Blood Loss and Visibility with Esmolol vs Labetalol in Endoscopic Sinus Surgery: A Randomized Clinical Trial

Philip F Lavere[1], Nikunj A Rana[1], Michael P Kinsky[2], J Sean Funston[2], Sharif S Mohamed[2] and Mohamad R Chaaban[1]

[1]Department of Otolaryngology, The University of Texas Medical Branch, Galveston, TX, USA.
[2]Department of Anesthesiology, The University of Texas Medical Branch, Galveston, TX, USA.

Clinical Medicine Insights:
Ear, Nose and Throat
Volume 12: 1–8

DOI: 10.1177/1179550619847992
SAGE

ABSTRACT

OBJECTIVES: Improved intraoperative visibility during functional endoscopic sinus surgery (FESS) decreases the risk of serious orbital or skull base injuries. Esmolol and labetalol have been used to reduce bleeding and achieve better visibility, but it remains unclear which drug is more effective. This study aims to measure visibility scores and mucosal bleeding rates for esmolol and labetalol in FESS.

METHODS: This is a 1-year randomized double-blind trial of adults undergoing FESS at a tertiary academic center. The inclusion criteria were as follows: age 18 or older; history of chronic rhinosinusitis (CRS) with or without nasal polyps; undergoing FESS for CRS; and American Society of Anesthesiologists (ASA) physical status 1 (healthy) or 2 (patient with mild systemic disease). The exclusion criteria were as follows: pregnancy; asthma, chronic obstructive pulmonary disease (COPD), bradycardia, heart failure, end-stage renal disease, cerebrovascular accident, diabetes mellitus; preoperative use of nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or beta-blockers; and body mass index (BMI) greater than 40 kg/m^2. Patients received either dose-infused esmolol or intravenous push labetalol. The primary outcome was intraoperative visibility determined by surgeon using validated scoring systems (Boezaart, Wormald). The secondary outcome was hemodynamic control (rate of blood loss, average mean arterial pressure [MAP], average heart rate [HR]). Hypothesis of no difference between drugs formed before data collection.

RESULTS: Of the 32 adults given drug (mean age = 50), 28 patients (13 esmolol and 15 labetalol) with complete data were included in the final analysis. There were no statistically significant differences between esmolol and labetalol in rate of blood loss (0.59 [0.28] vs 0.66 [0.37] mL/min, $P = 0.62$), average MAP (79.7 [7.5] vs 79.4 [7.7] mm Hg, $P = .93$), HR (72 [8.7] vs 68 [11.7] bpm, $P = .26$), or mean visibility scores for the Boezaart (3.1 [0.69] vs 3.1 [0.89], $P = .85$) and Wormald (6.1 [1.7] vs 5.9 [1.9], $P = .72$) grading scales.

CONCLUSIONS: There were no significant differences between esmolol and labetalol in rate of blood loss, MAP control, HR, or surgical visibility in FESS. Either drug may be used, and other considerations (availability, cost) can dictate choice.

KEYWORDS: chronic rhinosinusitis, functional endoscopic sinus surgery, mucosal bleeding, operative visibility, esmolol, labetalol

RECEIVED: February 5, 2019. **ACCEPTED:** April 1, 2019.

TYPE: Original Research

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Mohamad R Chaaban, Department of Otolaryngology, The University of Texas Medical Branch, 700 University Boulevard, Galveston, TX 77550, USA.
Email: mrchaaba@utmb.edu

Introduction

Chronic rhinosinusitis (CRS) is an inflammation of the nose and paranasal sinuses that persists for 12 or more weeks.[1,2] When appropriate medical therapy fails to resolve symptoms of CRS, functional endoscopic sinus surgery (FESS) is indicated.[3] Problematically, the nasal and sinus mucosa is highly vascularized and therefore prone to bleeding when performing functional endoscopic surgery.[4,5] Excessive mucosal oozing decreases intraoperative visibility, prolongs surgery time, and increases the risk of serious orbital or skull base injuries, including blindness and cerebrospinal fluid (CSF) leak.[6] Certain surgical and anesthetic techniques such as head elevation with the reverse Trendelenburg position, nasal decongestion, local anesthetics, and controlled hypotension (ie, safely reducing mean arterial pressure [MAP]) can limit intraoperative mucosal bleeding, thereby improving visibility.[4,5,7] Given the possibility of drug interactions, it is important to identify medications used in these methods that optimize a safe blood pressure (BP) goal without interfering with surgical field visibility.

Labetalol is a mixed alpha-beta adrenergic blocker that reduces BP and heart rate (HR); however, its alpha-blockade may offset the decongestant effects of topical epinephrine, a potent adrenergic receptor agonist used to improve visibility.[8,9] Esmolol, a selective beta-1 adrenergic blocker, reduces HR and MAP, and is not expected to interfere with topical epinephrine.[10] Our study is a double-blind randomized trial comparing the effects of esmolol and labetalol on intraoperative visibility and hemodynamic parameters during FESS.

Materials and Methods

Patients

A total of 172 patients were assessed for inclusion in the study. Among these, 134 patients were excluded and 38 patients were enrolled (Figure 1). Written informed consent was obtained from each patient enrolled in the study. The University of Texas Medical Branch Institutional Review Board approved the study (IRB # 15-0309). Our inclusion criteria included age

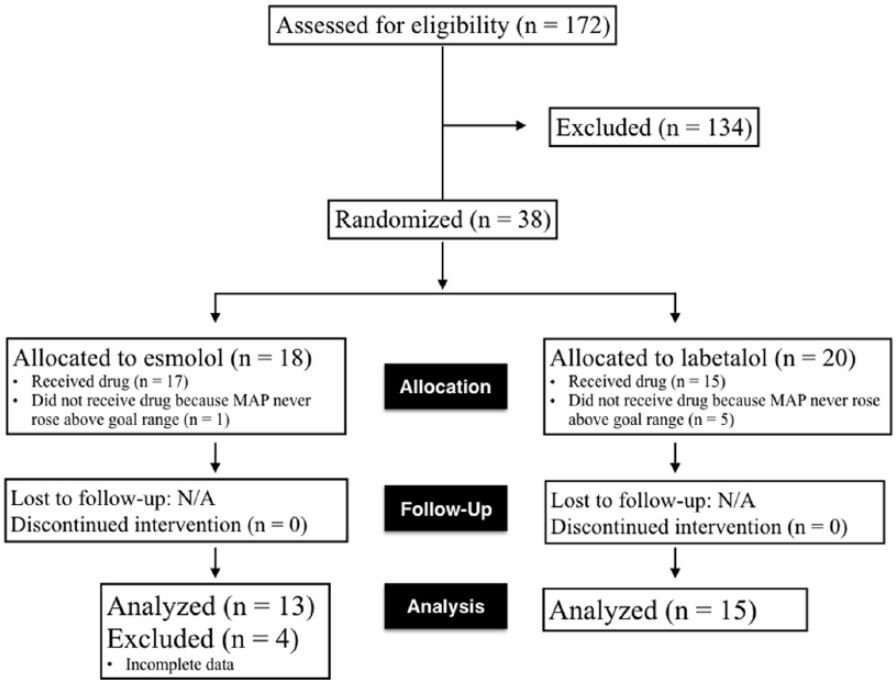

Figure 1. Study recruitment and allocation.
MAP indicates mean arterial pressure.

18 or older; a history of CRS with or without nasal polyps; planning to undergo FESS for CRS; and classified by the American Society of Anesthesiologists (ASA) as either physical status 1 (healthy) or 2 (patient with mild systemic disease). Exclusion criteria included pregnancy; a history of asthma, obstructive pulmonary disease, sinus bradycardia, severe bradycardia, heart failure, end-stage renal disease, cerebrovascular accident, or diabetes mellitus; preoperative use of nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or beta-blockers; and body mass index (BMI) greater than 40 kg/m^2.

Assignment and blinding

Patients were assigned to receive either esmolol or labetalol based on a computer-generated random sequence of binary numbers (0 = esmolol, 1 = labetalol) obtained before the enrollment period. This random sequence was used for drug assignment during sequential recruitment throughout the trial. Only the study coordinator knew the drug assignments, until it was disclosed to the anesthesiologists the day of operation. The surgeon was blinded to drug assignments and their administration with drapes, concealment tape on drug bags, and anesthesiologist discretion.

Anesthesia protocol

Anesthesia for this procedure used a balanced technique. The anesthesia protocol was developed to anticipate surgical stimulation as well as application of vasoactive agents administered for surgical exposure. Induction for patients in both drug groups consisted of 1 to 2 mg of midazolam, 1 to 3 μg/kg of fentanyl, 40 to 100 mg of lidocaine, and 2 to 4 mg/kg of propofol. After adequate ventilation and oxygenation were established, 0.05 to 0.10 mg/kg of intravenous (IV) vecuronium was administered prior to intubation.

Sevoflurane was used to achieve safe, controlled hypotension (MAP: 70 mm Hg for normotensive subjects and 80 mm Hg if the subjects had a history of hypertension) and an HR of 70 bpm and was initially adjusted up to 2% end-expired sevoflurane. Once 2% end-expired sevoflurane was reached, the anesthesiologist had the liberty to administer an additional 2 μg/kg of fentanyl for the entire surgery. Once sevoflurane and fentanyl reached their maximum acceptable dose, labetalol or esmolol was used to restore MAP and HR. For the labetalol drug group, aliquots of 10 mg were administered via slow intravenous push (IVP) every 10 minutes to achieve the MAP goal and HR goal, with a maximum dose of 300 mg for the duration of the surgery. For the esmolol group, IV esmolol (10 mg/mL solution) was infused at a rate of 0.1 mg/kg/min and titrated to achieve the MAP goal and HR goal, with a maximum dose of 0.3 mg/kg/min. If the maximum dosage was exceeded in either group and MAP remained 10 mm Hg above the target range, the anesthesiologist had discretion to administer other agents. If MAP fell below 60 mm Hg (70 mm Hg in subjects with a history of hypertension), the vasopressor phenylephrine was administered to re-establish MAP.

Surgical technique

For the entire procedure, the patients were placed in a supine position with 30 degrees of reverse Trendelenburg position. Initial local vasoconstriction was achieved with bilateral endonasal

application of oxymetazoline-soaked pledgets for 5 to 10 minutes. Topical 1:1000 epinephrine was also applied with cottonoid pledgets to the lateral nasal wall mucosa over the sphenopalatine recess, to the middle meatus, and to all polyps when present, and was then applied every 15 minutes to control bleeding and visibility. Endoscopic sinus surgery was then performed in the routine fashion by M.R.C.

Patients undergoing an inferior turbinate submucous resection and/or septoplasty also received injections of local anesthesia with 1:100 000 epinephrine into their septal and/or turbinate mucosa. Computed tomography (CT) scans of the patients were reviewed, and the severity of their sinus disease was rated using the Lund-Mackay (LM) scoring system.[11]

Outcome measures and statistical analysis

The primary outcome in this study was a comparison of hemodynamic parameters (rate of blood loss defined as estimated blood loss [EBL] per minute [EBL/min]) and surgical field visibility during FESS between the esmolol and labetalol groups.

All procedures were recorded and reviewed for their entire duration to determine intraoperative visibility at 15-minute intervals. Scores were given using validated surgical field grading scales (Boezaart, Wormald).[12–15] The minimum Boezaart score of 0 indicates no bleeding (cadaveric conditions), whereas the maximum score of 5 indicates severe bleeding (constant suctioning required). The minimum Wormald score of 0 indicates no bleeding, whereas the maximum score of 10 indicates severe bleeding (sphenoid fills < 10 seconds). The mean and SD for both grading scales were then determined. EBL was determined at the conclusion of the case, and rate of blood loss was calculated by dividing the total operative EBL by the duration of the procedure in minutes. In a previous study, we found suction canister volume estimation to be equivalent to calculating blood loss based on precise hemoglobin concentration measurements.[16]

Secondary outcomes included the duration of anesthesia, duration of surgery, time spent in the post-anesthesia care unit (PACU), average MAP, average HR, usage and amount of rescue pressor medication (phenylephrine), amount of fentanyl administered (μg/kg), average end-tidal expired sevoflurane, and average end-tidal carbon dioxide ($ETCO_2$). The mean values and SD were then determined for each of these secondary outcomes.

All data for the study outcomes were analyzed with the Wilcoxon rank sum test, which was used to compare the location shifts between the groups in 2-sided hypothesis testing. The *P*-value was based on asymptotic Wilcoxon 2-sample test with a continuity correction of 0.5. The 95% confidence interval for the location shift was based on Hodges-Lehmann estimation. Categorical data (sex) were analyzed with the chi-square test. Results were analyzed using the statistical program IBM SPSS Statistics (Version 24). *P*-value < .05 was considered significant a priori to the study.

Results

Of the 38 patients recruited for the study, 32 received either study drug, with 17 patients receiving esmolol and 15 patients receiving labetalol. Six patients enrolled did not require their allocated study drug and were thus excluded from the analysis. The operative video recordings of 2 esmolol patients were not recovered, so they were excluded from the analysis. In the electronic medical record of 2 esmolol patients, there were no CT scans available, and therefore their LM scores could not be determined; they were also excluded from the analysis. The demographic information and baseline characteristics (age, sex, BMI, LM scores, concurrent septoplasty) were not statistically different between the 2 drug groups (Table 1). The operating surgeon did not note a difference in nasal polypoid disease between the 2 drug groups.

There were no complications during surgery and all cases were completed as intended. There were no statistically significant differences in the duration of surgery, anesthesia, or PACU stay between the drug groups (Table 2).

The group comparisons on all outcomes did not show a significant difference ($P > .05$). There was no statistically significant difference between esmolol and labetalol in the Boezaart surgical field visibility grading scale (3.12 [0.69] vs 3.09 [0.89], $P = .85$, $df = 28$). There was also no statistically significant difference between esmolol and labetalol using the Wormald surgical field visibility grading scale (6.12 [1.72] vs 5.93 [1.91], $P = .72$, $df = 28$).

There were no statistically significant differences in total EBL or rate of blood loss between the 2 drug groups. Total EBL was 85.67 (54.01) mL in the esmolol group and 78.33 (48.28) mL in the labetalol group ($P = .79$, $df = 30$). The average rate of blood loss was 0.59 (0.28) mL/min in the esmolol group and 0.67 (0.37) mL/min in the labetalol group ($P = .62$, $df = 30$).

There were no statistically significant differences in any of the secondary outcomes. The esmolol average MAP was 79.69 (7.47) mm Hg, whereas the labetalol average MAP was 79.37 (7.70) mm Hg ($P = .93$). There were also no statistically significant differences in HR: the average intraoperative HR in the esmolol group was 72.14 (8.68) bpm, compared with labetalol with 67.81 (11.65) bpm ($P = .26$, $df = 30$). The average amount of fentanyl given to the esmolol group was (2.06 [1.2] μg/kg) and that given to the labetalol group was (2.31 [1.2] μg/kg) ($P = .58$). There was no statistically significant difference between the average intraoperative $ETCO_2$ concentration in the esmolol (36.8 [3.0] mm Hg) vs labetalol (35.6 [2.4] mm Hg) group. There was no statistically significant difference in the pressor use between the esmolol (296.3 [363.1] μg) and labetalol (650.0 [940.3] μg) groups ($P = .15$). The difference in mean end-expired sevoflurane percentage was not statistically significant between the 2 groups (1.68% esmolol vs 1.66% labetalol, $P = .81$).

Patients stratified according to their severity of sinus disease, as measured by the LM scoring system (more severe ≥ 10 LM subgroup vs less severe ≤ 9 LM subgroup), did not show any statically significant differences in any of the study outcomes between esmolol and labetalol (Tables 3 and 4). There were no statistically significant differences in age, BMI, or sex

Table 1. Demographic information and baseline characteristics of study patients.

CHARACTERISTICS	ESMOLOL (N = 13)	LABETALOL (N = 15)
Age (years)		
Mean (SD)	48.93 (18.35)	51.60 (18.42)
Median (Q1, Q3)	58.0 (30.0, 64.0)	57.0 (34.0, 67.0)
Male, No. (%)	9/13 (69)	10/15 (67)
BMI (kg/m^2)		
Mean (SD)	30.36 (4.87)	27.58 (3.32)
Median (Q1, Q3)	30.8 (25.2, 34.7)	27.0 (25.2, 29.1)
Lund-Mackay score		
Mean (SD)	10.38 (6.78)	9.80 (3.23)
Median (Q1, Q3)	10.0 (6.0, 14.0)	10.0 (7.0, 12.0)
Septoplasty, No. (%)	10 (67)	10 (67)

BMI, body mass index.

distribution between esmolol patients in both stratified groups. This was also true for the 2 stratified labetalol groups.

Discussion

Surgical management for CRS is indicated when appropriate medical therapy fails. However, mucosal bleeding represents a major limitation to FESS by increasing the risk of intraoperative injuries to the skull base and orbit. A variety of methods have been used to reduce mucosal bleeding; these include reverse Trendelenburg position, controlled hypotension, topical decongestants (eg, oxymetazoline and epinephrine), local anesthetic injection (eg, lidocaine), preoperative steroids, and selective use of anesthesia (eg, total intravenous anesthesia [TIVA], inhalational).[17–22] The aim of this study was to compare the effects of labetalol and esmolol on hemodynamic parameters and surgical visibility outcomes during FESS.

Our results showed that the rate of blood loss was comparable between the groups, and that both esmolol and labetalol are thus reasonable choices while performing FESS. In this regard, our findings are consistent with a number of other studies comparing either esmolol or labetalol with alternative agents such as sodium nitroprusside and nitroglycerin.[13,23–25]

We did not observe any difference in visibility scores between esmolol and labetalol; both drugs provided adequate visibility for the FESS procedure. This finding is noteworthy because, as mentioned earlier, labetalol can theoretically counteract the decongestant effects of topical epinephrine. As the surgeon assigning visibility scores was blinded to the study drug, our results suggest that labetalol does not limit the benefits of topical epinephrine. The reasons for this limited interaction are unclear. Regardless of the mechanisms involved, however, our findings suggest that either labetalol or esmolol may be used in conjunction with topical epinephrine to optimize visibility in the surgical field. Although our study suggests that these agents are equally effective in improving FESS visibility, at equivalent effective doses, labetalol is on average far cheaper than esmolol (one half to one tenth the price).[26–28] This price difference should be considered in cost-benefit analysis to help clinicians and hospitals select the most appropriate medications for FESS.

To address potential concerns over our limited sample size, we ran a futility analysis based on the EBL data to see how many patients would be required to show significant differences in blood loss, and therefore mucosal visibility, between the drug groups. Given the small differences in blood loss per minute during surgery between the treatment groups (0.59 compared with 0.66), and given the relatively large SDs obtained (0.28 and 0.37), 1245 patients would be required in each drug group (total N = 2490), using a unpaired *t*-test for the comparison, to show a statistically significant difference between the 2 treatments with a power of 0.8 and a type I error of 0.05. We thus conclude that a very large sample would be needed to show a significant difference in mucosal bleeding and visibility between esmolol and labetalol, and that continuing our study for this purpose would be futile.

Strengths of our study include the use of validated visibility scores, recording the entire procedure with intraoperative video, and calculating the average bleeding rate from data points taken throughout the surgery. We also held MAP constant at a safe hypotensive goal to better isolate the rate of bleeding effects on FESS visibility. In addition, we randomized patients and they and our surgeon were blinded. However, our study has several limitations. First, all the patients analyzed received either study drug, and there were no control patients receiving placebo. A control group would have allowed us to assess the role of either agent on hemodynamics and surgical visibility compared with baseline anesthesia. Second, our blood loss measurements were estimated, which can result in minor deviations from the actual blood loss values. Third, our mean HR values did not drop below 60, a level achieved by other beta-blocker studies that found significant reductions in surgical bleeding and improvements in visualization.[4,29] Finally, our study enrolled only ASA class 1 and 2 patients, so our results may not be applicable to FESS patients with other health comorbidities and higher ASA classifications.

Further research is needed to determine which anesthetic agents, when used in conjunction with either esmolol or labetalol, can result in the greatest improvement in intraoperative visibility during FESS. The manner in which intraoperative visibility can be best improved in patients with factors predisposing to hemodynamic instability (eg, heart failure, end-stage renal disease) should also be explored.

Conclusions

Our double-blind randomized trial found that esmolol and labetalol are equally effective during FESS; the 2 drugs did not yield statistically significant differences in the rate of blood loss or validated surgical field visibility scores.

Table 2. Comparing anesthesia and surgical parameters.

CHARACTERISTICS	ESMOLOL (N = 13)	LABETALOL (N = 15)	*P*-VALUE LOCATION SHIFT[a] (95% CI)
Duration (minutes)			
Surgery			
Mean (SD)	140.5 (49.73)	120.9 (28.62)	.24 –20.0 (–53.0, 12.0)
Median (Q1, Q3)	136.0 (95.0, 173.0)	129.0 (104.0, 138.0)	
Anesthesia			
Mean (SD)	193.2 (47.23)	175.2 (28.97)	.32 –16.0 (–49.0, 17.0)
Median (Q1, Q3)	193.0 (165.0, 217.0)	185.0 (151.0, 198.0)	
PACU			
Mean (SD)	113.0 (41.50)	90.73 (45.71)	.23 –19.0 (–56.0, 12.0)
Median (Q1, Q3)	109.0 (91.0, 139.0)	93.0 (69.0, 123.0)	
EBL (mL)			
Mean (SD)	85.67 (54.01)	78.33 (48.28)	.79 0.0 (–50.0, 30.0)
Median (Q1, Q3)	70.0 (50.0, 150.0)	65.0 (50.0, 100.0)	
Rate of blood loss (mL/min)			
Mean (SD)	0.59 (0.28)	0.66 (0.37)	.62 0.03 (–0.20, 0.32)
Median (Q1, Q3)	0.5 (0.3, 0.7)	0.6 (0.3, 0.9)	
Heart rate (bpm)			
Mean (SD)	72.14 (8.68)	67.81 (11.65)	.26 –4.0 (–12.4, 3.6)
Median (Q1, Q3)	69.0 (65.0, 78.2)	66.8 (61.1, 72.6)	
Mean MAP			
Mean (SD)	79.69 (7.47)	79.37 (7.70)	.93 –0.5 (–5.9, 6.5)
Median (Q1, Q3)	80.5 (72.2, 87.1)	79.1 (76.5, 84.7)	
Mean Boezaart score			
Mean (SD)	3.12 (0.69)	3.09 (0.89)	.85 0.0 (–0.8, 0.6)
Median (Q1, Q3)	3.0 (2.6, 3.6)	3.0 (2.3, 3.6)	
Mean Wormald score			
Mean (SD)	6.12 (1.72)	5.93 (1.91)	.72 –0.3 (–2.0, 1.0)
Median (Q1, Q3)	6.0 (5.0, 7.7)	5.4 (4.3, 7.0)	

CI, confidence interval; EBL, estimated blood loss; MAP, mean arterial pressure; PACU, post-anesthesia care unit.
[a]Location shift = group B – group A.

Table 3. Subjects with more mild sinus disease based on Lund-Mackay scoring system (<10).

CHARACTERISTICS	ESMOLOL (N=6)	LABETALOL (N=5)	*P*-VALUE LOCATION SHIFT[a] (95% CI)
Duration (minutes)			
Surgery			
Mean (SD)	132.8 (41.20)	101.0 (32.98)	.32 –31.0 (–96.0, 24.0)
Median (Q1, Q3)	130.0 (95.0, 154.0)	104.0 (94.0, 119.0)	
Anesthesia			
Mean (SD)	185.5 (41.56)	150.0 (30.85)	.12 –35.5 (–96.0, 20.0)
Median (Q1, Q3)	185.5 (148.0, 208.0)	143.0 (135.0, 168.0)	
PACU			
Mean (SD)	116.0 (62.93)	87.60 (38.70)	.52 –30.0 (–109.0, 55.0)
Median (Q1, Q3)	123.0 (68.0, 151.0)	97.0 (69.0, 119.0)	
EBL (mL)			
Mean (SD)	62.50 (24.44)	56.00 (26.08)	.63 0.0 (–50.0, 30.0)
Median (Q1, Q3)	60.0 (50.0, 75.0)	50.0 (50.0, 50.0)	
Rate of blood loss (mL/min)			
Mean (SD)	0.48 (0.17)	0.61 (0.34)	.65 0.1 (–0.3, 0.6)
Median (Q1, Q3)	0.4 (0.3, 0.6)	0.4 (0.4, 1.0)	
Heart rate (bpm)			
Mean (SD)	75.13 (10.65)	70.78 (2.83)	.78 –4.4 (–17.2, 10.0)
Median (Q1, Q3)	73.6 (67.9, 85.1)	71.7 (71.7, 72.1)	
Mean MAP			
Mean (SD)	78.45 (8.21)	83.95 (4.91)	.24 6.5 (–3.4, 16.9)
Median (Q1, Q3)	80.4 (70.3, 80.9)	82.1 (80.8, 87.2)	
Mean Boezaart score			
Mean (SD)	3.21 (0.60)	2.72 (1.07)	.41 –0.8 (–1.8, 1.3)
Median (Q1, Q3)	3.0 (3.0, 3.5)	2.3 (2.0, 3.3)	
Mean Wormald score			
Mean (SD)	6.08 (1.77)	5.89 (1.90)	.78 –0.6 (–2.5, 2.7)
Median (Q1, Q3)	6.0 (5.5, 6.5)	5.0 (4.8, 7.0)	

CI, confidence interval; EBL, estimated blood loss; MAP, mean arterial pressure; PACU, post-anesthesia care unit.
[a]Location shift = group B – group A.

Table 4. Subjects with more severe sinus disease based on Lund-Mackay scoring system (⩾10).

CHARACTERISTICS	ESMOLOL (N = 7)	LABETALOL (N = 10)	*P*-VALUE LOCATION SHIFT[a] (95% CI)
Duration (minutes)			
Surgery			
Mean (SD)	162.7 (45.31)	130.8 (21.49)	.09 –39.0 (–74.0, 12.0)
Median (Q1, Q3)	172.0 (119.0, 199.0)	131.0 (118.0, 146.0)	
Anesthesia			
Mean (SD)	216.1 (41.25)	187.8 (18.79)	.14 –24.0 (–72.0, 17.0)
Median (Q1, Q3)	215.0 (168.0, 260.0)	191.5 (174.0, 201.0)	
PACU			
Mean (SD)	114.1 (24.98)	92.30 (50.75)	.41 –18.5 (–69.0, 24.0)
Median (Q1, Q3)	123.0 (99.0, 136.0)	92.0 (71.0, 134.0)	
EBL(mL)			
Mean (SD)	121.4 (56.69)	89.50 (53.93)	.24 –37.5 (–100.0, 30.0)
Median (Q1, Q3)	150.0 (50.0, 150.0)	85.0 (50.0, 125.0)	
Rate of blood loss (mL/min)			
Mean (SD)	0.75 (0.32)	0.68 (0.40)	.66 –0.1 (–0.5, 0.3)
Median (Q1, Q3)	0.7 (0.5, 1.0)	0.7 (0.3, 0.9)	
Heart rate (bpm)			
Mean (SD)	69.89 (7.32)	66.33 (14.15)	.22 –4.9 (–16.8, 9.3)
Median (Q1, Q3)	67.1 (63.2, 76.2)	64.0 (58.0, 72.6)	
Mean MAP			
Mean (SD)	79.22 (7.33)	77.07 (8.00)	.73 –2.5 (–11.1, 7.0)
Median (Q1, Q3)	80.9 (72.2, 87.1)	77.6 (71.2, 84.7)	
Mean Boezaart score			
Mean (SD)	2.87 (0.75)	3.28 (0.77)	.38 0.3 (–0.6, 1.2)
Median (Q1, Q3)	3.0 (2.0, 3.6)	3.1 (2.8, 3.6)	
Mean Wormald score			
Mean (SD)	5.75 (1.85)	5.96 (2.02)	.88 0.2 (–2.3, 2.3)
Median (Q1, Q3)	6.0 (3.6, 7.7)	5.6 (4.3, 7.0)	

CI, confidence interval; EBL, estimated blood loss; MAP, mean arterial pressure; PACU, post-anesthesia care unit.
[a]Location shift = group B – group A.

Acknowledgements

The authors would like to thank Drs William Whitehead, Nicholas Defilippis, Husong Li, Nicole Ribeiro, Jeffrey Richards, and Adam Wacher in the Department of Anesthesiology, University of Texas Medical Branch, for their assistance in administering intraoperative anesthesia to the study patients. M.R.C. has full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of data analysis. This article was presented in an oral presentation at the Triological Society 121st Annual Meeting at COSM, National Harbor, MD, USA, April 20-21, 2018.

Author Contributions

Conceived and designed the analysis (NR, MK, JSF, MC, Collected the data (PL), Contributed data analysis or tools (PL, MC), Performed the analysis (PL, MC), Wrote the paper (PL, MK, MC), Other contributions - administered anesthesia protocol (MK, JSF, SM).

Data Sharing Statement

Individual participant de-identified data forming the results reported in this article will be shared with researchers who provide a methodologically sound proposal. This data sharing is to facilitate the aims of their approved proposal. In addition, the study protocol, statistical analysis plan, and analytic code will be available. The window for sharing begins upon publication and ends 5 years after article publication. Proposals should be directed to the corresponding author (mrchaaba@utmb.edu).

Trial Registration

This trial was registered at ClinicalTrials.gov under Trial # 03661346 (https://clinicaltrials.gov/ct2/show/NCT03661346).

ORCID iD

Philip F Lavere https://orcid.org/0000-0002-4943-8201

REFERENCES

1. Scadding GK, Durham SR, Mirakian R, et al. BSCAI guidelines for the management of rhinosinusitis and nasal polyposis. *Clin Exp Allergy*. 2008;38:260–275.
2. Shin HW. Animal models in CRS and pathophysiologic insights gained: a systematic review. *Laryngoscope Investig Otolaryngol*. 2016;1:116–123.
3. Lee JY, Lee SW, Lee JD. Comparison of the surgical outcome between primary and revision endoscopic sinus surgery for chronic rhinosinusitis with nasal polyposis. *Am J Otolaryngol*. 2008;29:379–384.
4. Jacob SM, Chandy TT, Cherian VT. Oral bisoprolol improves surgical field during functional endoscopic sinus surgery. *J Anaesthesiol Clin Pharmacol*. 2014;30:59–64.
5. Tewfik MA, Wormald PJ. Ten pearls for safe endoscopic sinus surgery. *Otolaryngol Clin North Am*. 2010;43:933–944.
6. Krings JG, Kallogjeri D, Wineland A, Nepple KG, Piccirillo JF, Getz AE. Complications of primary and revision functional endoscopic sinus surgery for chronic rhinosinusitis. *Laryngoscope*. 2014;124:838–845.
7. Degoute CS. Controlled hypotension: a guide to drug choice. *Drugs*. 2007;67:1053–1076.
8. Gunaratne DA, Barham HP, Christensen JM, Bhatia DD, Stamm AC, Harvey RJ. Topical concentrated epinephrine (1:1000) does not cause acute cardiovascular changes during endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2016;6:135–139.
9. MacCarthy PE, Bloomfield SS. Labetalol: a review of its pharmacology, pharmacokinetics, clinical uses and adverse effects. *Pharmacotherapy*. 1983;3:193–219.
10. Esmolol Wiest D. A review of its therapeutic efficacy and pharmacokinetic characteristics. *Clin Pharmacokinet*. 1995;28:190–202.
11. Lund VJ, Mackay IS. Staging in rhinosinusitis. *Rhinology*. 1993;31:183–184.
12. Fromme GA, MacKenzie RA, Gould AB Jr, Lund BA, Offord KP. Controlled hypotension for orthognathic surgery. *Anesth Analg*. 1986;65:683–686.
13. 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.
14. 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.
15. Athanasiadis T, Beule A, Embate J, Steinmeier E, Field J, Wormald PJ. Standardized video-endoscopy and surgical field grading scale for endoscopic sinus surgery: a multi-centre study. *Laryngoscope*. 2008;118:314–319.
16. 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.
17. Beule AG, Wilhelmi F, Kühnel TS, Hansen E, Lackner KJ, Hosemann W. Propofol versus sevoflurane: bleeding in endoscopic sinus surgery. *Otolaryngol Head Neck Surg*. 2007;136:45–50.
18. 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.
19. Carlton DA, Govindaraj S. Anesthesia for functional endoscopic sinus surgery. *Curr Opin Otolaryngol Head Neck Surg*. 2017;25:24–29.
20. Khosla AJ, Pernas FG, Maeso PA. Meta-analysis and literature review of techniques to achieve hemostasis in endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2013;3:482–487.
21. Blau WS, Kafer ER, Anderson JA. Esmolol is more effective than sodium nitroprusside in reducing blood loss during orthognathic surgery. *Anesth Analg*. 1992;75:172–178.
22. Laguna D, Lopez-Cortijo C, Millan I, Gonzalez FM, Garcia-Berrocal JR. Blood loss in endoscopic sinus surgery: assessment of variables. *J Otolaryngol Head Neck Surg*. 2008;37:324–330.
23. 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.
24. 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.
25. Hadavi MR, Zarei Y, Tarogh S. Comparison of effects of labetalol and nitroglycerine on intraoperative blood loss and surgical field quality in rhinoplasty surgery. *World J Plast Surg*. 2015;4:60–65.
26. Singh PP, Dimich I, Sampson I, Sonnenklar N. A comparison of esmolol and labetalol for the treatment of perioperative hypertension in geriatric ambulatory surgical patients. *Can J Anaesth*. 1992;39:559–562.
27. Drop L, Castelli I, Kaufmann M. Comparative doses and cost: esmolol versus labetalol during electroconvulsive therapy. *Anesth Analg*. 1998;86:916–917.
28. Richter A, Sheng C, Maxfield K, Naslund T. PS6 Effectiveness and cost of different intravenous drugs used for patients presenting with acute Stanford type B aortic dissection. *J Vasc Surg*. 2014;59:37S.
29. Nair S, Collins M, Hung P, Rees G, Close D, Wormald PJ. The effect of beta-blocker premedication on the surgical field during endoscopic sinus surgery. *Laryngoscope*. 2004;114:1042–1046.