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Surgical Field Visualization during Functional Endoscopic Sinus Surgery: Comparison of Propofol- versus 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 one of three 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 remifentanyl was titrated to decrease the mean arterial pressure to 60–70 mmHg, but not 30% from baseline. Surgical bleeding scores were recorded along with bleeding rates and hemodynamic parameters including cardiac

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Authors' Contributions:

Study conception, design: SG, DMP, MLR.

Data acquisition, analysis, interpretation: SG, DAG, DMP, TAL, MLR.

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output and systemic vascular resistance through pulse contour analysis from a radial arterial line. Statistics: Multiple comparison tests and regression analyses; $\alpha = 0.05$.

Results: 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 min), extubation time (9, 7, 8 min), recovery room time (65, 61, 61 min) or any hemodynamic parameters among groups 1 through 3, respectively. Group 1 required lower remifentanyl infusions than group 2 (0.11 vs 0.26 $\mu\text{g kg}^{-1} \text{min}^{-1}$; $P=0.01$). The bleeding score correlated positively with height ($P=0.014$) and the Lund-MacKay score ($P=0.013$). Bi- vs unilateral surgery led to longer surgery duration ($P=0.001$) and recovery room time ($P=0.004$).

Conclusion: When remifentanyl 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; remifentanyl; TIVA; volatile anesthetics

Introduction

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 importantly – controlled systemic hypotension, with target mean arterial pressures (MAP) generally between 50 and 70 mmHg.⁸

Bleeding from vascularized capillary beds is determined by central venous pressure (CVP) and MAP. With systemic 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, if 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, i.e. bleeding scores. All patients received a titratable remifentanyl 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™).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, WI, USA. All participants provided written informed consent before enrollment. Reporting adheres to the Helsinki Declaration and the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Eligibility

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

Enrollment

We screened 102 eligible American Society of Anesthesiologists (ASA) class one to three patients who underwent uni- or bilateral FESS under general anesthesia. Seventy-three patients consented, three 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 pre-determined sample size had been 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 three-group analysis of variance (ANOVA) with a power of 80%.

All patients were monitored with standard ASA monitoring: electrocardiogram, non-invasive blood pressure, pulse oximeter, concentration of inhaled O₂ and end-tidal CO₂, and temperature. After pre-oxygenation, general anesthesia was induced intravenously with propofol 2 mg kg⁻¹, lidocaine 1 mg kg⁻¹ and a remifentanyl infusion starting at 0.15 µg 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 sec later. To decrease bleeding, the surgeon (DMP or TAL) used topical epinephrine (1:1,000) on cotton pledgets (2 each side) for approximately five minutes prior to surgical start. This was followed by local anesthetic (5 to 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 of topical epinephrine (1:1,000) was provided from pharmacy for each patient.

Randomization, Blinding and Interventions

Before the procedure, patients were randomized to one of three anesthetic groups by the respective principal investigators of the study (SG and MLR) through sealed envelope technique with equal distribution of the three 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 µg kg⁻¹ min⁻¹ throughout the entire case; 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 µg kg⁻¹ min⁻¹ was given throughout the entire case. Since patient allocation to one of the three 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 post-anesthesia 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 three groups, remifentanyl was titrated to effect with the goal of achieving a MAP between 60 and 70 mmHg, 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™ platform¹² (both from Edwards Lifesciences Corp, Irvine, CA, USA) to measure arterial blood pressure, CO, cardiac index (CI equals CO divided by the body surface area which was calculated using the Mosteller formula¹⁴), and SVR. Hydromorphone 0.2 – 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 O₂ delivered via a face mask. The arterial line was removed in the PACU.

Outcomes

Primary outcomes: the surgeon provided a subjective surgical bleeding score every 15 min 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 non-site 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 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 min 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 Inc, San Jose, CA, USA). Categorical data were calculated as percentages, non-parametric data as median (1st, 3rd 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 non-parametric as were ranked data. Anesthetic groups were compared with each other by Chi-Square tests for categorical data, Kruskal-Wallis tests for non-parametric data and ANOVA for parametric data. If a difference was found among the three anesthetic groups by Kruskal-Wallis or ANOVA tests, post-hoc comparisons were done by Dunn's 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 $P < 0.05$ (two-tailed). Independent parameters included patient demographics such as gender, age, height, weight, body mass index (BMI), ASA score, Lund-MacKay score¹⁶ (LMS, determined by author DMP, 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, and the secondary outcomes of surgery duration, time from end of surgery to extubation, and PACU LOS, as well as 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, twenty-five patients with TIVA and twenty-three 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 three groups except for age ($P=0.04$). 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 remifentanyl rate which was found to be higher in the TIVA than in the desflurane group (median 0.26 vs 0.11 $\mu\text{g kg}^{-1} \text{min}^{-1}$; $P=0.01$), the type of anesthesia did not significantly affect any primary or secondary 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 ($P=0.014$) and LMS ($P=0.013$). Bilateral vs unilateral surgery (table 5) led to a 32% longer duration of surgery ($P=0.001$) and a 47% longer PACU LOS ($P=0.004$), but not to a higher EBL rate ($P=0.61$), or surgical bleeding score ($P=0.81$).

Because patients in the TIVA group required a significantly higher remifentanyl rate than in the desflurane group, we tested if the remifentanyl 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 ($P=0.04$). Within the range of our patients, MAP itself did not correlate with EBL rate ($P=0.29$).

Unintended Effects

We observed temporary hypertension in four patients and temporary and completely reversible ST changes in two patients with the injection of the local anesthetic with epinephrine; intra-operative hypotension in three patients; postoperative nausea in the PACU in six patients; postoperative hypertension in the PACU in two patients; prolonged postoperative sedation in seven patients; and postoperative epistaxis in two 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 of negative inotropic and chronotropic drugs have been tested. Sodium nitroprusside⁴ and nitroglycerin,¹⁸ have no advantage, whereas pre-operative metoprolol administration,¹⁹ intra-operative labetalol²⁰ or intra-operative esmolol administration consistently led to improved conditions.^{4,21,22} Studies using magnesium sulfate came to positive²² and negative conclusions.²³ Decreasing preload and improving venous drainage by reverse Trendelenburg has also been reported⁴ and became important to decrease intra-operative 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} were found to decrease blood loss in FESS and have, therefore, been used to compare TIVA with inhaled anesthesia.^{15,25,32,33} They 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 two (independent variable). In contrast, remifentanil (reported as a dependent variable) was titrated to effect to achieve controlled hypotension (MAP 60–70 mmHg). 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 three 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 either 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 remifentanyl to achieve the same MAP and subsequently EBL rate. Though 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 remifentanyl, HR, MAP, CO, CI or remifentanyl 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 non-parametric testing, it cannot be excluded that some outcome measurements are underpowered and fail to detect a true difference. We deliberately chose to titrate remifentanyl, routinely used as part of TIVA, to target 60–70 mmHg MAP instead of a fixed remifentanyl 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 remifentanyl infusion rate. Remifentanyl is an indirect sympatholytic drug⁸ with no further vasodilatory or directly cardiodepressant effects; esmolol may have led to a similar effect.^{4,18,21,22,38} We chose FloTrac¹² to measure CO and calculate its hemodynamic derivatives; a pulmonary artery catheter would not have been ethical, and the less invasive ClearSight^{TM39} 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. Lastly, 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 remifentanyl. 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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Figure 1. shows patient flow diagram in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. TIVA = total intravenous anesthesia.

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, and 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

Table 2**Baseline Demographics**

	Des (n=22)	Comb (n=23)	TIVA (n=25)	P
Age in years	50 (14)	46 (11)	41 (13) *	0.04
Female n (%)	16 (73)	15 (65)	16 (64)	0.79
Height in m	1.72 (0.12)	1.73 (0.09)	1.71 (0.10)	0.79
Weight in kg	85.6 (73.0, 97.0)	87.1 (68.9, 102.0)	78.9 (68.0, 103.4)	0.96
BMI in kg m ⁻²	28.6 (25.8, 32.5)	27.9 (23.4, 35.2)	28.3 (24.6, 34.0)	0.90
ASA Class >2 n (%)	7 (32)	6 (26)	6 (24)	0.83
Lund-MacKay Score	9 (6, 10)	8 (5, 11)	9 (6, 14)	0.63
Unilateral n (%)	4 (18)	6 (26)	5 (20)	0.79

Categorical data are given as percentage, non-parametric data as median (1st, 3rd quartile), and parametric data as mean (standard deviation). Des = inhaled anesthesia with Desflurane; Comb = combination of inhaled and intravenous anesthesia; TIVA = total intravenous anesthesia; BMI = body mass index; ASA = American Society of Anesthesiologists. P<0.05:

*
vs Des (two-tailed).

Table 3

Primary and Secondary Outcomes

	Des (n=22)	Comb (n=23)	TIVA (n=25)	P
Total EBL in ml	57 (32, 79)	61 (32, 81)	84 (39, 100)	0.21
EBL Rate in ml min ⁻¹	0.58 (0.48, 1.05)	0.57 (0.40, 0.72)	0.85 (0.50, 1.23)	0.29
Surgical Bleeding Score	2.1 (1.9, 2.4)	2.0 (1.8, 2.3)	2.0 (1.8, 2.6)	0.82
Surgery Duration in min	79 (65, 98)	86 (66, 123)	81 (67, 118)	0.59
Time to Extubation in min	9 (6, 12)	8 (5, 10)	7 (4, 8)	0.14
PACU LOS in min	65 (30)	61 (25)	61 (19)	0.80

Non-parametric data are given as median (1st, 3rd quartile), and parametric data as mean (standard deviation). Des = inhaled anesthesia with Desflurane; Comb = combination of inhaled and intravenous anesthesia; TIVA = total intravenous anesthesia; EBL = estimated blood loss; PACU LOS = length of stay in post-anesthesia care unit.

Table 4

Other Dependent Variables

	Des (n=22)	Comb (n=23)	TIVA (n=25)	P
HR in bpm	67.4 (7.5)	67.6 (10.4)	69.7 (11.0)	0.69
MAP in mmHg	63 (60, 67)	67 (63, 70)	67 (63, 73)	0.08
CO in l min ⁻¹	5.5 (4.5, 6.9)	5.9 (5.5, 7.5)	6.4 (5.5, 7.8)	0.21
CI in l min ⁻¹ m ⁻²	2.6 (2.5, 3.3)	3.1 (2.5, 3.9)	3.2 (2.7, 3.6)	0.18
SVR in dynes sec cm ⁻⁵	921 (248)	865 (235)	908 (257)	0.72
Remifentanyl in µg kg ⁻¹ min ⁻¹	0.11 (0.07, 0.15)	0.13 (0.10, 0.40)	0.26 (0.13, 0.47) *	0.01

Non-parametric data are given as median (1st, 3rd quartile), and parametric data as mean (standard deviation). Des = inhaled anesthesia with Desflurane; Comb = combination of inhaled and intravenous anesthesia; TIVA = total intravenous anesthesia; HR = heart rate; MAP = mean arterial pressure, CO = cardiac output; CI = cardiac index; SVR = systemic vascular resistance. P<0.05:

* vs Des (two-tailed).

Table 5

Uni- vs Bilateral Surgery

	Unilateral (n=15)	Bilateral (n=55)	P
Lund-MacKay Score	7 (5, 9)	9 (6, 13)	0.06
Duration of Surgery in min	65 (42, 80)	86 (68, 124) [†]	0.001
Total EBL in ml	50 (29, 71)	69 (39, 99)	0.09
EBL Rate in ml min ⁻¹	0.68 (0.50, 1.03)	0.69 (0.45, 1.12)	0.61
Surgical Bleeding Score	2.0 (1.9, 2.3)	2.0 (1.8, 2.4)	0.81
PACU LOS in min	45 (19)	66 (24) [†]	0.004

Non-parametric data are given as median (1st, 3rd quartile), and parametric data as mean (standard deviation). EBL = estimated blood loss; PACU LOS = length of stay in post-anesthesia care unit. P<0.05:

[†] vs unilateral (two-tailed).