PERIODICUM BIOLOGORUM
VOL. 127, No 1–2, 39–44, 2025
DOI: 10.18054/pb.v127i1-2.35797

UDC 57:61
CODEN PDBIAD
ISSN 0031-5362

Review article

Airway management pharmacology: a narrative review

DAVOR KRIŽANOVIĆ[1,2]*
VLADIMIR DOLINAJ[1,2]
VEDRAN BALTA[3]
ALEKSANDRA PLEĆAŠ ĐURIĆ[1,2]
NATAŠA MARKOVIĆ[1,2]
DANIJELA MILENKOVIĆ[1,2]

[1] University Clinical Centre of Vojvodina, Clinic for Anaesthesia, Intensive Care, and Pain Therapy, Novi Sad, Serbia

[2] University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

[3] Faculty of Science, University of Zagreb, Zagreb, Croatia

***Correspondence:**
Davor Križanović
E-mail address: 911056d24@mf.uns.ac.rs

Keywords: anaesthetics; pharmacology; airway management; awake intubation

Abbreviations
ARDS – acute respiratory distress syndrome
ASA – American Society of Anesthesiologists
EDTA – ethylenediaminetetraacetic acid
ETI – endotracheal intubation
GABA – γ-aminobutyric acid subtype a
IV – intravenous
NMDA – N-methyl-D-aspartate

Received March 28, 2025
Revised June 28, 2025
Accepted July 3, 2025

Abstract

Background and purpose: *The selection of anaesthetics and their correct dosage when securing the airway by endotracheal intubation are crucial for patient safety. In this context, different classes of drugs play an essential role. Intravenous anaesthetics, such as propofol, are often used to induce anaesthesia. Knowledge of the pharmacokinetic and pharmacodynamic characteristics of intravenous anaesthetics is extremely important due to the possibility of adequate drug selection in relation to the patient's condition and the side effects produced by these drugs. Ketamine is an anaesthetic that provides dissociative anaesthesia, analgesia and amnesia, and is often used in emergency situations because of its favourable hemodynamic effects. In recent years, the use of ketamine has undergone significant expansion, as has the study of its anaesthetic effects. Muscle relaxants that facilitate intubation and ventilation during anaesthesia are an essential part of the complex process of establishing the airway. These drugs, in combination with hypnotics and opioid analgesics, facilitate endotracheal intubation. Opioid analgesics, such as fentanyl, are necessary drugs to establish an airway, given that endotracheal intubation is one of the most painful interventions in anaesthesia. for analgesia during procedures and immediate postoperative treatment of acute pain. Benzodiazepines are used in elective airway management with the aim of sedation and anxiety reduction.*

Conclusions: *The correct application of drugs and intubation techniques is directly related to the safety and efficiency of establishing the airway; thus, the quality of healthcare is significantly improved.*

INTRODUCTION

Airway establishment and endotracheal intubation (ETI) are life-saving interventions frequently performed in emergency medicine, intensive care, and prehospital medicine. Despite its prevalence, ETI is associated with significant patient morbidity and mortality and is considered the riskiest procedure frequently performed in emergency settings *(1,2)*. Airway manipulation in emergency situations can cause life-threatening hemodynamic changes in patients, and arterial hypotension usually prompts aggressive resuscitation efforts *(3)*.

Critically ill patients usually require endotracheal intubation (ETI) to improve oxygenation and ventilation *(3)*. However, the need to provide an airway poses a challenge for patients who are often hemodynamically unstable and cannot compensate for this procedure *(4)*.

According to several guidelines, difficult intubation is defined as when an experienced resuscitation physician anticipates or encounters difficulties with ventilation using a face mask, direct or video laryngoscopy, identifying anatomical structures, utilising supraglottic devices, or requiring urgent surgical airway establishment (5). Objective signs of

difficult intubation can be represented by objective classifications, such as the Mallampati classification, which assigns a severity score of 3 or 4. A patient in respiratory distress due to low oxygen reserve, as well as anatomical malformations of the mandible, palate, tongue, uvula, and aryepiglottic folds, is also a predictor of difficult intubation (*6,7,8*).

Difficult or unsuccessful airway establishment under anaesthesia is a significant cause of patient morbidity and mortality, including potentially preventing adverse outcomes such as airway trauma, brain damage, or patient death *(3,4)*. Difficult or unsuccessful intubation is a responsibility and challenge for anaesthesiologists. Updated airway guidelines and the implementation of new airway devices in practice may affect patient safety *(9)*.

Difficult intubation can occur due to various anatomical, physiological, or pathological factors and represents a crucial step in treatment. In such circumstances, the correct choice of drugs and their administration become crucial to ensure successful intubation and reduce potential complications. Understanding the pharmacology and mechanisms of action of drugs used in difficult intubation can contribute to patient safety and the efficiency of the intubation procedure *(9)*. Training for providing an airway is a continuous process that should begin with theoretical training, followed by training on phantom mannequins, and later in the operating room under controlled conditions under the supervision of an experienced anaesthesiologist, culminating in emergency care in the field itself *(10)*.

Inadequate planning of airway management and errors in judgment contribute to the harm suffered by the patient. The results of several studies emphasise the need to improve practical skills and establish protocols for handling difficult or failed tracheal intubation *(9)*. Although standard laryngoscopy is the most common emergency intubation technique, flexible endoscopy is a valuable skill within a physician's procedural capabilities. This has long been the gold standard method for patients considered too risky for neuromuscular blockade. Although video laryngoscopes have largely replaced direct laryngoscopy, according to guidelines, the use of flexible endoscopy has remained fairly constant, serving as the gold standard in difficult intubation (*6,7*).

ANAESTHETICS AND HYPNOTICS

The most commonly used drugs for hypnosis before patient intubation are propofol, ketamine (a racemic mixture of R and S forms of ketamine), etomidate and thiopentone *(7)*.

Ketamine is a phenylcyclidine derivative that causes dissociation of the thalamus from the limbic cortex. It belongs to NMDA (N-methyl-D-aspartate) receptor antagonists. It has an effect on opioid, noradrenergic, serotonin, dopamine and muscarinic effects. In addition to the hypnotic effect, it also shows effects on amnesia and an antidepressant effect. Due to its high solubility in lipids, it readily crosses the blood-brain and placental barriers (7). A dissociative dose of ketamine through the NMDA receptor desensitises the patient to ETI (or any other painful stimulus) while inducing amnesia, while airway reflexes, breathing, and arterial blood pressure are usually maintained, albeit at moderately elevated levels compared to the initial state *(6,*7). When ketamine is administered intravenously (IV) as a rapid bolus dose of 0.5 to 1 mg for the S form and 2 to 2.2 mg for the racemic mixture of R and S forms of ketamine. Fast application of ketamine may cause a brief period of apnoea that usually resolves quickly but is undesirable and can often be avoided by slowly administering ketamine over 30-60 seconds. This may require dilution of the drug or the creation of a combination with propofol, known as Ketofol (*6,7,8*). Ketamine can antagonise the effects of histamine and is used in the treatment of status asthmaticus (*7*). Ketamine causes dissociation of the cortex from brainstem functions; the eyes can remain open, but the patient is anesthetised. Because many brainstem reflexes remain intact, vomiting can occur when upper airway structures are stimulated. Vomiting occurs in approximately 5-15% of cases of ketamine administration in adults *(5)*. Due to the muscarinic effects, lacrimation and salivation are increased, and pupil dilation and nystagmus may occur. Involuntary movements of arms, legs, head and trunk are characteristic (*7*). Contraindications for the use of ketamine are cardiac dysfunction, unregulated hypertension and threatening aneurysmal ruptures. Additionally, due to the muscarinic effect and hypersalivation, the prior administration of atropine or glycopyrrolate intramuscularly is required as premedication for the patient if the operative field is in the oral cavity. The beneficial effects of ketamine are bronchodilatory in asthma and chronic obstructive pulmonary disease, primarily due to its potent bronchodilator effect on the smooth muscles of the tracheobronchial tree *(7)*. As a weak sympathomimetic, ketamine is more likely to maintain tissue perfusion during and after rapid intubation, compared to fentanyl, midazolam, thiopental, and especially propofol *(11)*. The increasing interest in the independent use of ketamine during the induction of general anaesthesia requires the existence of experience. This induction allows ETI to be performed while the patient continues to breathe, often referred to as awake intubation; however, the term 'awake' refers to a conscious but dissociated patient *(9)*.

Propofol (2,6-di-isopropyl-phenol) is an intravenous anaesthetic used for procedural sedation, for maintenance of anaesthesia, or as an induction agent for general anaesthesia. It can be administered as a bolus or infusion or in combination with other hypnotics. Propofol is prepared in a lipid emulsion, which gives it its characteristic milky-

white appearance and the colloquial name "milk of amnesia" The formula contains soybean oil, glycerol, egg lecithin and a small amount of the preservative EDTA (ethylenediaminetetraacetic acid). A strict aseptic technique must be employed when preparing propofol because the emulsion provides a favourable environment for bacterial growth *(12,13,14)*. EDTA (ethylenediaminetetraacetic acid) is used as an emulsifier to inhibit bacterial growth. There is a 1% emulsion, and another formulation is 2%. Commercial formulations are stable at room temperature and can be diluted with 0.9% NaCl or 5% glucose solution. In contact with air, propofol oxidises in 6 hours and turns yellow. After opening, it can only be used once *(7)*. Propofol exerts sedative and general anaesthetic effects by reducing excitation and increasing the activity of the GABA (γ-aminobutyric acid subtype a) neurotransmitter (*15,16)*. Due to its high liposolubility, it quickly crosses the blood-brain barrier. It is distributed rapidly in the tissues and quickly eliminated. Propofol is metabolised in the liver with the help of oxidases, and the metabolite is 1,4-diisopropyl quinol *(7)*. Intravenous administration of propofol creates a euphoric mood and long-term relaxation; the increase in dopamine levels in the nucleus accumbens is responsible for the pleasant feeling (1*7*). Propofol can cause hemodynamic instability through vasodilation and reduced myocardial contractility *(18)*. The induction dose for intubation is 2 to 2.5 mg/kg/tm. It results in a decrease in arterial blood pressure of 24% to 40% compared to the initial values. A decrease in heart rate can explain a decrease in cardiac output. Due to the inhibition of the baroreceptor effect, there is no compensatory tachycardia after hypotension. The response to atropine after propofol administration was also reduced. The distribution time is 2 to 4 minutes, and the half-elimination time is 1 to 3 hours. Duration of hypnosis after iv bolus is 5 to 10 minutes. Since even short-term hypotension is associated with mortality, impaired hemodynamics may contribute to increased mortality (7*,19,20)*. There are several beneficial effects of propofol, including antioxidant properties, suppression of apoptosis, and an anti-inflammatory effect, all of which may have a protective role on organs (2*1,22)*.

Etomidate is a non-barbiturate intravenous anaesthetic. This drug is a hydrolysed imidazole salt that achieves its sedative and anaesthetic effects mainly by binding to γ-aminobutyric acid subtype receptors in the central nervous system *(23)*. This anaesthetic is suitable for the induction of general anaesthesia in critically ill patients because it maintains hemodynamic stability (21,22). Cortisol levels return to baseline by the third postoperative day following an etomidate infusion. Cortisol recovery occurs within 24 hours after a single dose of etomidate. Therefore, continuous administration of etomidate is not recommended (*24)*. There is no evidence that adding corticosteroids after etomidate improves outcomes, including 28-day mortality, duration of mechanical ventilation, or length of stay in the intensive care unit *(25)*. A meta-analysis of 14 studies found increased mortality in patients with an ASA (American Standards Association) score of 4 who received a single dose of etomidate, but no differences in outcome were observed between etomidate and propofol in the ASA 3 subgroup *(26*). Etomidate has several significant side effects, such as adrenal suppression, muscle spasm, pain after drug application, nausea and vomiting, which limit its clinical use *(26,27,28,29)*. Induction of general anaesthesia with etomidate (as opposed to propofol) results in mild hypertension intraoperatively. Improved hemodynamic stability was observed with etomidate compared to propofol, especially in patients with a high risk of mortality, including those who are hemodynamically unstable, e.g. septic or bleeding *(30,31)*. A meta-analysis revealed no significant difference in emergency intubation success rates between using etomidate and ketamine as induction agents. This result potentially suggests that both hypnotics provide similar and appropriate conditions for intubation and enable the timely establishment of a definitive airway in acutely ill patients *(32)*.

Thiopental sodium is an intravenous anaesthetic and is the standard against which other anaesthetics are compared. The specificities of thiopental include its long elimination half-life. Indications are allergies to other hypnotics as well as neurosurgical patients where the goal is to lower elevated intracranial pressure. It has weak analgesic and muscle relaxant effects. The intubation dose applied during induction of anaesthesia is 5 mg per kilogram of body weight. The duration of action is about 6 to 8 minutes *(33)*. Loss of consciousness after administration of an intravenous dose (3 to 4 mg/kg of body weight) is usually achieved within 10 seconds, and anaesthesia lasts for 3 to 5 minutes, which is slightly shorter than with propofol. Caution is required in patients with chronic obstructive pulmonary disease, hypovolemia, cardiac, renal, and hepatic dysfunction, as well as in children *(7)*.

BENZODIAZEPINES

Midazolam is a short-acting benzodiazepine with an elimination half-life of 1.5 to 2.5 hours (*34)*. It is used to induce sedation, hypnosis, anxiolysis, amnesia and reduction of muscle tension. The place of application is conscious sedation, premedication, co-induction or as a co-anaesthetic for induction of anaesthesia as well as long-term sedation in intensive care units. Doses for premedication are 0.05 mg/kg of body weight *(7)*. It is a general rule to avoid deep sedation with complete respiratory paralysis during intubations outside the operating room. Analgesia with midazolam can be used for this purpose. Excessive sedation can reduce reflexes and airway patency. Then intubation is resorted to on an awake patient or with the use of sedatives from the group of short-acting benzodiazepines such as midazolam or a

combination of midazolam 0.05 to 2 mg/kg body weight and opioids, usually fentanyl in small doses of 0.05-1μ/kg body weight *(35)*.

LIDOCAINE

Careful upper airway anaesthesia is critical for successful awake intubation. When attention is paid to this procedure, we find that additional sedation drugs are often not even necessary. As lidocaine 4% contains 40 mg of lidocaine per ml of liquid, for a 70 kg adult, the safe dose is approximately 15 ml of solution. It is important to monitor and recognise the rare occurrence of local anaesthetic toxicity *(7)*. Rapid crash intubation uses anaesthesia induction and neuromuscular blockers for rapid induction with sedation and paralysis, facilitating placement of an endotracheal tube. Emergency and intensive care physicians should consider awake intubation in patients with a difficult airway or challenging physiologic characteristics to avoid the inability to oxygenate and ventilate *(24)*.

DEXMEDETOMIDINE

Dexmedetomidine is a very useful drug for intubation in an awake patient who retains the ability to breathe with an agonist effect on α-adrenoreceptors with a markedly increased affinity for α2 receptors. The effect on α2-adrenoreceptors within the pons mediates its sedative effects, while the action on spinal α2-adrenoreceptors produces analgesia. Its ability to produce sedation and analgesia without respiratory depression means it is increasingly being used for procedural sedation. Inhibition of noradrenaline release and bradycardia decrease cardiac output and result in hypotension. Direct effects on the vascular wall after IV bolus injections of 1mg per kg may result in the development of transient hypertension, causing further reflex bradycardia *(37)*.

MUSCLE RELAXANTS

Two large groups of muscle relaxants are used for recalcification during intubation. The only representative of depolarising relaxants is suxamethonium chloride, also known as succinylcholine. It is a depolarising muscle relaxant that acts within 30 seconds and has an average effect duration of three to five minutes *(7)*. Hyperkalaemia can cause heart rhythm disturbances due to its connection with the modulation of the acetylcholine receptor, which serves as the basic molecular mechanism. Activation of the acetylcholine receptor by succinylcholine, acetylcholine, or choline causes hyperkalaemia in the extracellular space. However, certain pathological conditions cause the proliferation of acetylcholine receptors and the appearance of immature receptors that are capable of a more significant efflux of potassium into the bloodstream. Pathological conditions include upper and lower neuron injuries, significant burns, trauma, immobility, muscle tumours, and muscular dystrophy *(38)*. Pseudocholinesterase is a serine hydrolase enzyme primarily produced in the liver that catalyses the hydrolysis of choline esters, most notably succinylcholine and mivacurium. The key is to distinguish this enzyme from "true" cholinesterase, also known as acetylcholinesterase. It occurs in higher concentrations within conductive tissues such as the central or peripheral nervous system and neuromuscular synapses. Due to its diverse functions and tissue distribution within the human body, pseudocholinesterase is often referred to by various names, including plasma cholinesterase, serum cholinesterase, acetylcholine acetyl hydrolase, and butyrylcholinesterase. A deficiency of cholinesterase can lead to prolonged relaxation after the administration of succinylcholine *(39)*.

Rocuronium bromide is one of the most important non-depolarizing muscle relaxants. Used to induce muscle relaxation during intubation, surgical procedures and lung ventilation in severe forms of acute respiratory distress ARDS (acute respiratory distress). Recognised for its rapid onset and reversibility within its drug class, rocuronium offers distinct advantages over other nondepolarizing relaxants (*40*). The standard dose for intubation during anaesthesia is 0.6 mg/kg rocuronium bromide, after which conditions for intubation are established within 60 seconds in almost all patients. A dose of 1.0 mg/kg rocuronium bromide is recommended to facilitate tracheal intubation during rapid induction of anaesthesia. If a dose of 0.6 mg/kg rocuronium bromide is used for rapid induction of anaesthesia, it is recommended that the patient be intubated 90 seconds after administration of rocuronium bromide *(7)*. The maintenance dose is 0.15 mg/kg rocuronium bromide. In the case of long-term inhalation anaesthesia, it is necessary to reduce the dose to 0.075-0.1 mg/kg *(40)*.

Cisatracurium is also a non-depolarizing muscle relaxant that does not cause histamine release, and therefore, it does not produce cardiovascular effects or affect bradycardia caused by other anaesthetics or vagal stimulation during surgery *(41)*. The recommended dose of the drug for intubation in adults is 0.15 mg/kg body weight. The given dose provides good conditions for tracheal intubation after 120 seconds of drug administration. During opioid or propofol anaesthesia, the median recovery time from 25% to 75% and from 5% to 95% is approximately 13 minutes and 30 minutes, respectively *(42)*.

CONCLUSION

Proper selection, knowledge of the mechanism of action, method of administration, and dosage of drugs are key to creating optimal conditions for patient intubation. Understanding the pharmacological properties of anaesthetics and muscle relaxants is crucial for minimising the risk of complications associated with this procedure. Staff

education and work on improvement, as well as the application of new methods and drugs, can significantly influence the outcome of patient treatment. Further research on the application of new drugs can contribute to the safety and efficacy of these medications, making it necessary to document experiences and publications related to this area to gain new knowledge and apply more effective protocols. The correct application of drugs and intubation techniques is directly related to the safety and efficiency of establishing the airway, and thus, the quality of healthcare is significantly improved.

REFERENCES

1. COOK T M, MACDOUGALL-DAVIS 2012 Complications and failure of airway management. Br J Anaesth 109 (Suppl 1): i68–i85. https://doi.org/10.1093/bja/aes393
2. KO B S, AHN R, RYOO S M, AHN S, SOHN C H, SEO D W, LIM K S, KIM W Y 2015 Prevalence and outcomes of endotracheal intubation-related cardiac arrest in the ED. Am J Emerg Med 33(11): 1642–1645. https://doi.org/10.1016/j.ajem.2015.07.083
3. HEFFNER A C, SWORDS D, KLINE J A, JONES A E 2012 The frequency and significance of postintubation hypotension during emergency airway management. J Crit Care 27(4): 417.e9-13. https://doi.org/10.1016/j.jcrc.2011.08.011
4. JABRE P, AVENEL A, COMBES X, KULSTAD E, MAZARIEGOS I, BERTRAND L, LAPOSTOLLE F, ADNET F 2011 Morbidity related to emergency endotracheal intubation a substudy of the Ketamine Sedation trial. Resuscitation 82(5): 517–522. https://doi.org/10.1016/j.resuscitation.2011.01.015
5. LAW J A, BROEMLING N, COOPER R M, DROLET P, DUGGAN L V, GRIESDALE D E, HUNG O R, JONES P M, KOVACS G, MASSEY S, MORRIS I R, MULLEN T, MURPHY M F, PRESTON R, NAIK V N, SCOTT J, STACEY S, TURKSTRA T P, WONG D T, CANADIAN AIRWAY FOCUS GROUP 2013 The difficult airway with recommendations for management part 1 difficult tracheal intubation encountered in an unconscious induced patient.Can J Anaesth 60(11): 1089–1118. https://doi.org/10.1007/s12630-013-0019-3
6. KOLLMEIER B, BOYETTE L, BEECHAM G, DESAIN, KHETALPAL S 2025 Difficult Airway. In statPearls Publishing Treasure Island (FL), [cited 2025 Jan 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK470224/
7. IVOŠEVIĆ T, JOVIČIĆ J, SREBRO D. 2023 Intravenski anestetici. In: Stevanović P (ed). Anesteziologija teorijske i praktične osnove savremene kliničke prakse. Univerzitet u Kragujevcu, Fakultet medicinskih nauka, Kragujevac, p. 345-377
8. HUITINK J M, BOUWMAN R A 2015 The myth of the difficult airway airway management revisited. Anaesthesia 70(3): 244–249. https://doi.org/10.1111/anae.12989
9. PETERSON G N, DOMINO K B, CAPLAN R A, POSNER K L, LEE L A, CHENEY F W 2005 Management of the difficult airway a closed claims analysis. Anesthesiology 103(1): 33–39. https://doi.org/10.1097/00000542-200507000-00009
10. SOLEIMANPOUR H, GHOLIPOURI C, PANAHI J R, AFHAMI M R, GHAFOURI R R, GOLZARI S E, SOLEIMANPOUR M, ESFANJANI R M 2011 Role of anesthesiology curriculum in improving bag mask ventilation and intubation success rates of emergency medicine residents a prospective descriptive study. BMC Emerg Med 11: 8. https://doi.org/10.1186/1471-227X-11-8
11. MORRIS C, PERRIS A, KLEIN J, MAHONEY P 2009 Anaesthesia in haemodynamically compromised emergency patients does ketamine represent the best choice of induction agent. Anaesthesia 64(5): 532–539. https://doi.org/10.1111/j.1365-2044.2008.05835.x
12. AGUDELO S C, MENCÍA S, FARO A, ESCUDERO V, SANAVIA E, LÓPEZ-HERCE J 2012 Continuous propofol perfusion in critically ill children. Med Intensiva 36(6): 410–415. https://doi.org/10.1016/j.medin.2011.11.018
13. VELDHOEN E S, HARTMAN B J, VAN GESTEL J P 2009 Monitoring biochemical parameters as an early sign of propofol infusion syndrome false feeling of security. Pediatr Crit Care Med 10(2): e19–e21. https://doi.org/10.1097/PCC.0b013e3181956bda
14. CORNFIELD D N, TEGTMEYER K, NELSON M D, MILLA C E, SWEENEY M 2002 Continuous propofol infusion in 142 critically ill children. Pediatrics 110(6): 1177–1181 https://doi.org/10.1542/peds.110.6.1177
15. WALSH C T 2018 Propofol Milk Of Amnesia. Cell 175(1): 10–13. https://doi.org/10.1016/j.cell.2018.08.031
16. KREUZER M, BUTOVAS S, GARCÍA P S, SCHNEIDER G, SCHWARZ C, RUDOLPH U, ANTKOWIAK B, DREXLER B 2020 Propofol Affects Cortico-Hippocampal Interactions via β3 Subunit Containing $GABA_A$ Receptors. Int J Mol Sci 21(16): 5844. https://doi.org/10.3390/ijms21165844
17. BRECHMANN T, MAIER C, KAISLER M, VOLLERT J, SCHMIEGEL W, PAK S, SCHERBAUM, N, RIST F, RIPHAUS A 2018 Propofol sedation during gastrointestinal endoscopy arouses euphoria in a large subset of patients. United European Gastroenterol J 6(4): 536–546. https://doi.org/10.1177/2050640617736231
18. EBERT T J, MUZI M, BERENS R, GOFF D, KAMPINE J P 1992 Sympathetic responses to induction of anesthesia in humans with propofol or etomidate. Anesthesiology 76(5): 725–733. https://doi.org/10.1097/00000542-199205000-00010
19. MAHESHWARI K, NATHANSON B H, MUNSON S H, KHANGULOV V, STEVENS M, BADANI H, KHANNA A K, SESSLER D I 2018 The relationship between ICU hypotension and in-hospital mortality and morbidity in septic patients. Intensive Care Med 44(6): 857–867. https://doi.org/10.1007/s00134-018-5218-5
20. DE LA HOZ M A, RANGASAMY V, BASTOS A B, XU X, NOVACK V, SAUGEL B, SUBRAMANIAM B 2022 Intraoperative Hypotension and Acute Kidney Injury Stroke and Mortality during and outside Cardiopulmonary Bypass A Retrospective Observational Cohort Study. Anesthesiology 136(6): 927–939. https://doi.org/10.1097/ALN.0000000000004175
21. ENGELHARD K, WERNER C, EBERSPÄCHER E, PAPE M, BLOBNER M, HUTZLER P, KOCHS E 2004 Sevoflurane and propofol influence the expression of apoptosis regulating proteins after cerebral ischaemia and reperfusion in rats. Eur J Anaesthesiol 21(7): 530–537. https://doi.org/10.1017/s0265021504007057
22. KAHRAMAN S, KILINÇ K, DAL D, ERDEM K 1997 Propofol attenuates formation of lipid peroxides in tourniquet induced ischaemia reperfusion injury. Br J Anaesth 78(3): 279–281. https://doi.org/10.1093/bja/78.3.279
23. VALK B I, STRUYS M M R F 2021 Etomidate and its Analogs A Review of Pharmacokinetics and Pharmacodynamics. Clin Pharmacokinet 60(10): 1253–1269. https://doi.org/10.1007/s40262-021-01038-6
24. CHUNG M, SANTER P, RAUB D, ZHAO Y, ZHAO T, STROM J, HOULE T, SHEN C, Eikermann M, YEH R W 2020 Use of etomidate in patients with heart failure undergoing noncardiac surgery. Br J Anaesth 125(6): 943–952. https://doi.org/10.1016/j.bja.2020.06.059
25. VAN DEN HEUVEL I, WURMB T E, BÖTTIGER B W, BERNHARD M 2013 Pros and cons of etomidate more discussion than evidence. Curr Opin Anaesthesiol 26(4): 404–408. https://doi.org/10.1097/ACO.0b013e328362a84c
26. ALBERT S G, ARIYAN S, RATHER A 2011 The effect of etomidate on adrenal function in critical illness a systematic review.

Intensive Care Med 37(6): 901–910. https://doi.org/10.1007/s00134-011-2160-1

27. KOMATSU R, YOU J, MASCHA E J, SESSLER D I, KASUYA Y, TURAN A 2013 Anesthetic induction with etomidate rather than propofol is associated with increased 30 day mortality and cardiovascular morbidity after noncardiac surgery. Anesth Analg 117(6), 1329–1337. https://doi.org/10.1213/ANE.0b013e318299a516

29. MINER J R, DANAHY M, MOCH A, BIROS M 2007 Randomized clinical trial of etomidate versus propofol for procedural sedation in the emergency department. Ann Emerg Med 49(1): 15–22. https://doi.org/10.1016/j.annemergmed.2006.06.042

30. EGAN E D, JOHNSON K B 2020 The Influence of Hemorrhagic Shock on the Disposition and Effects of Intravenous Anesthetics A Narrative Review. Anesth Analg 130(5): 1320–1330. https://doi.org/10.1213/ANE.0000000000004654

31. LU Z, ZHENG H, CHEN Z, XU S, CHEN S, MI W, WANG T, CHAI X, GUO Q, ZHOU H, YU Y, ZHENG X, ZHANG J, AI Y, YU B, BAO H, ZHENG H, HUANG W, WU A, DENG X, XIONG L 2022 Effect of Etomidate vs Propofol for Total Intravenous Anesthesia on Major Postoperative Complications in Older Patients A Randomized Clinical Trial. JAMA Surg 157(10): 888–895. https://doi.org/10.1001/jamasurg.2022.3338

32. SAGARIN M J, BARTON E D, CHNG Y M, WALLS R M, National Emergency Airway Registry Investigators 2005 Airway management by US and Canadian emergency medicine residents a multicenter analysis of more than 6000 endotracheal intubation attempts. Ann Emerg Med 46(4): 328–336. https://doi.org/10.1016/j.annemergmed.2005.01.009

33. SHETABI H, MORADI FARSANI D, ALLAFCHIAN Z. 2024 Effect of Etomidate Versus Midazolam-Sodium Thiopental on Attenuating the Cardiovascular Response to Laryngoscopy and Tracheal Intubation. Anesth Pain Med 14(2): e143382. https://doi.org/10.5812/aapm-143382

34. PROMMER E 2020 Midazolam an essential palliative care drug. Palliat Care Soc Pract 14: 2632352419895527. https://doi.org/10.1177/2632352419895527

35. YAO Y T, HE L X, FANG N X, MA J 2021 Anesthetic Induction With Etomidate in Cardiac Surgical Patients A Prima Compliant Systematic Review and Meta Analysis. J Cardiothorac Vasc Anesth 35(4): 1073–1085. https://doi.org/10.1053/j.jvca.2020.11.068

36. VOPRA J, LESILE D, STACEY M 2022 Awake tracheal intubation. BJA Educ 22(8): 298–305. https://doi.org/10.1016/j.bjae.2022.03.006

37. MAMA K R, GAYNOR J S, HARVEY R C, ROBERTSON S A, KOENIG R L, COZZI E M 2013 Multicenter clinical evaluation of a multi dose formulation of propofol in the dog. BMC Vet Res 9: 261. https://doi.org/10.1186/1746-6148-9-261

38. BENNER A, LEWALLEN N F, SADIQ N M 2025 Biochemistry, Pseudocholinesterase. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; [cited 2025 Feb 11]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK545284/

39. JAIN A, WERMUTH H R, DUA A, SINGH K, MAANI C V 2025 Rocuronium. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, [cited 2025 Feb 11]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK539888/

40. ILKIW J E 1999 Balanced anesthetic techniques in dogs and cats. Clin Tech Small Anim Pract 14(1): 27–37. https://doi.org/10.1016/S1096-2867(99)80024-3

41. INTERLANDI C, DI PIETRO S, COSTA G L, SPADOLA F, IANNELLI N M, MACRÌ D, FERRANTELLI V, MACRÌ F 2022 Effects of Cisatracurium in Sevoflurane and Propofol Requirements in Dog Undergoing Mastectomy Surgery. Animals (Basel) 12(22): 3134. https://doi.org/10.3390/ani12223134