

Effect of Total Intravenous Anesthesia and Inhalation Anesthesia on Edema and Ecchymosis in Rhinoplasty: A Prospective Randomized Clinical Trial

ABSTRACT

Background: Postoperative edema and ecchymosis are frequently observed in rhinoplasty patients. Total intravenous anesthesia and inhalation anesthesia are 2 of the common types of general anesthesia used for rhinoplasty surgery and affect circulation and coagulation. The aim of this study was to investigate the edema and ecchymosis effects of total intravenous anesthesia and inhalation anesthesia in patients undergoing rhinoplasty.

Methods: A total of 52 patients undergoing rhinoplasty surgery were enrolled. The patients were divided into 2 groups: total intravenous anesthesia (group T, n=26) and inhalation anesthesia (group S, n=26). All patients were photographed by a blinded observer on postoperative days 1, 2, and 7 and were evaluated on a scale ranging from 0 to 4 by 3 independent observers for periorbital edema and ecchymosis. Blood samples were taken from the patients preoperatively and at the second postoperative hour. At the end of the study, edema and ecchymosis of the patients, coagulation, and blood parameters were compared according to the anesthesia type.

Results: When rhinoplasty patients in group T and group S were evaluated according to edema and ecchymosis on postoperative days 1, 2, and 7, no statistically significant difference was found ($P > .05$). There was no difference between the groups in terms of coagulation and blood parameters ($P > .05$).

Conclusion: No difference between total intravenous anesthesia or inhalation anesthesia according to edema and ecchymosis can be seen in the postoperative period in rhinoplasty patients.

Keywords: Rhinoplasty, ecchymosis, edema, propofol, sevoflurane

INTRODUCTION

Rhinoplasty is a common surgical procedure performed today. Postoperative periorbital edema and ecchymosis, which are frequently seen after surgery, are 2 important causes of morbidity that affect the postoperative recovery process and social life of the patient.¹ The most important cause of edema and ecchymosis is trauma of the blood vessels in the osteotomy area of the performed rhinoplasty.²

Piezoelectric osteotomy or the conventional osteotomy technique with a chisel is used for osteotomy in rhinoplasty. Studies investigating the effects of both techniques on edema and ecchymosis have been carried out. Whereas no significant difference in edema and ecchymosis was found between patients undergoing a conventional osteotomy or piezosurgery in one study,³ in another study, higher edema and ecchymosis was found in conventional osteotomy than piezosurgery on days 1 and 7.⁴

Total intravenous anesthesia (TIVA) and inhalation anesthesia are 2 of the common types of general anesthesia used for rhinoplasty surgery. Total intravenous anesthesia has a more cardiac depressant effect, whereas inhalation anesthesia has a more peripheral vasodilation effect.⁵ Total intravenous anesthesia and inhalation anesthesia can affect circulation and coagulation, which affect edema and ecchymosis. It was found that TIVA compared to inhalation agents provided a better visual field and caused less bleeding in patients who underwent

Hakan Tapar¹ 
İbrahim Erdim² 
Mehtap Gürler Balta¹ 
Vildan Kölükçü¹ 
Tuğba Karaman¹ 
Ali Genç³ 
Gülçin Uysal² 
Serkan Karaman¹ 

¹Department of Anesthesiology and Reanimation, Tokat Gaziosmanpaşa University Faculty of Medicine, Tokat, Turkey

²Department of Otorhinolaryngology, Tokat Gaziosmanpaşa University Faculty of Medicine, Tokat, Turkey

³Turhal State Hospital, Tokat, Turkey

Cite this article as: Tapar H, Erdim İ, Gürler Balta M, et al. Effect of total intravenous anesthesia and inhalation anesthesia on edema and ecchymosis in rhinoplasty: A prospective randomized clinical trial. *ENT Updates*. 2023;12(3):114-119.

Corresponding author:

Hakan Tapar

E-mail: hakantapar@hotmail.com

Received: October 7, 2022

Accepted: January 24, 2023

Publication Date: June 16, 2023

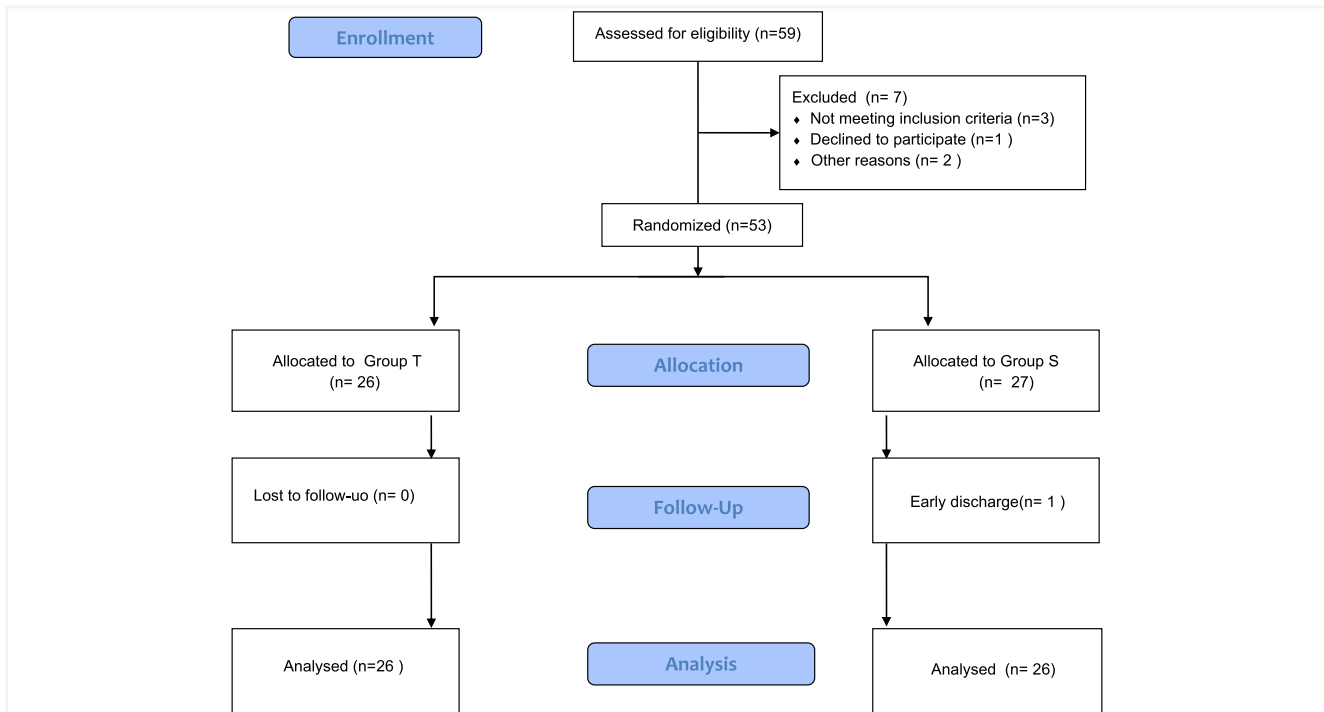


Figure 1. CONSORT flow diagram of the study.

endoscopic sinus surgery (ESS).⁶ However, there are studies that show that there is no difference between the 2 techniques.⁷

Comparison of the effects of these 2 anesthesia methods on edema and ecchymosis after rhinoplasty could affect the choice of anesthesia. Many studies have used steroids, periorbital cold packs, and different surgery techniques to prevent the development of periorbital edema and ecchymosis after rhinoplasty. We could not find a study in the literature investigating the effects of 2 different general anesthesia techniques on periorbital edema and ecchymosis after rhinoplasty. This study was designed to evaluate the effect of 2 different general anesthesia techniques in the prevention of periorbital ecchymosis and edema in patients undergoing rhinoplasty.

MATERIAL AND METHODS

This prospective randomized clinical trial study was carried out between March 2021 and August 2021. Ethics Committee of Tokat Gaziosmanpaşa University (21-KAEK-006) approved this study

and registered (clinicaltrials.gov; grant number NCT04773002). A total of 52 rhinoplasty patients who were aged between 18 and 45 years and with American Society of Anaesthesiologists (ASA) I and II were included. Written informed consent was obtained from the patients who agreed to take part in the study. Exclusion criteria of the study were bleeding disorder, abnormal coagulation findings, use of anticoagulant and anti-inflammatory drugs, and renal and hepatic disorders.

Patients were divided into 2 study groups, based on computer-generated randomization, according to TIVA (group T, n=26) and inhalation anesthesia (group S, n=26) (Figure 1). Premedication was not applied to patients, and surgery was performed by the same surgeon with open rhinoplasty technique.

Systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), heart rate, and blood oxygen saturation (SpO₂) were recorded before induction of anesthesia and during surgery for all patients. Anesthesia was induced with 1 µg/kg of fentanyl, 2 mg/kg of propofol, and 0.6 mg/kg of rocuronium for both groups. In group T, anesthesia maintenance was provided with propofol at a dose of 100-200 µg/kg/min and remifentanyl at a dose of 0.1-0.3 µg/kg/min (mixture of 50% air and 50% O₂). In group S, anesthesia maintenance was provided with sevoflurane and fentanyl. Sevoflurane remained constant at 1.2-1.5 minimum alveolar concentration (mixture of 50% air and 50% O₂). Sevoflurane concentration, propofol, and remifentanyl dosage were adjusted with the goal of maintaining an MAP of 55-65 mmHg. In this study, the chisel method was performed for osteotomy.

During the perioperative period, 5 mL/kg of Ringer's lactate solution was used for both groups. Only acetaminophen was used as a postoperative analgesic. All patients were photographed by a blinded observer on postoperative days 1, 2, and 7.

MAIN POINTS

- In rhinoplasty, total intravenous anesthesia (TIVA) and inhalation anesthesia are not effective for edema and ecchymosis.
- There is no difference between TIVA and inhalation anesthesia according to preoperative and postoperative hemogram in rhinoplasty.
- Total intravenous anesthesia and inhalational anesthesia have no different effects on bleeding in rhinoplasty.

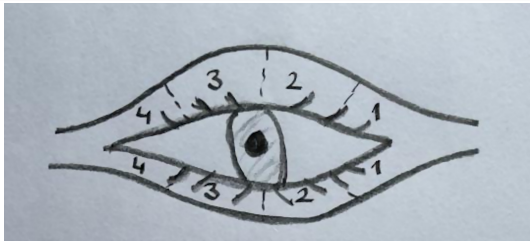


Figure 2. Level for periorbital ecchymosis: 0 (none), 1 (in the medial canthus), 2 (extending to the pupil), 3 (past the pupil), and 4 (extending to the lateral canthus).

For periorbital edema and ecchymosis, the scoring system developed by Kara and Gökalan,⁸ ranging from 0 to 4 (Figures 2 and 3), was used. Periorbital edema and ecchymosis were evaluated by 3 independent observers. Blood was taken from the patients at the preoperative and postoperative second hour. The blood values, amount of bleeding (with estimated amount of bleeding that accumulates in the surgical gauze and aspirator by an anesthetist), edema, and ecchymosis of the patients were compared according to the anesthesia procedure.

When ecchymosis score was accepted as 2.18 ± 0.13 mg in patients operated with TIVA from the study conducted by Valente et al⁹ and assuming a change by 5% on this value in patients with inhalation anesthesia, the accepted sample size to achieve a type 1 error ($\alpha = 0.05$) and power of 0.80 was 44 patients.

The Kolmogorov–Smirnov test was used to evaluate the normality of the distribution. The independent sample *t*-test, Mann–Whitney *U*-test, Pearson's chi-squared, and Fischer's exact test were performed to compare the data. All statistical analyses were done using Statistical Package for Social Sciences (SPSS) version 20.0 (IBM corp., Armonk, NY, USA). A *P*-value of $< .05$ was considered statistically significant.

RESULTS

A total of 52 patients undergoing open rhinoplasty were included in this study. Twenty-six patients were given TIVA (group T)

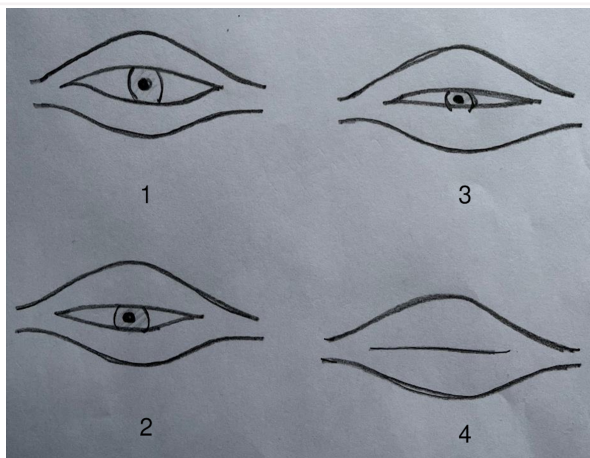


Figure 3. Scale for eyelid edema: 0 (none), 1 (minimal), 2 (covering to the iris), 3 (extending to the pupil), and 4 (massive edema).

Table 1. The Patients' Demographic Characteristics and Surgical Data

	Group T	Group S	P
Age (years)	26 (10)	27 (10)	1
Gender (n, %)			
Female	17 (65.4)	17 (65.4)	1
Male	9 (34.6)	9 (34.6)	
ASA (n, %)			
I	24 (92.3)	25 (96.1)	1
II	2 (7.7)	1 (3.9)	
Duration of surgery (minutes)	120 (100-150)	120 (90-150)	.06
Bleeding during surgery (mL)	200 (100-350)	225 (100-350)	.95
Intravenous fluids during surgery (mL)	600 (500-900)	550 (500-750)	.25
Room temperature (°C)	21.9 (20-23.1)	22.7 (20-24)	.06
Patient temperature (°C)	36.4 (36.0-37.3)	36.1 (36.0-37.3)	.30

ASA, American Society of Anaesthesiologists.

[mean age 26 (10) years] and 26 patients were given inhalation anesthesia (group S) [mean age 27 (10) years].

There was no statistically significant difference among the groups in terms of age, gender, ASA, duration of surgery, bleeding during surgery, intravenous fluids during surgery, room temperature, and patient temperature (Table 1, $P > .05$).

Table 2. The Patients' Laboratory Data

	Group T	Group S	P
PRO-HG	14.0 (12.5-17.30)	14.7 (12.0-18.7)	.52
POO-HG	12.75 (10.7-15.8)	13.10 (11.2-17.6)	.18
PRO-HTC	43.15 (3.86)	43.42 (3.83)	.80
POO-HTC	38.25 (32.4-47.3)	39.25 (33.4-50.6)	.39
PRO-PLT	279.73 (51.93)	272.23 (49.35)	.60
POO-PLT	240.12 (42.75)	252.5 (54.47)	.37
PRO-MPV	9.70 (7.7-11)	9.75 (8.10-11.5)	.78
POO-MPV	10 (8.2-10.9)	10 (7.59-11.10)	.90
PRO-INR	1.08 (0.094)	1.10 (0.133)	.53
POO-INR	1.19 (0.11)	1.18 (0.15)	.51
PRO-PT	14.37 (1.49)	14.76 (2.57)	.87
POO-PT	14.85 (1.93)	13.81 (2.42)	.10
PRO-PTT	27.66 (2.69)	27.53 (3.03)	.87
POO-PTT	27.17 (2.95)	28.32 (3.51)	.21
PRO-NT/LN	1.87 (0.78-3.82)	2.04 (0.75-7.68)	.10
POO-NT/LN	4.90 (1.69-2.47)	3.97 (1.38-26.87)	.31
PRO-PLT/LN	115.88 (48.16-262.5)	118.38 (68.24-231.03)	.87
POO-PLT/LN	131.71 (40.36-511.76)	125.40 (58.62-613.21)	.66

HG, hemoglobin; HTC, hematocrit; INR, international normalized ratio; LN, lymphocyte; MPV, mean platelet volume; NT, neutrophil; PLT, platelet; POO, postoperative; PRO, preoperative; PT, prothrombin time; PTT, partial thromboplastin time.

Table 3. The Patients' Edema and Ecchymosis Data

	Group T	Group S	P
<i>Right eye edema</i>			
First day	1 (0-2)	1 (0-1)	.12
Second day	1 (0-3)	1 (0-3)	.15
Seventh day	0 (0-1)	0 (0-1)	.64
<i>Left eye edema</i>			
First day	1 (0-2)	0 (0-3)	.19
Second day	1 (0-2)	1 (0-3)	.72
Seventh day	0 (0-2)	0 (0-1)	.60
<i>Right eye up ecchymosis</i>			
First day	1 (0-2)	1 (0-4)	.82
Second day	1 (0-3)	1 (0-4)	.07
Seventh day	0 (0-4)	0 (0-4)	.30
<i>Right eye down ecchymosis</i>			
First day	1 (0-4)	1 (0-4)	.48
Second day	1 (0-4)	1 (0-4)	.71
Seventh day	0 (0-3)	0 (0-4)	.08
<i>Left eye up ecchymosis</i>			
First day	1 (0-2)	1 (0-4)	.54
Second day	1 (0-4)	1 (0-4)	.23
Seventh day	0 (0-3)	0 (0-3)	.34
<i>Left eye down ecchymosis</i>			
First day	1 (0-4)	1 (0-4)	.13
Second day	1 (0-4)	1 (0-4)	.74
Seventh day	0 (0-3)	0 (0-3)	.84

There was no difference between the groups in terms of coagulation and blood parameters (Table 2, $P > .05$).

On postoperative days 1, 2, and 7, no differences were observed in terms of edema and ecchymosis between group T and group S (Table 3, $P > .05$).

DISCUSSION

This study is the first to compare edema and ecchymosis according to TIVA and inhalation anesthesia in patients with rhinoplasty. The results indicated that there is no difference between the effects of TIVA and inhalation anesthesia on edema and ecchymosis after rhinoplasty. Again, this study showed that both TIVA and inhalation anesthesia have the same effect on postoperative hemogram and conventional coagulation parameters.

Piezoelectric or chisel osteotomy technique is used for osteotomy in rhinoplasty. The 2 techniques have different effects. The piezoelectric technique causes less edema, ecchymosis, pain, and mucosal damage compared to the chisel method. But this method can increase the surgical time and the surgeon's injury. It is accepted that this problem can be overcome with experience.¹⁰

Inflammation and hemorrhage of soft tissues are the main causes of edema and ecchymosis.¹¹ Steroids reduce vascular permeability and migration of lymphocytes and neutrophils.⁹ There are many studies using steroids for this purpose. It showed that pre- and postoperative steroids reduce edema and ecchymosis.¹² In the literature, the neutrophil/lymphocyte ratio (NLR) and

platelet/lymphocyte ratio (PLR) are accepted as biomarkers of inflammation and immune suppression. In a study investigating the effects of TIVA and inhalation anesthesia on postoperative inflammation in pancreatic cancer patients, no difference was found between the groups according to NLR and PLR values.¹³ In this study, there was no difference between the postoperative NLR and PLR values of the patients who were operated on with TIVA and sevoflurane.

The endothelial glycocalyx (EG) is a layer on the luminal surface of the vascular endothelium. This layer is damaged under pathological conditions, such as inflammation, oxidative stress, and ischemia–reperfusion injury. Although it was shown that TIVA was superior to sevoflurane in EG protection, both TIVA and sevoflurane cannot prevent syndecan shedding, which is an indicator of EG damage.¹⁴

The stress response after trauma or injury causes immunological, hematological, and endocrine changes. Anesthesia can affect the inflammatory response by affecting the release of certain cytokines or neurotransmitters, as well as phagocytosis and apoptosis.¹⁵ A study evaluating the effects of stress response and apoptosis on leukocytes in TIVA and sevoflurane anesthesia showed that both techniques equally suppress endocrine, metabolic, and hemodynamic parameters and cell apoptosis markers in immune cells.¹⁶

Ecchymosis is usually caused by damage to the vessels. If bleeding continues in the lesion area and the remaining blood extravasates to the surface, ecchymosis begins to appear.⁹ The duration of surgery, the surgical procedure, and the patient's coagulation condition affect the formation of ecchymosis.¹¹ Studies have investigated the effects of TIVA and inhalation anesthesia on bleeding and coagulation. A study conducted on patients undergoing endoscopic sinus surgery found that TIVA provides a better field of view and causes less bleeding compared with sevoflurane anesthesia.⁶ This difference was generally attributed to the direct peripheral vasodilatation of sevoflurane causing an increase in both paranasal sinuses and cerebral blood flow¹⁷ and propofol causing controlled hypotension by depressing the central sympathetic tone without peripheral vasodilatation.¹⁸ However, another study showed no difference in terms of blood loss between the sevoflurane and TIVA groups.¹⁹

Both anesthesia and surgery are sources of stress for the patient. Surgical trauma results in vasodilation and increased vascular permeability. This causes the release of local chemicals such as bradykinin and prostaglandin, which are effective in inflammation and platelet activation.²⁰ Tissue trauma during surgery increases both coagulation factors and the release of stress hormones (such as cortisol, catecholamines, and glucagon) that cause blood hypercoagulability.²¹ Perioperative inflammatory response to surgery trauma causes hypercoagulopathy and vaso-occlusive events. This is known as the stress response to surgery. Sevoflurane has been shown to inhibit platelet aggregation in vitro studies. It shows this effect by suppressing thromboxane A2 formation and lasts for 1 hour postoperatively, although bleeding time is normal.²² Propofol inhibits adenosine diphosphate-induced platelet aggregation both in vitro and in vivo. It has a residual effect lasting 1 hour postoperatively. This effect disappears after 2 hours postoperatively and does not change the bleeding time.²³

In a study investigating the effects of propofol and sevoflurane on hemostasis, platelet function, and platelet aggregation by the thromboelastography method in patients undergoing endoscopic sinus surgery, no difference was found between the groups.²⁴ In a study that conducted tympanoplasty, the effect of TIVA and inhalation anesthesia on hemostasis according to platelet function, disseminated intravascular coagulopathy panel, and generalized D-dimer was negligible.²⁵ In a different study using rotational thromboelastometry analysis in elective ophthalmic surgery, there was no difference between the TIVA and sevoflurane groups in terms of hemostasis postoperatively.²⁶ In this study, there was no difference between the groups according to conventional hematological and coagulation parameters.

The NLR, PLR, and C-reactive protein are accepted as markers of stress response and inflammation. In a study related to case reports using remifentanyl and fentanyl, there were no differences between the groups.²⁷ We think that the remifentanyl we used in the study had no effect on edema and ecchymosis.

The first limitation is that a relatively small sample size was used in this study. The second limitation is that coagulation parameters were not studied using thromboelastography or rotational thromboelastometry. The third and fourth limitations are the subjective measurement of bleeding and the evaluation of edema and ecchymosis by blinded subjective raters.

CONCLUSION

In conclusion, the current study demonstrates that total intravenous or inhalational sevoflurane anesthesia has no effect on edema and ecchymosis in patients who underwent rhinoplasty. However, further studies in larger groups are required to better understand the clinical effects on postoperative edema and ecchymosis, and both anesthesia techniques can be preferable during rhinoplasty surgery.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Gaziosmanpaşa University (Approval No: 21-KAEK-006).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – H.T., İ.E.; Design – H.T., İ.E.; Supervision – H.T., İ.E.; Materials – H.T., M.G.B.; Data Collection and/or Processing – A.G., G.U.; Analysis and/or Interpretation – T.K.; Literature Review – H.T., V.K.; Writing – H.T.; Critical Review – S.K.

Acknowledgments: The authors would like to thank Tokat Gaziosmanpaşa University Departments of Anesthesiology and Reanimation and Otolaryngology for their valuable into the study.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: This study received no funding.

REFERENCES

- Levin M, Ziai H, Roskies M. Modalities of post-rhinoplasty edema and ecchymosis measurement: a systematic review. *Plast Surg (Oakv)*. 2022;30(2):164-174. [\[CrossRef\]](#)
- Chan DS, Roskies M, Jooya AA, Samaha M. Postoperative ecchymosis and edema after creation of subperiosteal tunnels in rhinoplasty: a randomized clinical trial. *JAMA Facial Plast Surg*. 2019;21(2):133-136. [\[CrossRef\]](#)
- Taşkın Ü, Batmaz T, Erdil M, Aydın S, Yücebaş K. The comparison of edema and ecchymosis after piezoelectric and conventional osteotomy in rhinoplasty. *Eur Arch Otorhinolaryngol*. 2017;274(2):861-865. [\[CrossRef\]](#)
- Koc B, Koc EAO, Erbek S. Comparison of clinical outcomes using a piezosurgery device vs. a conventional osteotome for lateral osteotomy in rhinoplasty. *Ear Nose Throat J*. 2017;96(8):318-326. [\[CrossRef\]](#)
- Deconde AS, Thompson CF, Wu EC, Suh JD. Systematic review and meta-analysis of total intravenous anesthesia and endoscopic sinus surgery. *Int Forum Allergy Rhinol*. 2013;3(10):848-854. [\[CrossRef\]](#)
- Brunner JP, Levy JM, Ada ML, et al. Total intravenous anesthesia improves intraoperative visualization during surgery for high-grade chronic rhinosinusitis: a double-blind randomized controlled trial. *Int Forum Allergy Rhinol*. 2018;8(10):1114-1122. [\[CrossRef\]](#)
- 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(9):1961-1962. [\[CrossRef\]](#)
- Kara CO, Gökalan I. Effects of single-dose steroid usage on edema, ecchymosis, and intraoperative bleeding in rhinoplasty. *Plast Reconstr Surg*. 1999;104(7):2213-2218. [\[CrossRef\]](#)
- Valente DS, Steffen N, Carvalho LA, Borille GB, Zanella RK, Padoin AV. Preoperative use of dexamethasone in rhinoplasty: a randomized, double-blind, placebo-controlled clinical trial. *JAMA Facial Plast Surg*. 2015;17(3):169-173. [\[CrossRef\]](#)
- Kisel J, Khatib M, Cavale N. A comparison between piezosurgery and conventional osteotomies in rhinoplasty on post-operative oedema and ecchymosis: a systematic review. *Aesthet Plast Surg*. 2022;1-11. [\[CrossRef\]](#)
- Tatar S, Bulam MH, Özmen S. Efficacy of adhesive strips to reduce postoperative periorbital edema and ecchymosis following rhinoplasty. *Turk J Med Sci*. 2018;48(1):34-39. [\[CrossRef\]](#)
- Aldhabaan SA, Hudise JY, Obeid AA. A meta-analysis of pre- and postoperative corticosteroids for reducing the complications following facial reconstructive and aesthetic surgery. *Braz J Otorhinolaryngol*. 2022;88(1):63-82. [\[CrossRef\]](#)
- Soliz JM, Ifeanyi IC, Katz MH, et al. Comparing postoperative complications and inflammatory markers using total intravenous anesthesia versus volatile gas anesthesia for pancreatic cancer surgery. *Anesthesiol Pain Med*. 2017;7(4):e13879. [\[CrossRef\]](#)
- Kim NY, Kim KJ, Lee KY, et al. Effect of volatile and total intravenous anesthesia on syndecan-1 shedding after minimally invasive gastrectomy: a randomized trial. *Sci Rep*. 2021;11(1):1511. [\[CrossRef\]](#)
- Song JW, Goligorsky MS. Perioperative implication of the endothelial glycocalyx. *Korean J Anesthesiol*. 2018;71(2):92-102. [\[CrossRef\]](#)
- Soto G, Pignolo F, Calero F, et al. Evaluation of Stress Response and Apoptosis on leucocytes in TIVA versus Balanced Anesthesia. *Open J Apoptosis*. 2017;6:1-16.
- Fraire ME, Sanchez-Vallecillo MV, Zernotti ME, Paoletti OA. Influencia de la premedicación con esteroides sistémicos en el sangrado y visualización del campo quirúrgico durante la cirugía endoscópica nasosinusal. *Acta Otorrinolaringol Esp*. 2013;64(2):133-139. [\[CrossRef\]](#)
- Cinčikas D, Ivaškevičius J, Martinkėnas JL, Balseris S. A role of anesthesiologist in reducing surgical bleeding in endoscopic sinus surgery. *Medicina (Kaunas)*. 2010;46(11):730-734. [\[CrossRef\]](#)
- 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(5):510-514. [\[CrossRef\]](#)
- Hahnenkamp K, Theilmeier G, Van Aken HK, Hoenemann CW. The effects of local anesthetics on perioperative coagulation, inflammation, and microcirculation. *Anesth Analg*. 2002;94(6):1441-1447. [\[CrossRef\]](#)

21. Rosenfeld BA, Faraday N, Campbell D, Dise K, Bell W, Goldschmidt P. Hemostatic effects of stress hormone infusion. *Anesthesiology*. 1994;81(5):1116-1126. [\[CrossRef\]](#)
22. Doğan IV, Ovalı E, Eti Z, Yayci A, Göğüş FY. The in vitro effects of isoflurane, sevoflurane, and propofol on platelet aggregation. *Anesth Analg*. 1999;88(2):432-436. [\[CrossRef\]](#)
23. Mizobe T, Nozuchi S, Aoki H, Nakajima Y, Shigemi K, Tanaka Y. Sevoflurane does not inhibit human platelet aggregation, possibly by compensating for the calcium mobilization by inositol 1,4,5-triphosphate. *Anesthesiology*. 1998;89(Supplement):144-152. [\[CrossRef\]](#)
24. Cattano D, Gomez-Rivera F, Altamirano AV, et al. Platelet function as affected by total intravenous and inhalational anesthesia. *J Anesth Clin Res*. 2012;4:1-6.
25. Özer E, Çeliker V, Aypar U, Başgül E. Influence of total intravenous and inhalational anaesthesia on haemostasis during tympanoplasty. *Acta Anaesthesiol Scand*. 2003;47(10):1242-1247. [\[CrossRef\]](#)
26. Koo B, Na H, Jeon Y, et al. The influence of propofol and sevoflurane on hemostasis : a rotational thromboelastographic study. *Anesth Pain Med*. 2014;9:292-297.
27. Agung Senapathi T, Subagiarta I, Utara Hartawan IAG, Thius A. Comparative effects of remifentanyl and fentanyl on inflammatory stress response in mastectomy surgery with general anesthesia: a case series. *Bali J Anesthesiol*. 2020;4(1):18-21. [\[CrossRef\]](#)