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Platelet Function as Affected by Total Intravenous and Inhalational Anesthesia

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Abstract

Background: Few studies have attempted to demonstrate a benefit of a total intraveneous anesthesia (TIVA) as the sole technique to optimize and reduce bleeding. Also few reports have linked the use of propofol to platelet dysfunction, and while Thromboelastography (TEG®) has been used previously, its complement platelet mapping (PM™) has not. The aim of the study was to exclude different causes for blood loss during surgery, including drug effects on platelet function.

Methods: After IRB approval, we studied 23 patients scheduled to undergo endoscopic sinus surgery. Using a double-blind experimental method, we randomly assigned patients to receive either TIVA with propofol/remifentanil (PR) or inhalational anesthesia with sevoflurane/remifentanil (SR).

Results: Estimated blood loss (PR 152.9 ± 161.3 cc/SR 355.9 ± 393.4 cc) showed no significant group difference. Platelet function was within the normal range for both groups, though several preoperative TEG® parameters were statistically different between the two groups (PR values were greater than SR values for MA Activator, ADP MA, AA MA and ADP Aggregation; SR value was greater than PR value for ADP Inhibition). Several TEG® PM™ parameters had statistically significant differences pre- and postoperatively in the SR group (Postoperative were greater for ADP MA and ADP Aggregation; Preoperative value was greater for ADP Inhibition). Individual patient abnormalities were noted.

Conclusion: The results do not indicate any significant difference between propofol and sevoflurane as concerns blood loss and platelet inhibition.

Keywords: Propofol; Sevoflurane; TIVA; Platelet function tests; Platelet aggregation

Introduction

The control of bleeding is important in any surgery, but particularly in endoscopic sinus surgery (ESS) where visibility of the field is crucial for the surgeon to perform surgical maneuvers. Hemostasis is important perioperatively in these surgeries and the choice of anesthesia can be a deciding factor in reducing patient blood loss.

Propofol is a frequent choice of hypnotic anesthetic for TIVA due to its role as a vasodilator [1]. The advantages for ESS of a lower patient blood pressure, however, may be negated by reports that propofol has an adverse effect on blood coagulation [1-6]. The choice of anesthesia regimen is further complicated by research indicating inhalational anesthetics also inhibit platelet aggregation [5,6].

The purpose of this study was to investigate the potential differences in effects of two anesthesia regimens by measuring blood loss and platelet function. It was our hypothesis that, for the purposes of ESS, TIVA with propofol/remifentanyl would result in reduced blood loss than inhalational anesthesia with sevoflurane/remifentanyl.

Methods

This study was registered with the National Institutes of Health and can be found at http://clinicaltrials.gov/ct2/show/NCT01214057. After obtaining approval from the Committee for the Protection of Human Subjects, 23 patients aged 18-80, American Society of Anesthesia (ASA) grade I or II, scheduled to undergo endoscopic sinus surgery (ESS) for chronic rhinosinusitis were screened, consented and enrolled. Exclusion criteria included known coagulopathy or use of any drug that could affect thrombocyte function (e.g., aspirin, clopidogrel).

Anesthetic Protocol

Patients were randomly assigned using a blocked randomization method to receive either propofol/remifentanil (PR, n=12) or sevoflurane/remifentanil (SR, n=11) general anesthesia. Both patients and surgeons were blinded to the type of anesthetic used. Patients were premedicated in the holding area with dexamethasone and midazolam. The patients were monitored by American Society of Anesthesia (ASA) standards with ECG, non-invasive blood pressure, pulse oximetry and temperature probe. Their blood pressure was recorded every 2 minutes for the first 10 minutes, then every 5 minutes.

In order to reduce the visual bias of a propofol infusion, anesthesia was induced in both SR and PR groups with lidocaine 0.5 mg/kg, propofol infusion at 250 mcg/kg/min and total volume infused was adjusted for an induction dose of 2-3 mg/kg before bolus of muscle relaxant, rocuronium 0.5 mg/kg. Remifentanil infusion was started at a rate of 0.4 mcg/kg/min one to two minutes before the propofol infu-

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sion and a 100 ml 0.9% normal saline bag was used to blind surgeons in the SR group. Sevoflurane 1-3% was administered to the SR group and the propofol infusion was stopped. After intubation the remifentanil infusion was changed to 0.2 mcg/kg/min in both groups. In order to limit the amount of fluids administered, remifentanil was diluted at a concentration of 4 mg in 100 ml.

The target mean arterial blood pressure (MAP) was maintained at 70-80 mm Hg by adjusting the propofol concentration within its range (100-150 mg) and the sevoflurane concentration within its range (1-3 vol%) according to the anesthesiologist's judgement and by surgeon request. If this failed, the remifentanil rate was adjusted by 0.05 mg/kg/min. The end-tidal CO_2 level was continuously monitored and adjusted to a concentration of 32-34 mm Hg.

Surgery Protocol

Patients were positioned in the reverse Trendelenburg position and four squeezed cottonoids soaked with a mixed solution of epinephrine and lidocaine (1:100000 epinephrine:lidocaine 2% at 1:1) were applied topically to each nasal cavity. The surgical procedures were performed by three fellowship-trained surgeons from the Department of Oto-rhinolaryngology at the University of Texas Health Science Center in Houston, TX with subspecialty training in endoscopic sinus surgery using a similar stepwise technique. The IV line and solutions were foiled to prevent the surgeon from seeing the color of the anesthetic agent used. All surgeries took place at Memorial Hermann Hospital – Texas Medical Center, Houston, TX.

Blood Samples

Blood samples for the TEG® PM™ (Haemonetics® Corp, Braintree, MA, US) were drawn pre-operatively before induction of anesthesia to provide a baseline for platelet function, and post-operatively in the post anesthesia care unit (PACU) to see the effects of the anesthetics on platelet function. Blood (3-4 ml) was collected in a 4 ml Vacuette® test tube containing lithium heparin 14.5 Uml^{-1} and whole fresh blood (2 ml) was collected in a 3 ml regular syringe for transfer to the vial containing kaolin. After transferring 1 ml of whole blood into the vial, the kaolin activated blood (360 µl) was transferred to the first TEG® cup and analyzed as a standard TEG®. Blood (360 µl) from the heparinized tube was transferred to the second TEG® cup along with 10 µl Activator F-reptilase. The third TEG® cup was filled with filled with 360 µl heparinized blood along with 10 µl adenosine diphosphate (ADP) and 10 µl Activator F. Similarly, the fourth TEG® cup was filled with 360 µl heparinized blood along with 10 µl arachidonic acid (AA) and 10 µl Activator F.

The TEG® PM™ assay quantitavely measures blood viscoelastic properties during clot formation [7]. The maximum amplitude in the thromboelastographic trace is dependent on platelet function. Four values that represent clot formation are determined by this test: the R value (or reaction time), the K value, the angle and the MA (maximum amplitude). The R value represents the speed of clot formation (time until the first evidence of a clot is detected). The K value is the time from the end, or R, until the clot reaches 20 mm and this represents the speed of clot formation. The angleα, is the tangent of the curve made as the K is reached and offers similar information to K. The MA is a reflection of clot strength. A mathematical formula determined by the manufacturer can be used to determine a Coagulation Index (CI) (or overall assessment of coagulability) which takes into account the relative contribution of each of these 4 values into 1 equation.

Fluid was collected during surgery by the Neptune Waste Management System (Stryker, Kalamazoo, MI). Blood loss was determined by subtracting the volume of irrigation used intraoperatively from the total volume of fluid in the collection canisters. Fluid management was strictly monitored during surgery.

Operative Time

Surgical operating time (SOT) was defined as the time from the moment of injection of local anesthetic in the nasal cavity to the end of application of the local hemostatic agents. SOT was documented for each patient.

Quality of Recovery

The quality of recovery of patients was based on alertness and ventilator support/oxygenation at arrival to the post anesthesia recovery unit (PACU) from the time of extubation and again 30 minutes after arrival to the PACU, degree of pain reported by patient in PACU, amount and type of opioid and non-opioid analgesic given at discharge (after second phase PACU or 23 hours day surgery), abnormal blood pressure or heart rate values that necessitated intervention after PACU transfer, incidence of nausea and vomiting, and delay in discharge (if patient was in day surgery unit).

Postoperative Analgesia

One microgram of fentanyl/kg was given if the patient's visual analog scale (VAS) of pain was more than 6 before leaving OR. In the PACU, morphine 1-2 mg IV bolus every 5-10 minutes and ondansetron 4 mg IV bolus were administered if VAS > 4 and per patient request.

Statistical Analysis

Intercooled Stata version 9.2 statistical software (Stata Corporation, College Station, TX) was used to perform data analysis. A p value < 0.05 was defined as statistically significant. The study was originally powered for the primary goals of assessing blood loss and surgical field visualization in patients undergoing ESS and it was determined that an N of 30 would be needed Because the effects, measured by TEG-PM, of sevoflurane and propofol *in vivo* have not previously been reported in the literature, the prospective collection of data on platelet function in the current study is of a pilot nature. Due to the lack of previously re-

This table describes the patient demographics and hemodynamic parameters of the PR and SR groups and includes age, gender, duration of surgery, duration of anesthesia, oral or intranasal steroid use, systolic and diastolic blood pressure measurements, and estimated blood loss.

Parameters	PR group (n=12)	SR group (n=11)	p-value
Age	51.3 ± 16.2	50.3 ± 16.0	0.89
Gender (male)	7 (58.3%)	6 (54.5%)	0.86
Duration of surgery (hours)	2.4 ± 1.2	3.6 ± 1.8	0.07
Duration of anesthesia (hours)	3.3 ± 1.3	4.7 ± 2.0	0.06
Oral steroids (%)	3 (25.0%)	7 (63.6%)	0.06
Intranasal steroids (%)	3 (25%)	5 (45.5%)	0.30
Systolic blood pressure (mm Hg)	140.8 ± 19.5	132.1 ± 15.6	0.25
Diastolic blood pressure (mm Hg)	80.3 ± 10.0	79.6 ± 11.0	0.89
EBL (cc)	152.9 ± 161.3	355.9 ± 393.4	0.12
EBL > 200 cc (%)	4 (33.3%)	5 (45.5%)	0.55

Data are presented as mean ± SD. There were no statistically significant differences between the two groups. SD = Standard Deviation; EBL = Estimated Blood Loss; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl.

Table 1: Patient Demographics and Hemodynamic Parameters.

ported data and the observational nature of this study, a power analysis was deferred for this aim; the main outcome variable was platelet function (inhibition) as measured by TEG-PM, yielding the following parameters: maximal amplitutude (MA) of the thrombin, fibrin, AA and ADP assessment as well as platelet inhibition. Data were analyzed using the two-tailed Student's t-test (normally distributed data), two-tailed Mann-Whitney *U* test (non-normally distributed data), and chi-square test (categorical data). Data are reported as mean ± standard deviation, median [1st quartile, 3rd quartile], or percentage where appropriate.

Results

Twenty-three patients completed the study and were included in analysis. No statistically significant differences were observed between the two groups with respect to age, gender, duration of surgery, duration of anesthesia, steroid use, blood pressure, or estimated blood loss (Table 1).

Table 2a summarizes the preoperative TEG® values of the two groups and table 2b summarizes their postoperative TEG® values. Table 3a displays the preoperative TEG® PM™ values of the two groups and table 3b displays their postoperative TEG® PM™ values. Statistical significance was found for the preoperative TEG® PM™ parameters MA Activator (PR 10.1, SR 6.3, p-value 0.01), ADP MA (PR 58, SR 47.3, p-value 0.01), AA MA (PR 60.4, SR 52, p-value 0.02), ADP Inhibition (PR 22.7%, SR 34.6%, p-value 0.03), and ADP Aggregation (PR 0.8%, SR 0.7%, p-value 0.03) (Table 3a).

Table 4 and Table 5 compare the TEG® and TEG® PM™ preoperative and postoperative results for the PR group and SR group, respec-

This table provides the preoperative TEG® measurements for both the PR and the SR groups. These measurements include R (clotting time), SP (earliest clotting activity), Δ (R-SP), K (speed of clot formation), α (rate of clot strengthening), MA (maximum clot strength), and G (overall clot strength).

Parameter	PR Group (n=12)		SR Group (n=11)		P value
	Mean	Median	Mean	Median	
R (min)	5.0 ± 1.63	4.9 [4.1, 5.8]	5.8 ± 1.65	5.9 [5.0, 6.4]	0.25
SP (min)	4.1 ± 1.49	3.9 [3.2, 4.9]	4.5 ± 1.83	4.6 [3.5, 5.7]	0.46
Δ (min)	0.9 ± 0.36	0.9 [0.7, 1.1]	1.2 ± 0.68	1.1 [0.7, 1.5]	0.23
K (mm)	2.1 ± 0.42	1.9 [1.8, 2.4]	2.9 ± 1.72	2.3 [1.8, 3.0]	0.38
MA (mm)	71.2 ± 4.80	71.4 [69.1, 74.0]	62.3 ± 11.91	67.8 [54.1, 71.8]	0.06
α (°)	62.8 ± 5.09	63.9 [59.3, 67.4]	55.8 ± 13.72	61.2 [50.3, 64.7]	0.23
G (K dynes/cm2)	12.8 ± 3.22	12.5 [11.2, 14.2]	9.7 ± 3.50	11.2 [7.6, 12.5]	0.07

Data are presented as mean ± SD and median [1st Quartile, 3rd Quartile]. Two-tailed *P* value determined using Mann-Whitney *U* test. There were no statistically significant differences between the two groups. SD = Standard Deviation; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl

Table 2a: Preoperative TEG® Data.

This table provides the postoperative TEG® measurements for both the PR and SR groups. These measurements include R, SP, Δ, K, α, MA, and G.

Parameters	PR Group (n=12)		SR Group (n=11)		P value
	Mean	Median	Mean	Median	
R (min)	4.8 ± 2.21	5 [3.7, 5.9]	4.9 ± 1.69	5.2 [3.8, 5.4]	1.0
SP (min)	3.8 ± 1.86	4.3 [2.6, 4.8]	3.4 ± 1.88	4.2 [2.8, 4.2]	0.41
Δ (min)	1.1 ± 0.75	0.9 [0.5, 1.6]	1.4 ± 1.42	0.8 [0.6, 1.2]	0.82
K (mm)	2.0 ± 0.45	2.2 [1.7, 2.2]	1.9 ± 0.84	1.6 [1.3, 2.6]	0.45
MA (mm)	71.9 ± 5.66	72.1 [67.5, 75]	68.7 ± 7.88	70.5 [66.3, 73.9]	0.60
α (°)	61.8 ± 6.30	60.7 [57.8, 67.5]	62.4 ± 11.55	67.4 [55.4, 70.4]	0.55
G (K dynes/cm2)	12.2 ± 5.90	10.9 [9.7, 15.1]	11.9 ± 3.73	13.4 [9.8, 14.4]	0.94

Data are presented as mean ± SD and median [1st Quartile, 3rd Quartile]. Two-tailed *P* value determined using Mann-Whitney *U* test. There were no statistically significant differences between the two groups. SD = Standard Deviation; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl

Table 2b: Postoperative TEG® Data.

This table provides the preoperative TEG® PM™ measurements for both the PR and SR groups. These measurements include G (overall clot strength), TEG® MA (maximum clot strength), MA Activator (maximum clot strength of activator added), ADP MA (maximum contribution of adenosine diphosphate channel to clot strength), AA MA (maximum contribution of arachidonic acid channel to clot strength), ADP Inhibition (percentage of ADP receptors inhibited), AA Inhibition (percentage of AA receptors inhibited), ADP Aggregation (percentage of ADP aggregation), and AA Aggregation (percentage of AA aggregation).

Parameter	PR Group (n=12)		SR Group (n=11)		P value
	Mean	Median	Mean	Median	
G (K dynes/cm2)	12.8 ± 3.22	12.5 [11.2, 14.2]	9.7 ± 3.50	11.2 [7.6, 12.5]	0.07
TEG® MA (mm)	71.2 ± 4.80	71.4 [69.1, 74.0]	62.3 ± 11.91	67.8 [54.1, 71.8]	0.06
MA Activator (mm)	18.2 ± 16.12	10.1 [8.8, 20.5]	7.4 ± 6.24	6.3 [3.1, 7.9]	0.01*
ADP MA (mm)	58.2 ± 10.84	58 [49.4, 62.7]	42.8 ± 12.07	47.3 [36.5, 50.8]	0.01*
AA MA (mm)	60.5 ± 15.01	60.4 [52.3, 71.7]	50.6 ± 14.64	52 [47.7, 58.7]	0.02*
ADP Inhibition (%)	23.4 ± 12.92	22.7 [13.8, 32.2]	36.6 ± 13.21	34.6 [28.7, 39.25]	0.03*
AA Inhibition (%)	19.6 ± 22.15	13.4 [8.0, 18.0]	25.9 ± 26.07	20.3 [9.4, 31.1]	0.49
ADP Aggregation (%)	0.8 ± 0.13	0.8 [0.7, 0.9]	0.6 ± 0.13	0.7 [0.6, 0.7]	0.03*
AA Aggregation (%)	0.8 ± 0.22	0.9 [0.8, 1.0]	0.7 ± 0.26	0.8 [0.7, 0.9]	0.49

Data are presented as mean ± SD and median [1st Quartile, 3rd Quartile]. Two-tailed *P* value determined using Mann-Whitney *U* test. SD = Standard Deviation; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl.

Table 3a: Preoperative TEG® PM™ Data.

This table provides the postoperative TEG® PM™ measurements for both the PR and SR groups. These measurements include G, TEG® MA, MA Activator, ADP MA, AA MA, ADP Inhibition, AA Inhibition, ADP Aggregation, AA Aggregation.

Parameter	PR Group (n=12)		SR Group (n=11)		P value
	Mean	Median	Mean	Median	
G (K dynes/cm2)	12.2 ± 5.90	10.9 [9.7, 15.1]	11.9 ± 3.73	13.4 [9.8, 14.4]	0.94
TEG® MA (mm)	71.9 ± 5.66	72.1 [67.5, 75]	68.7 ± 7.88	70.5 [66.3, 73.9]	0.60
MA Activator (mm)	9.4 ± 4.15	9.5 [8.1, 9.8]	9.9 ± 8.95	7.9 [4.9, 9.9]	0.47
ADP MA (mm)	51.7 ± 15.58	54.3 [43.1, 65.1]	55.1 ± 9.20	54.9 [51.1, 61.2]	0.86
AA MA (mm)	57.7 ± 19.28	64.1 [52.8, 68.4]	57.1 ± 16.32	63.7 [50.7, 67.8]	0.81
ADP Inhibition (%)	29.7 ± 21.81	24.8 [14.4, 43.9]	22.1 ± 15.09	20.5 [13.4, 30.4]	0.39
AA Inhibition (%)	24.3 ± 25.98	18.1 [11.2, 27.9]	19.5 ± 23.19	9.7 [5.0, 29.7]	0.56
ADP Aggregation (%)	0.7 ± 0.22	0.8 [0.6, 0.9]	0.8 ± 0.16	0.8 [0.7, 0.9]	0.45
AA Aggregation (%)	0.8 ± 0.26	0.8 [0.7, 0.9]	0.8 ± 0.23	0.9 [0.7, 1.0]	0.57

Data are presented as mean ± SD and median [1st Quartile, 3rd Quartile]. Two-tailed *P* value determined using Mann-Whitney *U* test. There were no statistically significant differences between the two groups. SD = Standard Deviation; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl.

Table 3b: Postoperative TEG® PM™ Data.

This table provides the pre- and postoperative TEG® and TEG® PM™ measurements for the propofol/remifentanyl group only.

Parameter	Preoperative (n=12)		Postoperative (n=11)		P value
	Mean	Median	Mean	Median	
R (min)	5.0 ± 1.63	4.9 [4.1, 5.8]	4.8 ± 2.21	5 [3.7, 5.9]	0.91
SP (min)	4.1 ± 1.49	3.9 [3.2, 4.9]	3.8 ± 1.86	4.3 [2.6, 4.8]	0.83
Δ (min)	0.9 ± 0.36	0.9 [0.7, 1.1]	1.1 ± 0.75	0.9 [0.5, 1.6]	0.83
K (mm)	2.1 ± 0.42	1.9 [1.8, 2.4]	2.0 ± 0.45	2.2 [1.7, 2.2]	0.87
TEG® MA (mm)	71.2 ± 4.80	71.4 [69.1, 74.0]	71.9 ± 5.66	72.1 [67.5, 75]	0.83
α (°)	62.8 ± 5.09	63.9 [59.3, 67.4]	61.8 ± 6.30	60.7 [57.8, 67.5]	0.83
G (K dynes/cm2)	12.8 ± 3.22	12.5 [11.2, 14.2]	12.2 ± 5.90	10.9 [9.7, 15.1]	0.65
MA Activator (mm)	18.2 ± 16.12	10.1 [8.8, 20.5]	9.4 ± 4.15	9.5 [8.1, 9.8]	1.00
ADP MA (mm)	58.2 ± 10.84	58 [49.4, 62.7]	51.7 ± 15.58	54.3 [43.1, 65.1]	0.53
AA MA (mm)	60.5 ± 15.01	60.4 [52.3, 71.7]	57.7 ± 19.28	64.1 [52.8, 68.4]	0.88
ADP Inhibition (%)	23.4 ± 12.92	22.7 [13.8, 32.2]	29.7 ± 21.81	24.8 [14.4, 43.9]	0.57
AA Inhibition (%)	19.6 ± 22.15	13.4 [8.0, 18.0]	24.3 ± 25.98	18.1 [11.2, 27.9]	0.41
ADP Aggregation (%)	0.8 ± 0.13	0.8 [0.7, 0.9]	0.7 ± 0.22	0.8 [0.6, 0.9]	0.89
AA Aggregation (%)	0.8 ± 0.22	0.9 [0.8, 1.0]	0.8 ± 0.26	0.8 [0.7, 0.9]	0.67

Data are presented as mean ± SD and median [1st Quartile, 3rd Quartile]. Two-tailed *P* value determined using Mann-Whitney *U* test. There were no statistically significant differences between the two groups. SD = Standard Deviation; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl

Table 4: PR Group Pre- and Postoperative TEG® and TEG® PM™ Data.

tively. Statistical significance was found for the SR group in the TEG® PM™ parameters ADP MA (Pre 47.3, Post 54.9, p-value 0.02), ADP Inhibition (Pre 34.6%, Post 20.5%, p-value 0.02), and ADP Aggregation (Pre 0.7%, Post 0.1%, p-value 0.01) (Table 5).

Three patients (all in the SR group) had preoperative alterations of their baseline MA; two of these 3 patients had significant blood loss (described as blood loss > 200 ml) and none had a postoperative alteration of their TEG® PM™. Twelve patients (8 in the SR group and 4 in the PR group) had subtle preoperative MA-ADP alterations but 2 of these patients had significant percent inhibition of ADP or AA combined. One patient (PR group) had a postoperative ADP inhibition of 70.5% but significant blood loss (50 mL); however, the surgeon complained of oozing. Another patient (PR group) had significant blood loss (460 ml) with the surgeon noticing excessive oozing. The postoperative TEG® PM™ assay illustrated ADP inhibition of 35.1% and AA inhibition of 32.9% although this same patient had a preoperative TEG® PM™ showing ADP inhibition of 42.9% and AA inhibition of 84.9%. Six patients who had a significant change to either their preoperative or postoperative MA-ADP exhibited significant blood loss, compared to 8 patients with significant change that did not demonstrate significant blood loss.

Discussion

This study is the first to incorporate point-of-care testing for patients scheduled to undergo endoscopic sinus surgery (ESS). The reliance on maintaining a surgical field as close to bloodless as possible in these types of surgeries makes including a platelet function test as part of the preoperative preparations advisable, especially when assays such as the TEG®PM™ are available for bedside use. While our study was not designed to guide the course of anesthesia and drugs used intraoperatively, the implications of utilizing the TEG® assay in the surgical theater for assisting with hemostasis are clear. Shore-Lesserson et al. [8] demonstrated in a prospective, randomized clinical study that cardiac surgical patients that were given point-of-care coagulation monitoring using TEG® intraoperatively received fewer transfusions postoperatively. They concluded that the reduction in transfusions may have been due to improved hemostasis of these patients who had earlier and specific identification of hemostatic abnormalities and were able to receive appropriate transfusion therapy intraoperatively.

While the statistically significant differences between the PR and SR preoperative TEG® PM™ parameters (Table 3a) and between the pre-and postoperative TEG® PM™ parameters in the SR group (Table 5) were within the normal range for all parameters (as provided by the Haemonetics® Operator's Manual), the differences were marked enough to indicate that the platelet function in the SR group was undergoing changes. We are unable to comment on the clinical value of these changes due to our limited sample size, but further study is merited as sevoflurane has been shown to inhibit platelet aggregation induced by adenosine diphosphate [9,10].

Our results indicate that there is no difference in blood loss between an anesthesia regimen using propofol and one that uses sevoflurane. A double-blinded clinical study by Beule et al. [5] investigated the possible effect of propofol on ESS. Their study parallels ours in that they also compared the analgesics propofol and sevoflurane, however they used them in combination with the anesthetic fentanyl. Total blood loss was calculated by analyzing the hemoglobin content of the fluid contained in the suction unit. Our findings are consistent with their results of no

This table provides the pre- and postoperative TEG® and TEG® PM™ measurements for the sevoflurane/remifentanyl group only.

Parameter	Preoperative (n=11)		Postoperative (n=10)		P value
	Mean	Median	Mean	Median	
R (min)	5.8 ± 1.65	5.9 [5.0, 6.4]	4.9 ± 1.69	5.2 [3.8, 5.4]	0.16
SP (min)	4.5 ± 1.83	4.6 [3.5, 5.7]	3.4 ± 1.88	4.2 [2.8, 4.2]	0.11
Δ (min)	1.2 ± 0.68	1.1 [0.7, 1.5]	1.4 ± 1.42	0.8 [0.6, 1.2]	0.55
K (mm)	2.9 ± 1.72	2.3 [1.8, 3.0]	1.9 ± 0.84	1.6 [1.3, 2.6]	0.16
TEG® MA (mm)	62.3 ± 11.91	67.8 [54.1, 71.8]	68.7 ± 7.88	70.5 [66.3, 73.9]	0.22
α (°)	55.8 ± 13.72	61.2 [50.3, 64.7]	62.4 ± 11.55	67.4 [55.4, 70.4]	0.21
G (K dynes/cm2)	9.7 ± 3.50	11.2 [7.6, 12.5]	11.9 ± 3.73	13.4 [9.8, 14.4]	0.13
MA Activator (mm)	18.2 ± 16.12	10.1 [8.8, 20.5]	11.9 ± 3.73	13.4 [9.8, 14.4]	0.31
ADP MA (mm)	58.2 ± 10.84	58 [49.4, 62.7]	68.7 ± 7.88	70.5 [66.3, 73.9]	0.02*
AA MA (mm)	60.5 ± 15.01	60.4 [52.3, 71.7]	9.9 ± 8.95	7.9 [4.9, 9.9]	0.17
ADP Inhibition (%)	23.4 ± 12.92	22.7 [13.8, 32.2]	55.1 ± 9.20	54.9 [51.1, 61.2]	0.02*
AA Inhibition (%)	19.6 ± 22.15	13.4 [8.0, 18.0]	57.1 ± 16.32	63.7 [50.7, 67.8]	0.47
ADP Aggregation (%)	0.8 ± 0.13	0.8 [0.7, 0.9]	22.1 ± 15.09	20.5 [13.4, 30.4]	0.01*
AA Aggregation (%)	0.8 ± 0.22	0.9 [0.8, 1.0]	19.5 ± 23.19	9.7 [5.0, 29.7]	0.33

Data are presented as mean ± SD and median [1st Quartile, 3rd Quartile]. Two-tailed *P* value determined using Mann-Whitney *U* test. SD = Standard Deviation; PR = propofol/remifentanyl; SR = sevoflurane/remifentanyl

Table 5: SR Group Pre- and Postoperative TEG® and TEG® PM™ Data.

significant group difference. Pavlin et al. [11] and Law et al. [12] also found the same lack of difference in blood loss between total intravenous anesthesia and inhalational anesthesia. These studies differ from ours in that both studies compared the effects of propofol against those of isoflurane. Comparisons may still be drawn between our study and theirs despite the change in anesthetic from sevoflurane to isoflurane because Pavlin et al., Law et al., and we analyzed the propofol group's pre- and postoperative values separately as well to check for abnormalities in platelet function. Pavlin et al.'s study comprised ESS patients and their total blood loss for the propofol group (mean=189 ml) is similar to ours (mean=159 ml).

In contrast to our findings, Beuel et al. [5] documented that propofol inhibits platelet aggregation. This difference may be due to the coagulation monitor their study utilized. While we used the TEG® and TEG® PM™ assays, Beuele et al. used the Platelet Function Analyzer 100 (PFA 100®, Dade Behring). Tsou [13] evaluated the PFA 100® and compared it against the TEG® and concluded that the TEG® may offer more information about platelet function, coagulation factors, fibrin and fibrinolysis than the PFA 100®. His conclusion was based on the TEG®'s ability to use 5 different reagents for detection (TEG-Kaolin, TEG-Heparinase, mTEG, Rapid TEG®, and functional fibrinogen test) whereas the PFA 100® uses collagen and epinephrine as agonists. Moreover, Tsou notes that when using the PFA 100® to measure aspirin-mediated platelet inhibition, the method faces severe limitations that include poor correlation with other measures of platelet performance [13].

While our study did not find statistical significance between each anesthesia regimen's effects on platelet function, individual patients from both groups demonstrated abnormalities in platelet function. Of interest were the 8 patients who registered a significant change in platelet function during surgery. An understanding of why these changes occurred is difficult to come to as many factors could have affected their platelet function. Several of the 8 patients used corticosteroids orally or nasally, but their use of steroids may not have affected their platelet function as research by Jørgensen et al. analyzed ivy bleeding time, capillary fragility, and threshold ADP concentration for secondary platelet aggregation and platelet adhesiveness and found them to be unchanged by 2 days and 6 weeks of treatment with prednisone in 22 consecutive patients with collagen or hematological diseases [14]. Thong et al. also researched the effect of orally administered prednisone on 12 healthy volunteers after 2 days in a double-blinded study and found no statistical significance in mean bleeding times [15].

Another factor to consider in attempting to understand why these patients suffered no abnormalities during or after surgery was their group identification. As 4 patients belonged to the PR group and 4 belonged to the SR group, their respective anesthetics seem to have played a minor role, if any, in their blood profiles. Other possibilities include genetics, mechanical changes wrought through surgery, and fluid interactions.

As this study included an analysis of blood drawn postoperatively and surgeries were of duration longer than two hours, the use of propofol to induce anesthesia is not a confounding factor due to its half-life of 30 minutes [16]. Lidocaine also has the reported effect of inhibiting platelet function [17]. However, research indicates that therapeutic doses of lidocaine have a minimal effect on platelet function [18]. In our study lidocaine was administered intravenously as a bolus before the induction dose of propofol and then locally to the sinuses; it was also administered in both groups. Given the short half-life of lidocaine [19], the initial administration would have been metabolized by the end of surgery. Any pharmacological effects it may have had would have been present in both groups and therefore negligible.

The results of this study should be considered in the context of its limitations. One major limitation in this study is its pilot nature. The findings in this study must therefore be viewed cautiously due to the small sample size. Another limitation is the postoperative use of the TEG® assay instead of an intraoperative reading. Due to this delay in platelet function assessment, surgeons and anesthesiologists were unable to receive real-time feedback and alter the anesthetic regimen accordingly.

Conclusions

The results do not indicate any significant difference between propofol and sevoflurane as concerns blood loss and platelet inhibition. Individual genotypic and phenotypic features may manipulate platelet interactions which could influence the platelet coagulation variability seen. The use of TEG® PM™ in larger prospective studies could enlighten on the test or patient variability and its significance.

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Disclosure

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