the confined space of a sinus, leading to prolonged surgery, incomplete procedures, and increased complications.[2,3] To decrease bleeding, different interventions have been proposed, including reverse Trendelenburg position,[4] the application of topical vasoconstrictors,[5] regional anesthesia, laryngeal mask airways,[6] different ventilation strategies,[7] and—most important—controlled systemic hypotension, with target mean arterial pressures (MAPs) generally between 50 and 70 mm Hg.[8]

Bleeding from vascularized capillary beds is determined by central venous pressure (CVP) and MAP. With systemic

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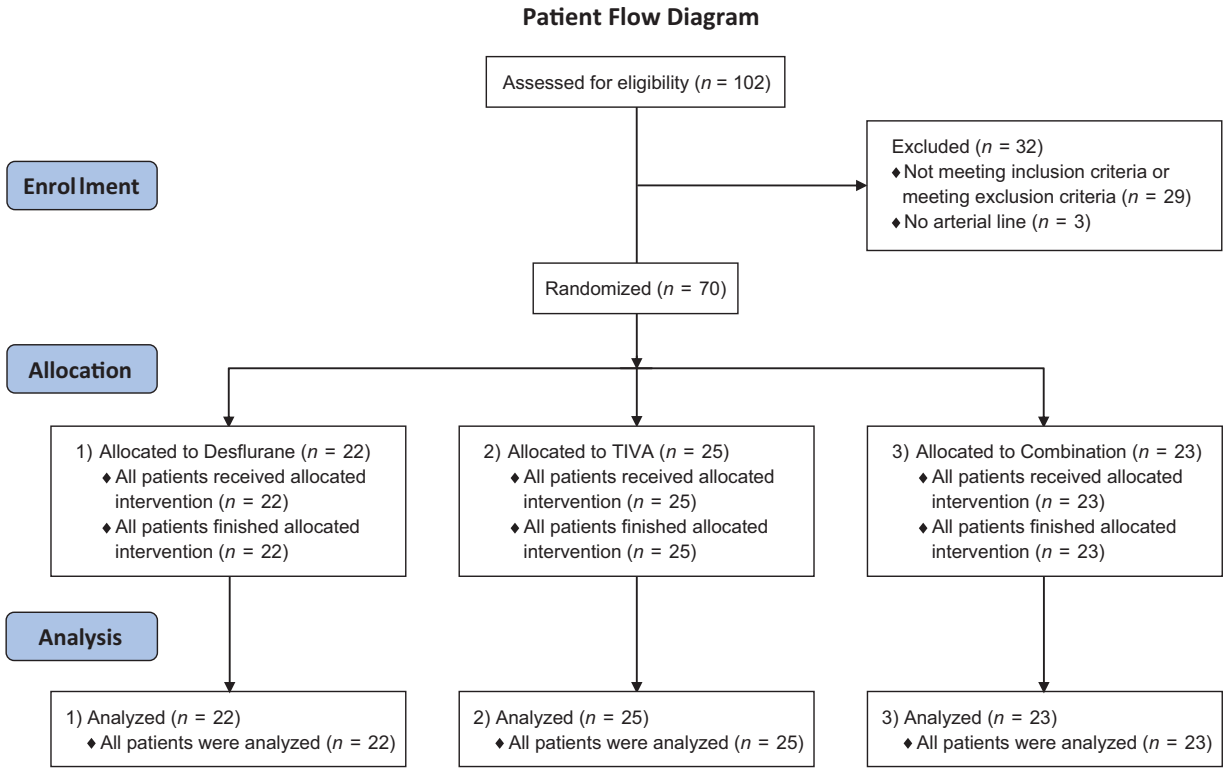

Figure 1. Patient flow diagram in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. TIVA, total intravenous anesthesia.

vascular resistance (SVR) equaling (MAP minus CVP) divided by cardiac output (CO), MAP is largely proportional to the product of CO and SVR. Thus, hypotension is achieved by decreasing SVR, CO, or both. Mucosal vasodilation, however, offsets the benefit of hypotension, and pure vasodilators lead to reflex tachycardia and increased CO; thus, drugs are preferred that directly or indirectly decrease CO.[3,8]

General anesthetics often have profound hemodynamic side effects: they decrease vascular tone and/or myocardial inotropy and chronotropy either directly or indirectly by decreasing sympathetic tone.[9,10] It has been postulated that some may have a distinct advantage over others in decreasing local bleeding by decreasing CO. Yet, whether total intravenous anesthesia (TIVA) with propofol is superior to volatile anesthetics remains largely unsettled to date.[2,11]

We aimed to compare (1) the volatile anesthetic desflurane, (2) TIVA with propofol, and (3) the combination of both with regards to estimated blood loss (EBL) and surgical field visualization (ie, bleeding scores). All patients received a titratable remifentanil infusion to maintain the blood pressure goals of controlled hypotension. To assess the impact of different anesthetics on hemodynamics, we used invasive blood pressure monitoring and pulse contour analysis (FloTrac; Edwards Lifesciences Corp, Irvine, California).[12]

Methods

Ethics and Trial Design

This prospective, randomized, controlled, clinical trial was approved by the Institutional Review Boards at Froedtert Hospital/Medical College of Wisconsin (#PRO00017972; Charles Cady, MD) and the Clement J. Zablocki VA Medical Center (#7435-04; Elizabeth Jacobs, MD) in Milwaukee, Wisconsin. All participants provided written informed consent before enrollment. Reporting adheres to the Declaration of Helsinki and the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Eligibility

Inclusion criteria were legally competent men and women 18 to 85 years of age undergoing uni- or bilateral FESS. Exclusion criteria were patient refusal, history of sinus surgery, pregnancy, uncontrolled hypertension, family or personal history of or clinically suspected susceptibility for malignant hyperthermia (contraindication for volatile anesthetics), allergy to any part of the propofol suspension (eg, egg yolk, soy bean oil), contraindications against placement of an arterial line (eg, limited collateral blood flow, local infection, vascular graft on same extremity), and any bleeding disorder as assessed by history and/or coagulation tests.

Enrollment

We screened 102 eligible American Society of Anesthesiologists (ASA) class 1 to 3 patients who underwent uni- or bilateral FESS under general anesthesia. Seventy-three patients consented, and 3 patients were not included secondary to inability to get an arterial line, resulting in 70 patients who were enrolled and finished the study (**Figure 1**), after which enrollment was stopped as the predetermined sample size had been

Table 1. Endoscopic Surgical Field Grading System.

Grade	Assessment
0	No bleeding (cadaveric conditions)
1	Slight bleeding, no suctioning required
2	Slight bleeding, occasional suctioning required
3	Slight bleeding, frequent suctioning required; bleeding threatens surgical field a few seconds after suction is removed
4	Moderate bleeding, frequent suctioning required; bleeding threatens surgical field directly after suction is removed
5	Severe bleeding, constant suctioning required; bleeding appears faster than can be removed by suction; surgical field severely threatened and surgery usually not possible

Adapted from Boezaart et al.[4] and Kelly et al.[2]

achieved. A power analysis based on the 20% reduction in bleeding scores between sevoflurane and propofol anesthesia reported by Wormald et al[13] had revealed a sample size of 23 patients per group in a 3-group analysis of variance (ANOVA) with a power of 80%.

All patients were monitored with standard ASA monitoring: electrocardiogram, noninvasive blood pressure, pulse oximeter, concentration of inhaled O_2 and end-tidal CO_2, and temperature. After preoxygenation, general anesthesia was induced intravenously with propofol 2 mg kg^{-1}, lidocaine 1 mg kg^{-1}, and a remifentanil infusion starting at 0.15 $\mu g\ kg^{-1}\ min^{-1}$. Following loss of consciousness and adequate mask ventilation, rocuronium 0.6 mg kg^{-1} was given followed by endotracheal intubation 90 seconds later. To decrease bleeding, the surgeon (D.M.P. or T.A.L.) used topical epinephrine (1:1000) on cotton pledgets (2 each side) for approximately 5 minutes prior to surgical start. This was followed by local anesthetic (5-8 mL of 1% lidocaine with 1:100,000 epinephrine) injected into the nasal mucosa in the region of the sphenopalatine artery and the ascending process of the maxilla on each side. Epinephrine-soaked pledgets were used during surgery on an as-needed basis to control bleeding. A total of 20 mL topical epinephrine (1:1000) was provided from pharmacy for each patient.

Randomization, Blinding, and Interventions

Before the procedure, patients were randomized to 1 of 3 anesthetic groups by the respective principal investigators of the study (S.G. and M.L.R.) through a sealed envelope technique with equal distribution of the 3 anesthetic groups: (1) in the desflurane group, general anesthesia was maintained by a fixed concentration of 1 minimum alveolar concentration (MAC) of desflurane (7.3% in a young adult) throughout the entire case; (2) in the TIVA group, general anesthesia was maintained by continuous intravenous infusion of propofol at a fixed rate of 100 $\mu g\ kg^{-1}\ min^{-1}$ throughout the entire case; and (3) in the combined group, an also fixed combination of (1) and (2) consisting of 0.5 MAC desflurane and a continuous intravenous infusion of propofol at 50 $\mu g\ kg^{-1}\ min^{-1}$ was given throughout the entire case. Since patient allocation to 1 of the 3 anesthetic regimens was strictly randomized, the preoperative diagnosis, including the subtype or severity of CRS, anticipated length of surgery, or uni- vs bilateral surgery did not affect treatment allocation.

The patient, the surgical team members, and the postanesthesia care unit (PACU) nurses were completely blinded to the anesthetic regimen. To ease blinding of the surgical team and to account for the 10% lipid emulsion given as vehicle in the TIVA and the combination groups, we ran a 10% Intralipid infusion in the desflurane group at the rate the propofol infusion would have run in the propofol group, so that the surgical team would always see ''white medication'' given to the patient. The propofol/Intralipid was administered by a syringe pump whose label was hidden from the surgeons' view; the anesthesia machine and its displays were also turned away from the surgeons, and the anesthetic vaporizer was covered with a towel.

In all 3 groups, remifentanil was titrated to effect with the goal of achieving a MAP between 60 and 70 mm Hg but not more than 30% lower than baseline. After induction of general anesthesia and endotracheal intubation, all patients received a radial arterial line for blood draws and invasive blood pressure monitoring using a FloTrac transducer connected to an EV1000 platform[12] (both from Edwards Lifesciences Corp) to measure arterial blood pressure, CO, cardiac index (CI equals CO divided by the body surface area, which was calculated using the Mosteller formula[14]), and SVR. Hydromorphone 0.2 to 0.4 mg was given to all patients before emergence. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate. Patients were extubated when they met the criteria of being awake, following commands, and achieving adequate tidal volumes on spontaneous ventilation. Patients were then taken to the PACU with O_2 delivered via a face mask. The arterial line was removed in the PACU.

Outcomes

The surgeon provided a subjective surgical bleeding score every 15 minutes ranging from 0 for no bleeding to 5 for severe bleeding with constant suctioning required and surgery usually not possible (**Table 1**).[2,4] These nonsite specific bleeding scores were averaged per patient. Possible changes in any given patient over time have not been taken into consideration. Objective total EBL was calculated by multiplying

Table 2. Baseline Demographics.[a]

Characteristic	Des (n = 22)	Comb (n = 23)	TIVA (n = 25)	*P* Value
Age, y	50 (14)	46 (11)	41 (13)[b]	.04
Female, n (%)	16 (73)	15 (65)	16 (64)	.79
Height, m	1.72 (0.12)	1.73 (0.09)	1.71 (0.10)	.79
Weight, kg	85.6 (73.0, 97.0)	87.1 (68.9, 102.0)	78.9 (68.0, 103.4)	.96
BMI, kg m^{-2}	28.6 (25.8, 32.5)	27.9 (23.4, 35.2)	28.3 (24.6, 34.0)	.90
ASA class >2, n (%)	7 (32)	6 (26)	6 (24)	.83
Lund-MacKay score	9 (6, 10)	8 (5, 11)	9 (6, 14)	.63
Unilateral, n (%)	4 (18)	6 (26)	5 (20)	.79

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; Comb, combination of inhaled and intravenous anesthesia; Des, inhaled anesthesia with desflurane; TIVA, total intravenous anesthesia.
[a]Categorical data are given as number (percentage), nonparametric data as median (first, third quartile), and parametric data as mean (standard deviation).
[b]$P < .05$ vs Des (2-tailed).

the amount of the blood/irrigation mixture in the suction canister by the ratio of the hematocrit in the canister to the patient's hematocrit at the halfway point of surgery as previously published by Ahn et al.[15] To account for surgery duration and to make EBL in patients with different surgery durations comparable, EBL rate was calculated by dividing EBL by surgery duration. Secondary outcomes were duration of surgery, time to extubation, and PACU length of stay (LOS). Other dependent variables included hemodynamic variables such as heart rate (HR), MAP, CO, CI and SVR measured every 5 minutes as well as the remifentanil infusion rate necessary to achieve the blood pressure goal of controlled hypotension.

Statistical Analysis

Statistical analysis was done with SigmaStat (version 3.4; Systat Software, San Jose, California). Categorical data were calculated as percentages, nonparametric data as median (first, third quartile), and parametric data as mean (standard deviation). The Kolmogorov-Smirnov test was used for all continuous data to test for normal distribution; not normally distributed data were treated as nonparametric, as were ranked data. Anesthetic groups were compared with each other by χ^2 tests for categorical data, Kruskal-Wallis tests for nonparametric data, and ANOVA for parametric data. If a difference was found among the 3 anesthetic groups by Kruskal-Wallis or ANOVA tests, post hoc comparisons were done by the Dunn or Student-Newman-Keuls test, respectively. Multiple regression and correlation analyses were used to test for possible associations among different variables; log-transformation was used to transform not normally distributed data to normal distribution. Differences were considered statistically significant when $P < .05$ (2-tailed). Independent parameters included patient demographics such as sex, age, height, weight, body mass index (BMI), ASA score, Lund-MacKay score[16] (LMS, determined by author D.M.P., a surgeon blinded to the group assignment), uni- vs bilateral surgery, and type of anesthesia. Dependent variables included the primary outcomes of total EBL, EBL rate, and surgical bleeding score, as well as the secondary outcomes of surgery duration, time from end of surgery to extubation, and PACU LOS, along with other dependent variables such as average CO, CI, average MAP, average HR, and average remifentanil infusion rate.

Results

Patients were enrolled between December 2012 and May 2015. Twenty-two patients received general anesthesia with desflurane, 25 patients with TIVA, and 23 patients with a combination of both (**Figure 1**). Among the continuous data, age, height, PACU LOS, HR, and SVR were normally distributed, whereas weight, BMI, duration of surgery, time to extubation, EBL, EBL rate, CO, CI, MAP, and remifentanil rate were not.

Baseline Data

Table 2 shows the relevant baseline demographics separated by type of anesthesia; there were no significant differences among the 3 groups except for age ($P = .04$). In further multiple regression analyses, however, age was not found to be an independent factor for any of the primary or secondary outcomes or other dependent variables. The patients' indications were CRS (92%) with (27%) or without (65%) nasal polyps, or recurrent acute rhinosinusitis (8%). All patients had lidocaine injected into the nasal mucosa (see Methods), 97% of the patients with 1:100,000 epinephrine, to decrease bleeding. There were no significant differences between the different anesthetic groups with regards to the patients' preoperative diagnoses, their medical treatment (consisting of an antibiotic [Augmentin, azithromycin, Bactrim, cefuroxime, or doxycycline] with or without the addition of prednisone starting approximately one week prior to surgery), the addition of epinephrine to the lidocaine injection, or the use of topical pledgets with epinephrine.

Primary and Secondary Outcomes and Other Dependent Variables

Except for the remifentanil rate, which was found to be higher in the TIVA than in the desflurane group (median 0.26 vs 0.11 $\mu g\ kg^{-1}\ min^{-1}$; $P = .01$), the type of anesthesia did not significantly affect any primary or secondary

Table 3. Primary and Secondary Outcomes.[a]

Characteristic	Des (n = 22)	Comb (n = 23)	TIVA (n = 25)	*P* Value
Total EBL, mL	57 (32, 79)	61 (32, 81)	84 (39, 100)	.21
EBL rate, mL min^{-1}	0.58 (0.48, 1.05)	0.57 (0.40, 0.72)	0.85 (0.50, 1.23)	.29
Surgical bleeding score	2.1 (1.9, 2.4)	2.0 (1.8, 2.3)	2.0 (1.8, 2.6)	.82
Surgery duration, min	79 (65, 98)	86 (66, 123)	81 (67, 118)	.59
Time to extubation, min	9 (6, 12)	8 (5, 10)	7 (4, 8)	.14
PACU LOS, min	65 (30)	61 (25)	61 (19)	.80

Abbreviations: Comb, combination of inhaled and intravenous anesthesia; Des, inhaled anesthesia with desflurane; EBL, estimated blood loss; PACU LOS, length of stay in postanesthesia care unit; TIVA, total intravenous anesthesia.
[a]Nonparametric data are given as median (first, third quartile) and parametric data as mean (standard deviation).

Table 4. Other Dependent Variables.[a]

Characteristic	Des (n = 22)	Comb (n = 23)	TIVA (n = 25)	*P* Value
HR, bpm	67.4 (7.5)	67.6 (10.4)	69.7 (11.0)	.69
MAP, mm Hg	63 (60, 67)	67 (63, 70)	67 (63, 73)	.08
CO, l min^{-1}	5.5 (4.5, 6.9)	5.9 (5.5, 7.5)	6.4 (5.5, 7.8)	.21
CI, l min^{-1} m^{-2}	2.6 (2.5, 3.3)	3.1 (2.5, 3.9)	3.2 (2.7, 3.6)	.18
SVR, dynes s cm^{-5}	921 (248)	865 (235)	908 (257)	.72
Remifentanil, μg kg^{-1} min^{-1}	0.11 (0.07, 0.15)	0.13 (0.10, 0.40)	0.26 (0.13, 0.47)[b]	.01

Abbreviations: CI, cardiac index; CO, cardiac output; Comb, combination of inhaled and intravenous anesthesia; Des, inhaled anesthesia with desflurane; HR, heart rate; MAP, mean arterial pressure; SVR, systemic vascular resistance; TIVA, total intravenous anesthesia.
[a]Nonparametric data are given as median (first, third quartile) and parametric data as mean (standard deviation).
[b]$P < .05$ vs Des (2-tailed).

Table 5. Unilateral vs Bilateral Surgery.[a]

Characteristic	Unilateral (n = 15)	Bilateral (n = 55)	*P* Value
Lund-MacKay score	7 (5, 9)	9 (6, 13)	.06
Duration of surgery, min	65 (42, 80)	86 (68, 124)[b]	.001
Total EBL, mL	50 (29, 71)	69 (39, 99)	.09
EBL rate, mL min^{-1}	0.68 (0.50, 1.03)	0.69 (0.45, 1.12)	.61
Surgical bleeding score	2.0 (1.9, 2.3)	2.0 (1.8, 2.4)	.81
PACU LOS, min	45 (19)	66 (24)[b]	.004

Abbreviations: EBL, estimated blood loss; PACU LOS, length of stay in postanesthesia care unit.
[a]Nonparametric data are given as median (first, third quartile) and parametric data as mean (standard deviation).
[b]$P < .05$ vs unilateral (2-tailed).

outcomes (**Table 3**) or other dependent variables (**Table 4**), namely, total EBL, EBL rate, surgical bleeding score, duration of surgery, time to extubation, PACU LOS, or any of the hemodynamic parameters.

Further multiple regression analysis did not reveal any parameter to be associated with EBL rate. The surgical bleeding score, however, correlated positively with height ($P = .014$) and LMS ($P = .013$). Bilateral vs unilateral surgery (**Table 5**) led to a 32% longer duration of surgery ($P = .001$) and a 47% longer PACU LOS ($P = .004$) but not to a higher EBL rate ($P = .61$) or surgical bleeding score ($P = .81$).

Because patients in the TIVA group required a significantly higher remifentanil rate than in the desflurane group, we tested if the remifentanil infusion rate correlated with EBL rate or MAP. It did not correlate with EBL rate ($P = 1.00$), but it did correlate positively with MAP ($P = .04$). Within the range of our patients, MAP itself did not correlate with EBL rate ($P = .29$).

Unintended Effects

We observed temporary hypertension in 4 patients and temporary and completely reversible ST changes in 2 patients

with the injection of the local anesthetic with epinephrine, intraoperative hypotension in 3 patients, postoperative nausea in the PACU in 6 patients, postoperative hypertension in the PACU in 2 patients, prolonged postoperative sedation in 7 patients, and postoperative epistaxis in 2 patients. None of these were significantly associated with the anesthetic technique.

Discussion

It has been postulated that lower MAP during FESS can have a positive effect on surgical conditions by reducing local bleeding, thus improving surgical field visualization.[17] As MAP is proportional to SVR and CO, the effects of vasodilators and negative inotropic and chronotropic drugs have been tested. Sodium nitroprusside[4] and nitroglycerin[18] have no advantage, whereas preoperative metoprolol administration,[19] intraoperative labetolol,[20] or intraoperative esmolol administration consistently led to improved conditions.[4,21,22] Studies using magnesium sulfate came to positive[22] and negative conclusions.[23] Decreasing preload and improving venous drainage by reverse Trendelenburg has also been reported[4] and became important to decrease intraoperative bleeding.[3,8] Deliberate hypocapnia, however, seems ineffective.[7]

In addition to above adjuncts, the choice of the general anesthetic may also have an impact on hemodynamics and bleeding. Despite extensive efforts, the use of TIVA vs inhaled anesthetics led to inconclusive outcomes.[17] Several studies reported TIVA improving surgical conditions,[13,15,24,25] while others failed to demonstrate a difference.[26-29] Many studies have limitations in design or sample size to allow a well-founded recommendation.[2,11,17]

Continuous infusion of μ-opioids sufentanil or remifentanil[30,31] was found to decrease blood loss in FESS and, therefore, has been used to compare TIVA with inhaled anesthesia.[15,25,32,33] These μ-opioids are thought to exert their beneficial effect on surgical conditions indirectly through a reduction in sympathetic tone.[8]

A major challenge remains: different agents are used in inhaled anesthetic as well as TIVA regimens, often with different drug combinations, dosing, and assignments of fixed vs titrated drugs, rendering comparisons or meta-analyses difficult to impossible. Furthermore, the effect of anesthetics on important hemodynamic parameters such as CO and SVR has rarely been measured[34-36] to allow a reasonable conclusion regarding possible mechanisms of action.

Consequently, we randomized our patients to a fixed concentration of desflurane, a fixed infusion rate of propofol, or a combination of the 2 (independent variable). In contrast, remifentanil (reported as a dependent variable) was titrated to effect to achieve controlled hypotension (MAP 60-70 mm Hg). We assessed CO and its derivatives by pulse contour analysis from radial arterial line-derived blood pressure to determine possible hemodynamic differences among the anesthetic groups.

Under those conditions, we did not find a significant difference between the 3 anesthetic regimens with regards to the clinically important primary outcomes of overall EBL, EBL rate, or surgical bleeding score (**Table 3**) or other relevant secondary outcomes such as surgery duration, extubation time, or PACU LOS (**Table 3**). In other words, when remifentanil is titrated to achieve controlled hypotension, the choice of general anesthetic—propofol, inhaled anesthetic, or their combination—does not matter. This is completely in line with several other studies.[26-29] Almost all other studies reporting propofol to be superior to inhaled anesthesia have not used the same opioid regimen in both groups,[13,24,25,37] have not titrated remifentanil to effect to achieve the same MAP, or have not recorded or stated the used propofol or remifentanil doses.[33] Commendable exceptions are the studies by Ahn et al[15] and Cho et al.[32] In the former, the median remifentanil rate was 40% higher and HR significantly lower in the propofol group. Interestingly, in both studies, the difference in outcome was amplified in patients with high LMS but not significant in patients with low LMS.

Another important finding from our study is that patients in the TIVA group required almost 2.5 times more remifentanil to achieve the same MAP and subsequently EBL rate. Although not significant, the latter tended to be on the higher side in TIVA compared to desflurane patients, underscoring the point that a standard infusion rate of propofol alone to achieve general anesthesia is not sufficient by itself to achieve the same surgical conditions in FESS as desflurane, not to mention that it is not superior to inhaled anesthesia.

Further pertinent negative findings were that, under the given conditions of controlled hypotension achieved with desflurane and/or propofol and titrated remifentanil, HR, MAP, CO, CI, or remifentanil infusion rate did not correlate with any of the primary or secondary outcomes. This is also remarkable as our study does not show a differential effect of propofol vs desflurane on CO/CI vs SVR within the hemodynamic range of our patients.

Some demographic parameters, however, had a significant effect on select outcomes. Not surprisingly, quantitatively increased sinus pathology requiring bilateral surgery was associated with longer surgery duration and PACU LOS but had no independent effect on bleeding rate or score. In contrast, qualitatively increased sinus pathology as evidenced by higher LMS was associated with increased bleeding scores as well as PACU LOS.

These results need to be interpreted within the natural constraints of our study. It is adequately powered to detect a 20% decrease in the surgical bleeding score as reported by Wormald et al[13] but possibly not for other analyses or subgroups. Based on the different effect sizes and variances in our study and more conservative nonparametric testing, it cannot be excluded that some outcome measurements are underpowered and fail to detect a true difference. We deliberately chose to titrate remifentanil, routinely used as part of TIVA, to target 60 to 70 mm Hg MAP instead of a fixed remifentanil regimen with a higher likelihood of different MAPs and EBL rates; in our mind, the latter is not compatible with standard of care based on pertinent literature. It would also likely not have resulted in a superiority of propofol as those patients in fact required a higher rather than

lower remifentanil infusion rate. Remifentanil is an indirect sympatholytic drug[8] with no further vasodilatory or directly cardiodepressant effects; esmolol may have led to a similar effect.[4,18,21,22,38] We chose FloTrac[12] to measure CO and calculate its hemodynamic derivatives; a pulmonary artery catheter would not have been ethical, and the less invasive ClearSight[39] (Edwards Lifesciences Corp, Irvine, California) was not available at the beginning of our study. Yet, most CO measurements share an inherent variability, which increases the likelihood for a type II error with regards to measurable differences in CO and its derivatives.[40] Nevertheless, to our knowledge, this is the first study reporting CO and CO-derived data in connection with other outcome data in FESS patients with different anesthetic regimen. Last, we have not assessed anesthetic depth as a variable or titrated propofol or desflurane to the same anesthetic depth target; different anesthetic depths might have affected MAP and bleeding.

Conclusions

With surgical field visualization and measured EBL as primary outcomes, we found no superiority of propofol-based compared with desflurane-based inhaled general anesthesia or vice versa when controlled hypotension at comparable blood pressure levels is achieved by remifentanil. Differential effects of propofol vs desflurane on CO vs SVR could not be detected under these conditions. Thus, the selection of general anesthetic becomes inconsequential in FESS patients as long as controlled hypotension is achieved. These findings provide important guidance to anesthesia providers and surgeons caring for this patient group.

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Author Contributions

Suneeta Gollapudy, study design, data acquisition, data analysis, manuscript written, final approval, agreement to be accountable; **Drake A. Gashkoff**, data analysis, manuscript written, final approval, agreement to be accountable; **David M. Poetker**, study design, data acquisition, data analysis, manuscript written, final approval, agreement to be accountable; **Todd A. Loehrl**, study design, data acquisition, manuscript written, final approval, agreement to be accountable; **Matthias L. Riess**, study design, data acquisition, data analysis, manuscript written, final approval, agreement to be accountable.

Disclosures

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References

1. Ramakrishnan VR, Kingdom TT, Nayak JV, Hwang PH, Orlandi RR. Nationwide incidence of major complications in endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2012;2:34-39.
2. Kelly EA, Gollapudy S, Riess ML, Woehlck HJ, Loehrl TA, Poetker DM. Quality of surgical field during endoscopic sinus surgery: a systematic literature review of the effect of total intravenous compared to inhalational anesthesia. *Int Forum Allergy Rhinol*. 2013;3:474-481.
3. Carlton DA, Govindaraj S. Anesthesia for functional endoscopic sinus surgery. *Curr Opin Otolaryngol Head Neck Surg*. 2017;25:24-29.
4. Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside- and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. *Can J Anaesth*. 1995;42:373-376.
5. Higgins TS, Hwang PH, Kingdom TT, Orlandi RR, Stammberger H, Han JK. Systematic review of topical vasoconstrictors in endoscopic sinus surgery. *Laryngoscope*. 2011;121:422-432.
6. Atef A, Fawaz A. Comparison of laryngeal mask with endotracheal tube for anesthesia in endoscopic sinus surgery. *Am J Rhinol*. 2008;22:653-657.
7. Nekhendzy V, Lemmens HJ, Vaughan WC, et al. The effect of deliberate hypercapnia and hypocapnia on intraoperative blood loss and quality of surgical field during functional endoscopic sinus surgery. *Anesth Analg*. 2007;105:1404-1409.
8. Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs*. 2007;67:1053-1076.
9. Bryson HM, Fulton BR, Faulds D. Propofol. An update of its use in anaesthesia and conscious sedation. *Drugs*. 1995;50:513-559.
10. Ebert TJ, Harkin CP, Muzi M. Cardiovascular responses to sevoflurane: a review. *Anesth Analg*. 1995;81:S11-2S2.
11. Boonmak P, Boonmak S, Laopaiboon M. Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS). *Cochrane Database Syst Rev*. 2016;10:CD006623.
12. Mayer J, Boldt J, Poland R, Peterson A, Manecke GR Jr. Continuous arterial pressure waveform-based cardiac output using the FloTrac/Vigileo: a review and meta-analysis. *J Cardiothorac Vasc Anesth*. 2009;23:401-406.
13. Wormald PJ, van Renen G, Perks J, Jones JA, Langton-Hewer CD. The effect of the total intravenous anesthesia compared with inhalational anesthesia on the surgical field during endoscopic sinus surgery. *Am J Rhinol*. 2005;19:514-520.
14. Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med*. 1987;317:1098.

15. Ahn HJ, Chung SK, Dhong HJ, et al. Comparison of surgical conditions during propofol or sevoflurane anaesthesia for endoscopic sinus surgery. *Br J Anaesth*. 2008;100:50-54.
16. Lund VJ, Mackay IS. Staging in rhinosinusitus. *Rhinology*. 1993;31:183-184.
17. Al-Bar MH, Ruiz JW, Casiano RR. Does total intravenous anesthesia provide significant blood loss reduction compared to inhalational anesthesia during endoscopic sinus surgery? *Laryngoscope*. 2016;126:1961-1962.
18. Bajwa SJ, Kaur J, Kulshrestha A, Haldar R, Sethi R, Singh A. Nitroglycerine, esmolol and dexmedetomidine for induced hypotension during functional endoscopic sinus surgery: a comparative evaluation. *J Anaesthesiol Clin Pharmacol*. 2016; 32:192-197.
19. Rahimzadeh P, Faiz SH, Alebouyeh MR. Effects of premedication with metoprolol on bleeding and induced hypotension in nasal surgery. *Anesth Pain Med*. 2012;1:157-161.
20. El-Shmaa NS, Ezz HAA, Younes A. The efficacy of labetalol versus nitroglycerin for induction of controlled hypotension during sinus endoscopic surgery: a prospective, double-blind and randomized study. *J Clin Anesth*. 2017;39:154-158.
21. Shen PH, Weitzel EK, Lai JT, Wormald PJ, Ho CS. Intravenous esmolol infusion improves surgical fields during sevoflurane-anesthetized endoscopic sinus surgery: a double-blind, randomized, placebo-controlled trial. *Am J Rhinol Allergy*. 2011;25:e208-e211.
22. Jangra K, Malhotra SK, Gupta A, Arora S. Comparison of quality of the surgical field after controlled hypotension using esmolol and magnesium sulfate during endoscopic sinus surgery. *J Anaesthesiol Clin Pharmacol*. 2016;32:325-328.
23. Bayram A, Ulgey A, Gunes I, et al. Comparison between magnesium sulfate and dexmedetomidine in controlled hypotension during functional endoscopic sinus surgery. *Rev Bras Anestesiol*. 2015;65:61-67.
24. Tirelli G, Bigarini S, Russolo M, Lucangelo U, Gullo A. Total intravenous anaesthesia in endoscopic sinus-nasal surgery. *Acta Otorhinolaryngol Ital*. 2004;24:137-144.
25. Milonski J, Zielinska-Blizniewska H, Golusinski W, Urbaniak J, Sobanski R, Olszewski J. Effects of three different types of anaesthesia on perioperative bleeding control in functional endoscopic sinus surgery. *Eur Arch Otorhinolaryngol*. 2013;270: 2045-2050.
26. Beule AG, Wilhelmi F, Kuhnel TS, Hansen E, Lackner KJ, Hosemann W. Propofol versus sevoflurane: bleeding in endoscopic sinus surgery. *Otolaryngol Head Neck Surg*. 2007;136: 45-50.
27. Yoo HS, Han JH, Park SW, Kim KS. Comparison of surgical condition in endoscopic sinus surgery using remifentanil combined with propofol, sevoflurane, or desflurane. *Korean J Anesthesiol*. 2010;59:377-382.
28. Ankichetty SP, Ponniah M, Cherian V, et al. Comparison of total intravenous anesthesia using propofol and inhalational anesthesia using isoflurane for controlled hypotension in functional endoscopic sinus surgery. *J Anaesthesiol Clin Pharmacol*. 2011;27:328-332.
29. Chaaban MR, Baroody FM, Gottlieb O, Naclerio RM. Blood loss during endoscopic sinus surgery with propofol or sevoflurane: a randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2013;139:510-514.
30. Manola M, De Luca E, Moscillo L, Mastella A. Using remifentanil and sufentanil in functional endoscopic sinus surgery to improve surgical conditions. *ORL J Otorhinolaryngol Relat Spec*. 2005;67:83-86.
31. Bairy L, Vanderstichelen M, Jamart J, Collard E. Clonidine or remifentanil for adequate surgical conditions in patients undergoing endoscopic sinus surgery: a randomized study. *PeerJ*. 2017;5:e3370.
32. Cho K, Lee JY, Park SK, et al. Comparison of surgical conditions during propofol or desflurane anesthesia for endoscopic sinus surgery. *Korean J Anesthesiol*. 2012;63:302-307.
33. Marzban S, Haddadi S, Mahmoudi Nia H, Heidarzadeh A, Nemati S, Naderi Nabi B. Comparison of surgical conditions during propofol or isoflurane anesthesia for endoscopic sinus surgery. *Anesth Pain Med*. 2013;3:234-238.
34. Yun SH, Kim JH, Kim HJ. Comparison of the hemodynamic effects of nitroprusside and remifentanil for controlled hypotension during endoscopic sinus surgery. *J Anesth*. 2015;29:35-39.
35. Gollapudy S, Riess ML. Non-invasive cardiac output monitoring during sinus surgery. *J Anesth*. 2015;29:639.
36. Ha TN, van Renen RG, Ludbrook GL, Wormald PJ. The effect of blood pressure and cardiac output on the quality of the surgical field and middle cerebral artery blood flow during endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2016;6:701-709.
37. Eberhart LH, Folz BJ, Wulf H, Geldner G. Intravenous anesthesia provides optimal surgical conditions during microscopic and endoscopic sinus surgery. *Laryngoscope*. 2003;113: 1369-1373.
38. Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A. Controlled hypotension for functional endoscopic sinus surgery: comparison of esmolol and nitroglycerine. *Indian J Otolaryngol Head Neck Surg*. 2013;65:440-444.
39. Di Mauro R, Lucci F, Martino F, et al. The role of intraoperative stroke volume variation on bleeding during functional endoscopic sinus surgery. *Minerva Anestesiol*. 2018;84(11): 1246-1253.
40. Sangkum L, Liu GL, Yu L, Yan H, Kaye AD, Liu H. Minimally invasive or noninvasive cardiac output measurement: an update. *J Anesth*. 2016;30:461-480.