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When it comes to proactive temperature management, degrees matter. Even a small drop in core body temperature can result in inadvertent perioperative hypothermia, a complication associated with an increased risk of surgical site infection,<sup>1,2</sup> longer length of stay,<sup>3</sup> and other costly, potentially deadly consequences.<sup>4</sup>

The 3M™ Bair Hugger™ Normothermia System allows clinicians to help maintain normothermia before, during and after surgery. The system includes:

- Convective air warming units, blankets, and gowns
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1. Kurz A, Sessler DI, et al. Perioperative Normothermia to Reduce the Incidence of Surgical-Wound Infection and Shorten Hospitalization. *New Engl J Med.* 1996;334:1209-1215.  
 2. Melling AC, Ali B, Scott Em, Leaper DJ. Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomized controlled trial. *The Lancet.* 2001;358(9285):876-880.  
 3. Bush H Jr., Hydo J, Fischer E, et al. Hypothermia during elective abdominal aortic aneurysm repair: The high price of avoidable morbidity. *J Vasc Surg.* 1995;21(3):392-402.  
 4. Sessler DI. Perioperative thermoregulation and heat balance. *The Lancet.* 2016;387(10038):2655-2664.

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# KOREAN JOURNAL of ANESTHESIOLOGY

2022 August

VOLUME 75 NUMBER 4

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## Stay 'Sedated' with Precedex<sup>1,2</sup>

**Precedex**  
showed better surgeon satisfaction score compared to  
midazolam-fentanyl under MAC ( $p=0.014$ ).<sup>3,\*</sup>



**Precedex injection/Precedex premix injection Safety Information<sup>1</sup>**

Precedex should be administered only by clinician and patients should be continuously monitored while receiving Precedex. Some patients receiving Precedex could be observed to be arousable and alert when stimulated. If Precedex is administered for greater than 24 hours and stopped abruptly, withdrawal symptoms similar to those reported for another alpha-2-adrenergic agent, clonidine, may result. In two trials for procedural sedation in which 318 adult patients received Precedex, respiratory depression (absolute and relative terms as respiratory rate (RR) <8 beats per minute and >25% decrease from baseline) was one of the adverse reactions with an incidence >2% in procedural sedation. The decrease in respiratory rate and hypoxia was similar between Precedex and comparator groups in both studies. The most frequent adverse reactions were hypotension, bradycardia, and dry mouth. Co-administration of Precedex with anesthetics, sedatives, hypnotics, and opioids is likely to lead to an enhancement of effects. Specific studies have confirmed these effects with sevoflurane, isoflurane, propofol, alfentanil, and midazolam. No pharmacokinetic interactions between Precedex and isoflurane, propofol, alfentanil and midazolam have been demonstrated. However, due to possible pharmacodynamics interactions, when co-administered with Precedex, a reduction in dosage of Precedex or the concomitant anesthetic, sedative, hypnotic or opioid may be required. Three randomized, active comparator trials were conducted for intensive care unit (ICU) patients for which the drug was administered 24 hours or more. Delirium occurred in 2.0-3.9% of patients. The incidence of delirium over time was found to be 2.0-3.9% in a randomized, active-controlled clinical trial in which precedex was continuously administered for 24 hours or longer in patients under intensive care management. Adverse reaction information is derived from the continuous infusion trials of Precedex for sedation in the Intensive Care Unit setting in which 1,007 adult patients received Precedex for less than 24 hours. The most frequent adverse reactions were hypotension, bradycardia and dry mouth.

Precedex Injection (dexmedetomidine hydrochloride) 200 mcg/2 mL / Precedex Premix Injection (dexmedetomidine hydrochloride) 80 mcg/20 mL, 200 mcg/50 mL, 400 mcg/100 mL abbreviated Product Information

(INDICATIONS) 1. Sedation in an Intensive Care Setting: Sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting. 2. Sedation of Non-intubated Patients Prior to and/or during Surgical and Other Procedures 1) Monitored Anesthesia Care (MAC) 2) Awake Fiberoptic Intubation (AFI) (DOSAGE AND ADMINISTRATION) 1. Intensive Care Unit (ICU) Sedation - Initiation: 1 mcg/kg over 10 to 20 minutes. - Maintenance: 0.2 to 0.7 mcg/kg/hr The rate of the maintenance infusion should be adjusted to achieve the desired level of sedation. 2. Procedural Sedation - Initiation: 1 mcg/kg over 10 minutes For less invasive procedures such as ophthalmic surgery, a loading infusion of 0.5 mcg/kg given over 10 minutes may be suitable. - Maintenance: 0.6 mcg/kg/hr and titrated to achieve desired clinical effect with doses ranging from 0.2 to 1 mcg/kg/hr. A maintenance infusion of 0.7 mcg/kg/hr is recommended until the endotracheal tube is secured for awake fiberoptic intubation. (WARNINGS) Precedex should be administered only by clinician and patients should be continuously monitored while receiving Precedex. Since Precedex clearance decreases with severity of hepatic impairment, dose reduction should be considered in patients with impaired hepatic function. (CONTRAINDICATIONS) Patients with hypersensitivity or a history of hypersensitivity to the active substance or to any of the excipients. (ADMINISTRATIONS WITH CAUTION) Patients with cardiovascular disorders. Patients with decreased cardiac function. Patients with hypovolemia. Patients with hepatic impairment. Patients with renal impairment. (ADVERSE REACTIONS) Because clinical trials are conducted under widely varying conditions, adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in practice. [Precedex injection latest HA approved date] 2021.07.21 [Precedex Premix injection latest HA approved date] 2021.07.21

\*The latest version of the product information can be found on the pfizer website.

**Study design** The objective of the study was to compare the efficacy of dexmedetomidine with midazolam-fentanyl combination on patient movement score in patients undergoing burr-hole surgery for CSDH under conscious sedation.

Fifty-two patients undergoing burr-hole surgery for chronic subdural hematoma under MAC were randomly assigned to receive either IV dexmedetomidine 1 µg/kg over 10 minutes followed by continuous infusion 0.03 to 0.07 µg/kg/h (group D) or IV fentanyl 0.5 µg/kg and midazolam 0.05 mg/kg over 10 minutes followed by continuous infusion of 0.5 to 1.16 µg/kg/h fentanyl and 0.03 to 0.07 mg/kg/h midazolam (group M/F) titrated to maintain Ramsay sedation scale 3. Total number of intraoperative patient movements, postoperative recovery time, and patient and surgeon satisfaction scores were recorded.

**References** 1. Precedex injection product information. Latest HA approved date: Jul 21, 2021. 2. Precedex Premix injection product information. Latest HA approved date: Jul 21, 2021. 3. Bishnoi V, et al. Comparison of Dexmedetomidine Versus Midazolam-Fentanyl Combination for Monitored Anesthesia Care During Burr-Hole Surgery for Chronic Subdural Hematoma. *J Neurosurg Anesthesiol*. 2016 Apr;28(2):141-146.



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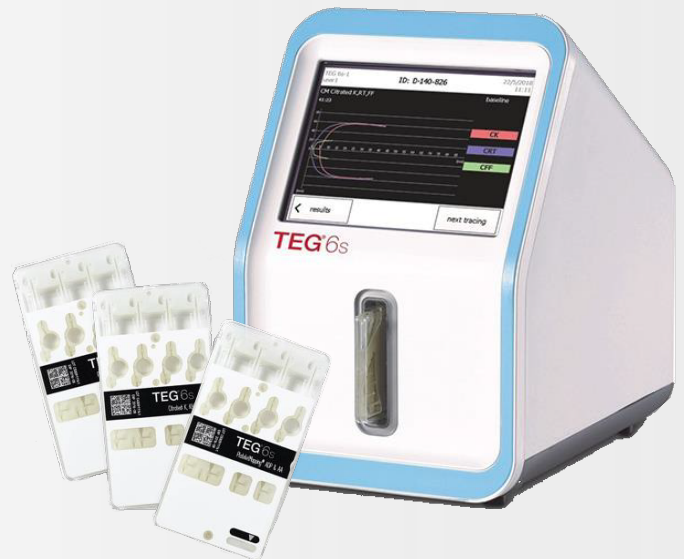
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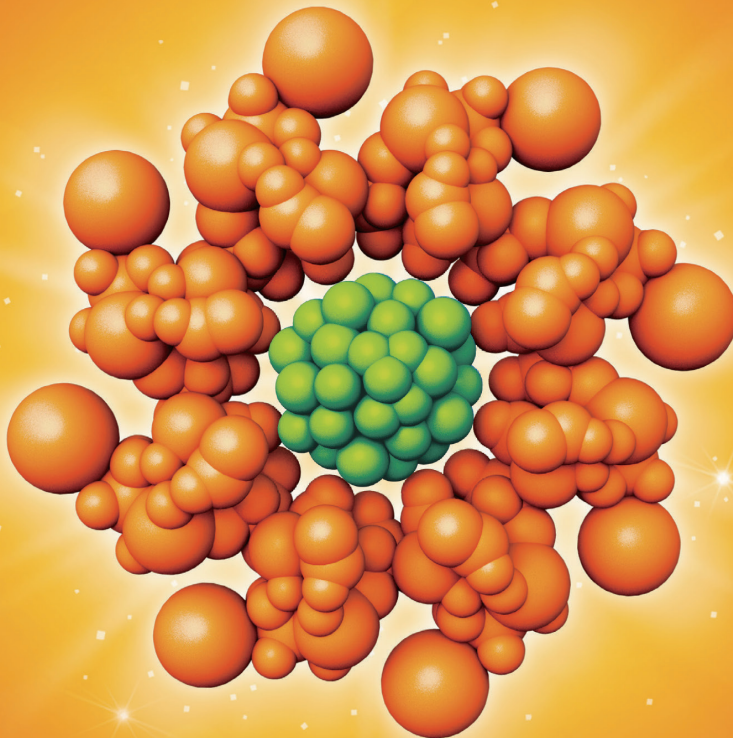
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# Because Every\* Kid is Special **Bridion**<sup>® 1,2,a,†</sup>

So that our precious child wakes up well<sup>2,a</sup>  
Bridion<sup>®</sup>, that a neuromuscular blockade reversal agent  
can be used by children over 2 years of age.<sup>1</sup>



\* 2 years and older **Primary endpoint result:** A TOF ratio of 0.9 or higher was attained in a median time of less than 2 min with a sugammadex dose of 2.0 mg/kg in all age groups, infants (0.6%), children (1.2%), adolescents (1.1%), adults (2.1).

**Study design a.** The aim of this multicenter, randomized, parallel-group, dose-finding, safety-assessor blinded study was to explore the dose-response relationship of sugammadex given at reoparance of the second twitch (T<sub>2</sub>) of the TOF stimulation for the reversal of rocuronium-induced neuromuscular blockade in infants, children, adolescents, and adults between May 2005 and May 2006. A total of 94 patients were randomized to receive sugammadex or placebo, of which 91 patients (8 infants, 24 children, 31 adolescents, and 28 adults) received the study medication (all subjects-treated group). Anesthetized patients (American Society of Anesthesiologists class 1–2) received 0.6 mg/kg rocuronium and were randomized to receive sugammadex (0.5, 1.0, 2.0, or 4.0 mg/kg) or placebo at reoparance of T<sub>2</sub>. Neuromuscular monitoring was performed using acceleromyography. Primary endpoint was time from sugammadex/placebo administration to recovery of the train-of-four ratio to 0.9.<sup>1</sup>

**References:** 1. BRIDION<sup>®</sup> Prescribing Information, MSD, 2. Flout B, et al. Reversal of rocuronium-induced neuromuscular blockade with sugammadex in pediatric and adult surgical patients. *Anesthesiology*. 2009 Feb; 110(2):284-94.

#### **Bridion<sup>®</sup> (Sugammadex) 100 mg Selected Safety Information**

**Indications and Usage:** Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults and pediatric patients aged ≥2 years old undergoing surgery. **[Dose and Administration Adult Patients:** Routine reversal. A dose of 4 mg/kg Bridion is recommended as IV injection if recovery has reached at least 1–2 post-tetanic counts (PTC) following rocuronium or vecuronium induced blockade. A dose of 2 mg/kg Bridion is recommended as IV injection, if spontaneous recovery has occurred up to at least the reappearance of T<sub>1</sub> following rocuronium or vecuronium induced blockade. **Immediate Reversal of Rocuronium-Induced Blockade:** A dose of 16 mg/kg Bridion is recommended if there is a clinical need to reverse neuromuscular blockade soon (approximately 3 minutes) after administration of rocuronium as IV injection. The safety and efficacy with the use of Bridion for immediate reversal following rocuronium induced blockade has not been established. **Renal Impairment:** No dosage adjustment is necessary for patients with mild or moderate renal impairment (creatinine clearance ≥30 mL/min and <80 mL/min). Bridion is not recommended for use in patients with severe renal impairment (creatinine clearance <30 mL/min) or dialysis. **Elderly Patients:** Elderly patients tend to delay recovery from neuromuscular blockade, but dose adjustment is not necessary. **Obese Patients:** The dose of this drug in obese patients should be based on actual weight (ABW). **Hepatic Impairment:** No dosage adjustment is necessary for patients with mild and moderate hepatic impairment. Since no clinical studies have been conducted with patients with hepatic impairment, caution should be taken in patients with severe hepatic impairment or hepatic impairment with coagulation disorders. **Pediatric Patients (2 years old):** Bridion 100 mg/mL may be diluted to a concentration of 10 mg/mL to increase the accuracy of dosing in the pediatric population. Routine Reversal: A dose of 4 mg/kg Bridion is recommended if spontaneous recovery of the twitch response has reached 1 to 2 post-tetanic counts (PTC) following rocuronium- or vecuronium-induced neuromuscular blockade. A dose of 2 mg/kg Bridion is recommended if spontaneous recovery has reached the reappearance of the second twitch (T<sub>2</sub>) in response to TOF stimulation following rocuronium- or vecuronium-induced neuromuscular blockade. **Immediate Reversal:** Immediate reversal in pediatric patients has not been studied. Preparation of dilution for pediatric use: To prepare the required dose, aseptically transfer all the contents of the 2 mL vial of Bridion 2 mL single-dose vial containing 200 mg Bridion (100 mg/mL) to a bottle of intravenous bag containing 18 mL of 0.9% sodium chloride injection, to achieve a final concentration of 10 mg/mL Bridion. **[Warnings and Precautions] Contraindications:** Patients with known hypersensitivity to Bridion or any of its components. **Careful Administration:** 1) Patients with renal impairment. 2) Patients with hepatic impairment. 3) Patients with decrease of cardiac output. 4) Patients with edema state. 5) Patients with a history of allergic reaction. 6) Patients with a history of pulmonary complications (possible occurrence of bronchospasm). 7) Patients with coagulation disorders. 8) Patients with anaphylaxis. 9) The elderly. 10) Pregnant or women who may be pregnant. **Adverse Reactions:** 1) The safety of Bridion has been evaluated based on an integrated safety database of approximately 1,700 surgical patients and 120 healthy adult volunteers. The most commonly reported adverse reactions in patients who experienced surgery were anesthetic complications. **Immune System:** 1) Hypersensitivity: (1/1,000, <1/100), the others: Anesthetic complication/body movement in the middle of anesthesia or operation, coughing, grimacing and sucking of the tracheal tube (1/100, <1/100), unintended intraoperative awareness (1/1,000, <1/100). 2) In clinical trials with surgical patients, hypersensitivity including anaphylaxis has been reported infrequently. The frequency of occurrence of hypersensitivity reactions in post-marketing surveys is unknown. Hypersensitivity reactions that occurred varied from isolated skin reactions to severe systemic reactions (i.e., anaphylaxis, anaphylactic shock) and have occurred in patients with no prior exposure to Bridion. Symptoms associated with these reactions can include: flushing, urticaria, erythematous rash, severe hypotension, tachycardia, swelling of tongue, swelling of pharynx, bronchospasm and pulmonary obstructive events. Severe hypersensitivity reactions can be fatal. Hypersensitivity reactions, including anaphylaxis, have occurred in patients treated with Bridion in clinical study for healthy volunteers (150 subjects received 4 mg/kg, 148 received 16 mg/kg and 150 received placebo). The incidence of adjudicated hypersensitivity was 0.7% (n=1) and 4.7% (n=7) in Bridion 4 mg/kg and Bridion 16 mg/kg groups, respectively. There were no reports of anaphylaxis after placebo. 3) In a dedicated clinical study in healthy volunteers, dyspnea, nausea and flushing were reported and showed a dose response relationship. 4) In a few patients receiving Bridion, unintended intraoperative awareness was reported. It cannot be determined whether this event was causally related to Bridion. 5) Cases of marked bradycardia, bradycardia with cardiac arrest, ventricular fibrillation and ventricular tachycardia have been observed within minutes after administration of Bridion. Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. If cardiac disorders should occur, appropriate treatment should be instituted. 6) In one dedicated clinical trial and in post-marketing data, in patients with a history of pulmonary complications, bronchospasm was reported as a possibly related adverse event. 7) Post-marketing clinical trial of obese patients (BMI ≥40 kg/m<sup>2</sup>) showed that the adverse reaction profile was generally similar between patients who were administered actual body weight (ABW) and patients who were administered ideal body weight (IBW). 8) One trial of 331 patients who were assessed as ASA Class 3 (Patients with severe systemic disease) or 4 (Patients with severe systemic disease that is a constant threat to life) investigated the incidence of treatment-emergent arrhythmias sinus bradycardia, sinus tachycardia, or other cardiac arrhythmias) after administration of Bridion. The incidence of treatment-emergent sinus bradycardia in patients receiving Bridion 2 mg/kg, 4 mg/kg, or 16 mg/kg was generally similar to those in patients receiving neostigmine (50 µg/kg up to 5 mg maximum dose) + glycopyrrolate (10 µg/kg up to 1 mg maximum dose). Incidence of treatment-emergent sinus bradycardia was statistically significantly lower in Bridion treatment group (mg/kg) compared to neostigmine treatment group (p=0.026). Incidence of treatment-emergent sinus tachycardia was statistically significantly lower in Bridion treatment group (2 mg/kg, 4 mg/kg) compared to neostigmine treatment group (p=0.007, 0.036). 9) During post-marketing surveillance period of 6 years in 718 subjects for re-examination, AEs were reported in 26.6% (91/1718 subjects, 281 events), regardless of causal relationship. Among those, serious AE was hypertensive crisis, pruritus, purpura, urticaria, urinary retention, atrial fibrillation, etc. and there was no serious AE that cannot rule out relationship to Bridion. **General Cautions:** 1) Ventilatory support is mandatory for patients until adequate spontaneous respiration is restored following reversal of neuromuscular blockade. 2) In order to prevent recurrence of neuromuscular blockade, the recommended doses for routine should be used. 3) When drugs which potentiate neuromuscular blockade are used in the post-operative phase, special attention should be paid to the possibility of recurrence of neuromuscular blockade. 4) Recurrence of neuromuscular blockade may occur due to displacement of rocuronium or vecuronium from Bridion by other drugs (i.e., Torsemide, fentanyl, acid). 5) When neuromuscular blockade was reversed intentionally in the middle of anesthesia in clinical trials, signs of light anesthesia were noted occasionally (movement, coughing, grimacing and sucking of the tracheal tube). 6) In patients for whom intubation is expected to be difficult, the method of airway maintenance should be considered beforehand. 7) Rocuronium-induced neuromuscular blockade cannot or does not allow airway intubation, it should be promptly restored from neuromuscular blockade. 7) Coagulation parameters should be carefully monitored in patients with known coagulopathies when Bridion is administered. 8) In patients with severe renal failure (creatinine clearance <30 mL/min), the excretion of Bridion or the Bridion-ocuronium complex was delayed; however, in these patients there were no signs of re-occurrence of neuromuscular blockade. The drug is not recommended for use in patients with severe renal impairment. 9) Dedicated studies in patients with hepatic impairment have not been conducted. Patients with severe hepatic impairment or hepatic impairment with coagulation disorders should be cautious when administering this drug. 10) Bridion has not been studied for reversal following rocuronium or vecuronium administration in the ICU. 11) Do not use Bridion to reverse neuromuscular blockade induced by nonsteroidal neuromuscular blocking agents such as succinylcholine or benzylisoquinolium compounds, steroidal neuromuscular blocking agents, pancuronium other than rocuronium or vecuronium. 12) Conditions associated with prolonged circulation time such as cardiovascular disease, old age or edema state (i.e., severe hepatic impairment) may be associated with longer recovery times. 13) The patients should be carefully observed for the possibility of drug hypersensitivity reactions (including anaphylactic reactions). If any abnormality is observed, appropriate measures should be taken immediately. 14) Each 1 mL solution contains 9.1 mg sodium. If more than 2.4 mL contain approximately 22 mg sodium solution needs to be administered, this should be taken into consideration by patients on a controlled sodium diet. 15) In rare instances, cases of marked bradycardia, some of which have resulted in cardiac arrest, have been observed within minutes after the administration of Bridion for reversal of neuromuscular blockade. **Drug Interactions:** 1) Torsemide: For torsemide, which has a relatively high binding affinity for Bridion and for which relatively high plasma concentrations might be present, some displacement of vecuronium or rocuronium from the complex with this drug could occur. 2) Fentanyl: In administration of fentanyl acid in the pre-operative phase may give some delay in the recovery of the T<sub>1</sub> ratio to 0.9. No recurrence of neuromuscular blockade is expected in the recovery of the T<sub>1</sub> ratio to 0.9. No recurrence of neuromuscular blockade is expected in the recovery of the T<sub>1</sub> ratio to 0.9. There are no clinical trial data for exposure to this drug during pregnancy. It is administered only if the benefits of administration exceed the risks. No data are available regarding the presence of Bridion in human milk, the effects of Bridion on the breast-fed infant, or the effects of Bridion on milk production. Breastfeeding is not recommended during the administration of this drug. **Pediatric Administration:** In clinical study for pediatric patients 2 to <17 years of age, the safety profile of Bridion 4 mg/kg maximum dose is generally consistent with that observed in adults. Safety and effectiveness in patients younger than 2 years of age have not been established. **Elderly Administration:** Exercise caution when administering Bridion to elderly patients who tend to delay recovery from neuromuscular blockade. (Revised: 2012.10.14)

† Before prescribing BRIDION, please refer to the full prescribing information for further details.





## Aims and Scope

The Korean Journal of Anesthesiology (Korean J Anesthesiol; KJA/ISSN: 2005-6419), an official journal of the Korean Society of Anesthesiologists, is an English-language, peer-reviewed journal that publishes articles in the fields of anesthesiology, critical care, and pain medicine. KJA aims to publish high-quality clinical and scientific materials on all aspects of anesthesiology, critical care, and pain medicine. Its regional focus is mainly Korea, but it also welcomes submissions from researchers all over the world.

In addition to publishing original articles, KJA features reviews, editorials, case reports, and letters to the editor. KJA also features statistical rounds to provide its readers with educational fundamentals and practical implications for clinical and experimental statistics. Additionally, KJA gladly publishes negative results, which will benefit clinical practice and promote further research activity.

The primary considerations for publication are clarity, uniqueness, and advancement in design, performance, and knowledge.

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## Anatomical classification and clinical application of thoracic paraspinal blocks

흉추부 척추 주위 블록의 해부학적 분류 및 임상 적용

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현재 임상에서 흉곽의 부위마취와 진통을 위한 다양한 블록 방법들이 사용되고 있다. 흉추부 척추 주위 블록(thoracic paraspinal block)은 해부학적인 목표점의 차이를 바탕으로 방척추 블록(paravertebral block), 후추궁판 블록(retrolaminar block), 척추기립근막 블록(erector spinae plane block), 횡돌기사이 블록(intertransverse process block)의 4가지 유형으로 분류한다. 이러한 블록 방법은 서로 다른 해부학적 목표점을 가지고 있으므로 주입 시 주사액이 퍼지는 양상이 다르게 되며, 결과적으로 신경 차단 특성이 다르게 나타날 수 있다. 방척추 블록은 척추 신경축 영역 바로 바깥의 방척추 공간(paravertebral space)을 직접 대상으로 하며, 경막외 차단과 비슷한 진통 효과를 가지고 있다. 그러나 이 블록은 술기와 관련된 몇 가지 잠재적인 위험성을 가지고 있다. 후추궁판 블록과 척추기립근막 블록은 각각 척추체의 추궁판과 횡돌기의 척추기립근막을 목표로 한다. 해부학 연구에서, 등 근육과 근막으로의 주사제 확산 양상은 이 두 블록에서 서로 다르게 나타났다. 후추궁판 블록의 경우 사체 연구에서 방척추 공간 내로의 확산은 일부 확인되었지만, 일관되지 않은 결과를 보였다. 많은 임상 연구와 증례 보고의 결과로 볼 때, 척추기립근막 블록에서는 방척추 공간으로의 주사제 확산이 이루어진다고 여겨지고 있다. 두 가지 방법 모두 대조군에 비해 수술 후 통증을 감소시키는 것으로 밝혀졌지만, 임상 결과는 전통적 방척추 블록보다는 가변적이었다. 마지막으로, 횡돌기사이 블록은 위늑골횡돌기 인대(superior costotransverse ligament) 뒤쪽의 조직 복합체를 해부학적 목표점으로 한다. 최근 사체 연구에 따르면 이 방법은 후추궁판 블록 또는 척추기립근막 블록보다 방척추 공간 내로 통하는 더 직접적이고 가까운 주사제 확산 경로를 가지고 있다고 보고되었다. 이러한 해부학적 발견을 확실히 검증하기 위해서는 이 횡돌기사이 블록을 사용한 추가적 임상 연구들이 더 필요해 보인다.

**Keywords:** Analgesia; Anatomy; Anesthesia; Nerve block; Postoperative pain; Ultrasonography.



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# Remimazolam – current knowledge on a new intravenous benzodiazepine anesthetic agent

레미마졸람, 새로운 벤조디아제핀 정맥 마취제

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일반적으로 마취와 진정의 목적으로 미다졸람(midazolam), 프로포폴(propofol) 그리고 케타민(ketamine)과 같은 정맥 마취제들이 사용된다. 이러한 정맥 마취제들은 환자의 기억상실과 진정 그리고 최면을 효과적으로 유도 및 유지하는 것으로 알려져 있다. 그렇지만, 모든 정맥 마취제를 사용함에 있어 혈액학적 불안정, 호흡억제 또는 수술 후 진정작용이 길어져 회복이 느려지는 등 원치 않는 부작용을 일으킬 가능성을 항상 가지고 있다. 최근 국내에서 전신마취 및 수술에서 진정 목적으로 승인된 벤조디아제핀 계열의 레미마졸람은 기억상실, 진정 그리고 최면을 성공적으로 달성하면서 혈액학적 불안정, 호흡억제 등은 최소화하여 여러 임상 환경에서 다양한 환자들에게 사용되고 있다. 그렇지만, 현재까지 각 임상 환경 및 각 환자의 특성에 맞는 레미마졸람의 사용 방법 등에 대해서는 아직까지 구체적으로 확립되어 있지 않은 실정이다. 레미마졸람의 약동학과 약력학 특성을 고려하면 레미마졸람의 사용은 계속해서 증가할 것으로 예상된다. 본 리뷰를 통해 레미마졸람의 약리학적인 측면을 미다졸람 및 프로포폴과 비교하여 설명함으로써 보다 다양한 임상 환경 및 다양한 환자에게서 레미마졸람의 사용에 대한 기초 지식을 전달하고자 한다.

**Keywords:** Amnesia; Anesthesia; Benzodiazepine; Conscious sedation; Hypnosis; Remimazolam.



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# Comparison of the clinical performance of the i-gel™, LMA Supreme™, and Ambu AuraGain™ in adult patients during general anesthesia: a prospective and randomized study

## 전신마취하 성인 환자의 일회용 후두마스크 i-gel™, LMA Supreme 및 Ambu AuraGain™의 임상 성능 비교: 전향적 무작위 연구

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**배경:** 성문 상부 기도 장치(supraglottic airway devices, SADs)는 일반적으로 기도를 보호하기 위해 사용한다. 본 연구에서는, 전신마취를 하는 성인환자에게 사용하는 세 가지의 SADs와 관련된 임상 실무를 비교하였다.

**방법:** 미국 마취과학회의 신체적인 상태 I-III의 피험자들을 i-gel™ (I), LMA Supreme™ (L), 혹은 Ambu AuraGain™ (A) 그룹(그룹마다 30개)으로 무작위 배정하였다. 본 연구의 주요 목적은 삽입 시간을 비교하는 것이었다. 또한, 삽입 용이성, 시도 횟수, 구강인두 누출 압력(OLP), 기도 처치 시 요구 사항, 위관 설치의 어려움 및 합병증이 평가되었다.

**결과:** 인구통계학적 자료는 그룹 간에 차이가 없었다. 그룹 I (16.9 ± 4.9초)는 그룹 L (19.6 ± 5.2초) 및 그룹 A (22.1 ± 5.7초)보다 삽입 시간이 상당히 짧았다( $p = 0.001$ ). 그룹 A의 OLP (29.8 ± 3.0 cmH<sub>2</sub>O)는 그룹 L (24.1 ± 6.3 cmH<sub>2</sub>O)과 그룹 I (9.4 ± 6.1 cmH<sub>2</sub>O)의 OLP보다 높았다( $p < 0.001$ ). 삽입 시도 횟수( $p = 0.232$ ), 삽입 용이성( $p = 0.630$ ), 기도 처치 시 요구 사항( $p = 0.585$ ), 위관 설치의 어려움( $p = 0.364$ ) 그리고 합병증( $p = 0.873$ )은 그룹 간에 큰 차이가 없었다.

**결론:** 세 가지 기구 모두 다 전신마취 상태에서 성인 기도 관리에 편리하고 효과적이다. 그러나 i-gel 삽입 시 필요한 시간이 짧을수록 소생 및 응급 상황에 더 적합할 수 있으며, 높은 OLP (oropharyngeal leak pressure)를 고려할 때 Ambu AuraGain으로 흡인 위험을 줄일 수 있다.

**Keywords:** Airway management; General anesthesia; Elective surgical procedures; Laryngeal masks; Pressure; Ventilation.



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# Comparison between the coronal diameters of the cervical spinal canal and spinal cord measured using computed tomography and magnetic resonance imaging in Korean patients

컴퓨터 단층촬영(CT)과 자기공명영상(MRI)을 이용하여 측정된 한국인 환자들의 척추관 및 척수의 관상면 비교

So Young Lee<sup>1</sup>, In Young Kim<sup>1</sup>, Kyung Wook Jeong<sup>1</sup>,  
Taeha Ryu<sup>1</sup>, Sang Kyu Kwak<sup>2</sup>, Jin Yong Jung<sup>1</sup>

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**배경:** 경부 경막의 신경차단술 시 C-arm 투시 촬영으로도 척수강내 척수의 비율을 미리 파악할 수 있다면, 척수를 천자하지 않고 경막의 공간에 바늘을 안전하게 거치할 수 있다. 이 연구의 목적은 각각의 경추에서 척수 대 척추관 가로직경 비율을 측정하는 것이었다.

**방법:** 저자들은 병원에서 경추 컴퓨터 단층촬영(CT)과 자기공명영상(MRI)을 모두 받은 환자 100명의 영상 자료를 소급 평가하였다. 환자의 경추 CT와 MRI 영상을 이용하여 3번 경추(C3)에서 1번 흉추(T1)에 이르기까지 척추관과 척수의 길이를 각각의 단계(level)에서 측정하였다. 척수 및 척추관 길이는 각각 경추 MRI 및 CT 영상의 가로면(transverse plane)에서 측정하였다.

**결과:** 척수 대 척추관 길이의 비율은 4번과 5번 경추( $0.64 \pm 0.07$ )에서 가장 컸고, 1번 흉추( $0.55 \pm 0.06$ , 99% CI: 0.535, 0.565)에서 가장 작았다.

**결론:** 본 연구 결과는 C-arm 투시 촬영에서 경부 경막외차단 중 척수 대 척추관 가로직경 비율을 앞으로써 직접적인 척수 손상을 줄이기 위한 참고기준으로 사용될 수 있을 것이다. C-arm 투시 촬영에서 1번 흉추의 고리뿌리(pedicle)에서 좌우 가장 안쪽 선을 잇는 가상의 선을 그리고, 이를 5등분하여 좌우의 바깥쪽 5분의 1에 바늘을 거치하면 척수를 천자할 위험이 상대적으로 줄어들 것이다.

**Keywords:** Cervical cord; Cervical vertebrae; Epidural injections; Fluoroscopy; Safety management; Spinal canal; Spinal cord injuries; Three-dimensional imaging.



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# Video laryngoscope versus USB borescope-aided endotracheal intubation in adults with anticipated difficult airway: a prospective randomized controlled study

어려운 기관내 삽관이 예상되는 성인에서 비디오 후두경과 USB 보스코프(borescope) 보조 기관내 삽관 비교: 전향적 무작위 대조군 연구

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**배경:** 비디오 후두경은 어려운 기관내 삽관을 위해 입증된 기구이다. 코로나바이러스 (COVID-19) 시대에 소개된 USB 보스코프(borescope)는 후두경 날 위에 바로 배치되어 실용적인 비디오 후두경을 제공하였다. 이 연구에서, 우리는 보스코프를 기관내 튜브 안에 장착하여 비디오 후두경과 비교하였다.

**방법:** 정규 수술이 예정되어 있고 어려운 기관내 삽관이 예상되는 성인 환자 120명에게 사전 동의를 받은 뒤 이 연구에 포함시켰다. 환자들은 보스코프와 비디오 후두경 그룹으로 무작위 배정되었다. 1차 목표는 삽관 성공 시간이었으며, 2차 목표는 혈액학적 변화, 마취통증의학과 의사의 만족도, 그리고 합병증 발생률이었다.

**결과:** 삽관 시간은 두 그룹(비디오 후두경 = 30.63초, 보스코프 = 28.35초,  $P = 0.166$ ) 간에 유사했다. 그러나 비디오 후두경은 보스코프에 비해 시야가 더 분명하고( $P = 0.026$ ), 김서림 발생률이 낮았다( $P = 0.015$ ). 반대로, 마취통증의학과 의사의 만족도는 비디오 후두경보다 보스코프에서 더 높았다( $P < 0.001$ ).

**결론:** 비디오 후두경은 보스코프와 비슷한 삽관 시간이 소요되었고, 더 나은 시야를 제공하고 삽관 시 김서림이 적었다. 그러나 비디오 후두경의 가격이 높아 구비하는 데 제한이 있다. 반면, 보스코프는 저비용으로 구비하여 어려운 기관내 삽관이 예상되는 환자에서 사용할 수 있다.

**Keywords:** Airway management; Endotracheal intubation; General anesthesia; Intubation; Laryngoscopy; Trachea.



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## Clinical Research Article

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# Microvascular reactivity as a predictor of major adverse events in patients with on-pump cardiac surgery

## 심폐체외순환하에서 시행하는 심장 수술 환자의 주요 부작용 예측 변수로서의 미세혈관 반응성

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**배경:** 미세 순환계 장애는 일반적으로 심장 수술 중에 발생하는 심폐 우회술(cardiopulmonary bypass, CPB) 동안 가장 심각하다. CPB 동안 미세혈관 반응성이 미세순환 장애를 보상하면 조직 저산소혈증을 최소화할 수 있다. 이 연구의 주요 목적은 CPB 동안 미세혈관 반응성이 심장 수술 후 주요 부작용(major adverse events, MAE)을 예측할 수 있는지 여부를 평가하는 것이다.

**방법:** 이 전향적 관찰 연구에는 심폐체외순환하에서 시행하는 계획 심장 수술을 받은 115명의 환자가 포함되었다. 근적외선 분광법을 적용한 혈관폐색검사(VOT)는 환자별로 전신마취 유도 전, 전신마취 유도 후 30분, CPB 적용 후 30분, 프로타민 주사 후 10분, 흉골봉합 후와 관련하여 5회 실시했다. 수술 후 MAE가 기록되었다. 수신자 조작 특성 곡선 아래 영역(AUROC) 분석을 이용하여 회복 기율기의 MAE의 예측력을 분석하였다.

**결과:** 109명의 환자 중 MAE는 32명(29.4%)에서 발생했다. CPB 중 VOT의 회복기율기에 대한 AUROC 곡선은 0.701이었다( $P < 0.001$ ; 95% CI [0.606, 0.785]). CPB 중 VOT의 회복기율기가  $< 1.08\%/s$ 인 경우, 민감도 62.5%, 특이도 72.7%로 MAE가 예측되었다.

**결론:** 우리의 연구는 CPB 동안 VOT의 회복기율기가 심장 수술 후 MAE를 예측할 수 있다는 것을 입증했다. 이러한 결과는 CPB에 의해 유도된 미세 순환계의 장애가 불량한 임상 결과의 발달을 예측할 수 있다는 생각을 뒷받침하며, 따라서 심장 수술 후 MAE의 초기 예측인자로서 미세 혈관 반응성의 잠재적 역할을 입증한다.

**Keywords:** Cardiac surgical procedures; Cardiopulmonary bypass; Hemodynamics; Microcirculation; Near-infrared spectroscopy; Postoperative complications.

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## Editorial

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# The golden era of videolaryngoscopy: costs we should consider

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Direct laryngoscopy has been considered the gold standard for endotracheal intubation for several decades. A more advanced intubation device has thus been sorely needed and has now become a reality. Since the first videolaryngoscopy (VL) device, known as the Glidescope, was introduced in 2001, many types of VL have grown considerably [1]. VL was initially recognized as a critical option for difficult airway management, but it has now permeated the clinical setting so thoroughly that it may be considered an alternative to direct laryngoscopy for intubation in both adults and children, and it has assumed a central role in both difficult and routine airway management.

Additionally, the COVID-19 pandemic has further justified VL applications, particularly given its associated efficacy and safety profile. VL has become the only option for minimizing direct contact between the operator and virus-transmitting aerosols. Because of the COVID-19 pandemic, many countries' airway management guidelines now recommend VL as the first-line device for all patients requiring endotracheal intubation [2]. VL has not only been embedded in most difficult airway algorithms but has also become a core skill in airway management, and the use of awake VL has also increased. Indeed, it is not an exaggeration to say that we have entered the golden era of VL.

As the VL market is continuously evolving, the costs associated with the use of this technology must be considered. As may be expected, the costs vary depending on the circumstances in which VL is used. According to the findings of an economic analysis conducted in 2021 on the use of VL versus direct laryngoscopy in the surgical setting, VL may be associated with a reduction in total cost, length of hospital stay, and the likelihood of postoperative ICU admission [3]. Given the unique benefits of VL, this result is not surprising. Some would posit that the costs of VL per se would not pose a substantial barrier to its application [4]. Indeed, the costs of VL have been decreasing in recent years, and with increased use, disposable blades may become more affordable. Therefore, it would not be unrealistic for every operating room to invest in VL. However, if we take a closer look at the current clinical reality, it appears that not all settings where airway management is practiced use VL on a routine basis; their use in many centers is limited to a few devices in the main theater area [5]. The use of VL also appears to be restricted in areas with a dearth of medical resources or where the cost of VL is relatively high.

In this issue of the *Korean Journal of Anesthesiology*, Elshazly et al. [6] compared the effectiveness of USB borescopes (which are intended for industrial use) aided direct laryngoscopy to provide low-cost with VLs for adult intubation. The intubation time was comparable between the two devices, though VL provided a better environment for visibility and fogging, whereas operators reported higher levels of satisfaction with the borescope. The study suggests that borescopes could be used in place of VL at a low cost. Although the issue of whether borescopes can be used as clinical instruments has remains to be clearly addressed, they may be a useful alternative in situations where VL is limited or unavailable, especially when a difficult airway is expected or aerosol-transmission is a

concern.

Borescopes can also be a cost-effective tool for educating novices, such as trainees and medical students. VL is an excellent educational tool for teaching laryngoscopy techniques since the anatomy can be better visualized through the magnified screen, and endotracheal intubation training can be conducted more effectively through sharing the screen with the instructor [7]. Another view considers the cost in the educational field that may result from increased use of VL [8]. These authors reported a 38.3% reduction in the number of asleep fiberoptic intubations (FOIs) performed after the implementation of VL at their hospital. FOIs are essential for education because they offer a path for endotracheal intubation when VL is not accessible. Thus, the increased use of VL should not come at the cost of decreased trainee experience in FOIs.

VL is not a tool that can be made available for simple convenience, but rather, an essential technology developed as a result of medical innovation from which both healthcare workers and patients can optimally benefit. As VL becomes more prevalent in medical environment, we should be able to consider the costs associated with VL from various balanced perspectives.

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No potential conflict of interest relevant to this article was reported.

## References

1. Rai MR, Dering A, Verghese C. The Glidescope system: a clinical assessment of performance. *Anaesthesia* 2005; 60: 60-4.
2. Cook TM, El-Boghdadly K, McGuire B, McNarry AF, Patel A, Higgs A. Consensus guidelines for managing the airway in patients with COVID-19: Guidelines from the Difficult Airway Society, the Association of Anaesthetists the Intensive Care Society, the Faculty of Intensive Care Medicine and the Royal College of Anaesthetists. *Anaesthesia* 2020; 75: 785-99.
3. Zhang J, Jiang W, Urdaneta F. Economic analysis of the use of video laryngoscopy versus direct laryngoscopy in the surgical setting. *J Comp Eff Res* 2021; 10: 831-44.
4. Zaouter C, Calderon J, Hemmerling TM. Videolaryngoscopy as a new standard of care. *Br J Anaesth* 2015; 114: 181-3.
5. Cook TM, Kelly FE. A national survey of videolaryngoscopy in the United Kingdom. *Br J Anaesth* 2017; 118: 593-600.
6. Elshazly M, Medhat M, Marzouk S, Samir EM. Video laryngoscope versus USB borescope aided endotracheal intubation in adults with anticipated difficult airway: a prospective randomized controlled study. *Korean J Anesthesiol* 2022; 75: 331-7.
7. Malito ML, Mathias LA, Kimura Junior A, Correa GH, Bardauil VR. The impact of introducing a videolaryngoscope in the initial training of laryngoscopy for undergraduate medical students: a simulation randomized trial. *Braz J Anesthesiol* 2021. Advance Access published on Apr 3, 2021. doi:10.1016/j.bjane.2021.02.048.
8. Dawson SR, Taylor L, Farling P. The true cost of videolaryngoscopy may be trainee experience in fibreoptic intubation. *Br J Anaesth* 2015; 115: 134-5.



## Review Article

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# Anatomical classification and clinical application of thoracic paraspinal blocks

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Various techniques for regional anesthesia and analgesia of the thorax are currently being used in clinical practice. A recent international consensus has anatomically classified paraspinal blocks in the thoracic spinal region into the following four types: paravertebral, retrolaminar, erector spinae plane, and intertransverse process blocks. These blocks have different anatomical targets; thus, the spreading patterns of the injectates differ and consequently exhibit different neural blockade characteristics. The paravertebral block directly targets the paravertebral space just outside the neuraxial region and has an analgesic efficacy comparable to that of the epidural block; however, there are multiple potential risks associated with this technique. Retrolaminar and erector spinae plane blocks target the erector spinae plane on the vertebral lamina and transverse process, respectively. In anatomical studies, these two blocks showed different injectate spreading patterns to the back muscles and the fascial plane. In cadaveric studies, paravertebral spread was identified, but variable. However, numerous clinical reports have shown paravertebral spread with erector spinae plane blocks. Both techniques have been found to reduce postoperative pain compared to controls; however, the results have been more inconsistent than with the paravertebral block. Finally, the intertransverse process block targets the tissue complex posterior to the superior costotransverse ligament. Anatomical studies have revealed that this block has pathways that are more direct and closer to the paravertebral space than the retrolaminar and erector spinae plane blocks. Cadaveric evaluations have consistently shown promising results; however, further clinical studies using this technique are needed to confirm these anatomical findings.

**Keywords:** Analgesia; Anatomy; Anesthesia; Nerve block; Postoperative pain; Ultrasonography.

## Introduction

Performing a paravertebral block (PVB) in the thoracic region is a well-established technique for perioperative analgesia and chronic pain management of the thorax [1-3]. PVBs directly target the thoracic paravertebral space (TPVS), which contains the roots of the spinal nerves, making PVBs distinct from peripheral nerve blocks [4]. Clinically, successful PVBs result in a blockade of the ipsilateral, segmental, somatic, and sympathetic nerves in the dermatomes adjacent to the hemithorax [3]. This technique was first described by Hugo Sellheim in 1905 [1] and has since been modified and improved. However, even with ultrasound guidance, the potential risk of a pneumothorax, neurovascular damage, or unintentional neuraxial injection remain a concern [5-7].

Ultrasound-guided regional anesthesia techniques are fundamental components of



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multimodal perioperative care [8]. The utility of ultrasound has led to the development of many novel approaches of anesthesia and analgesia delivery, including the interfascial plane block, in which local anesthesia is injected into a fascial plane to indirectly access target nerves [9]. Since the erector spinae plane (ESP) block was first described by Forero et al. [10] in 2016, it has attracted considerable attention and has stimulated an explosion of interest in interfascial plane blocks. As a result, many block techniques have since been introduced; however, similar techniques carry different names, and techniques with the same name can have different technical approaches and targets. To standardize this, a recent international consensus has anatomically classified paraspinal blocks in the thoracic region into four types: PVBs, ESP blocks, retrolaminar blocks (RLBs), and intertransverse process (ITP) blocks [11]. Each paraspinal block is associated with different spreading patterns of injectate following different anatomical target points and consequently have different neural blockade characteristics when used clinically.

The purpose of this review is to outline the proposed mechanisms of action of each thoracic paraspinal block based on the available anatomical evidence and discuss clinical findings that have been reported to date.

## Paravertebral block

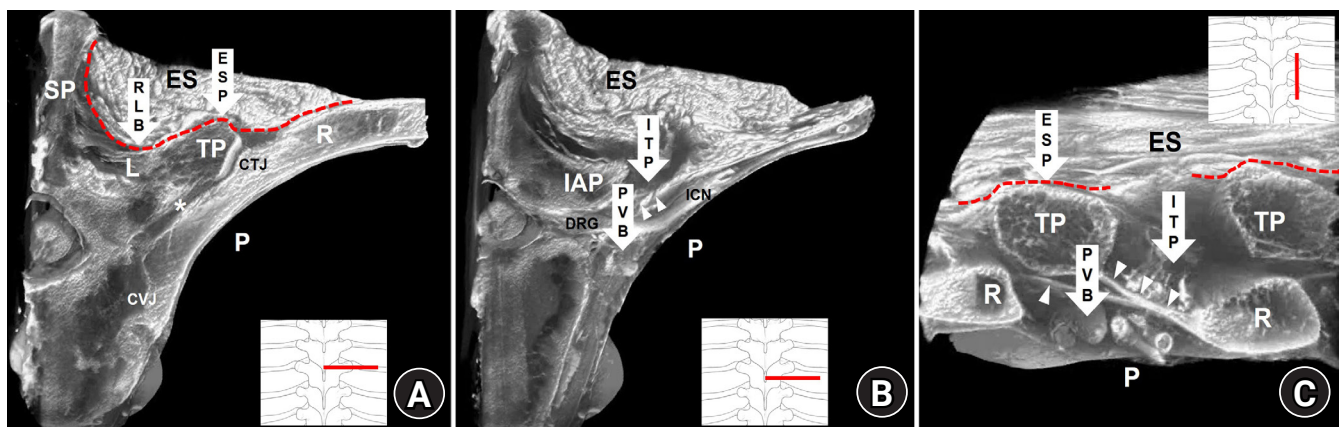
### Anatomical description

A PVB is anatomically described as a block injected into the

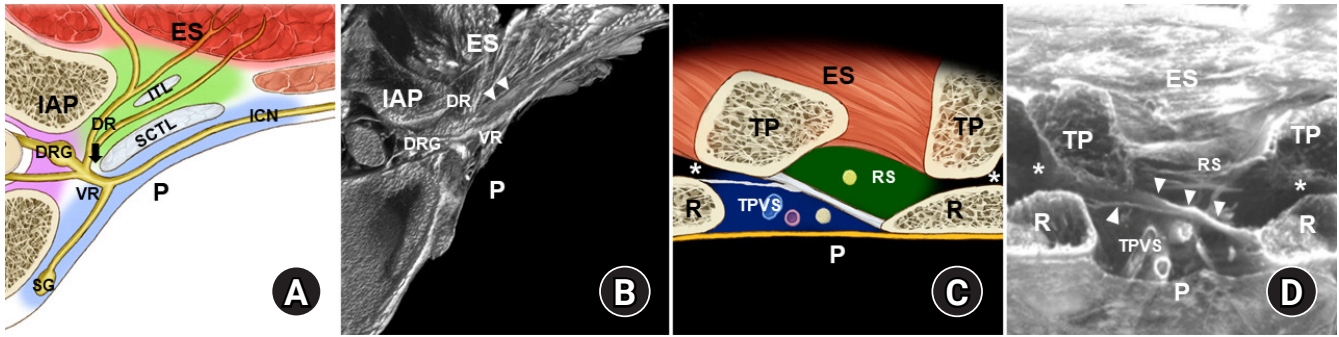
paravertebral space between the superior costotransverse ligament (SCTL) and the parietal pleura in the thoracic region (Fig. 1) [11].

### Anatomical considerations

The TPVS contains the roots of the spinal nerve along with its dorsal and ventral branches and their plexuses, white and gray rami communicantes, the sympathetic ganglion, and sympathetic chain (Fig. 2) [2,4]. Thus, PVBs may be the closest anatomical approach to the concept of ‘paraneuraxial’ nerve blocks [12]. Even established anatomy textbooks, such as Gray’s Anatomy, do not use the term ‘paravertebral space’ [13]. The concept of the TPVS appears to have been shaped by clinical needs, as it has not been fully elucidated as a clearly delineated space from an anatomical perspective. Posteriorly, the TPVS is bounded by the transverse process, a rib, and the SCTL, and the needle should pass the SCTL to reach the TPVS for the conventional PVB [1,2]. In the classic literature, a subtle ‘pop’ or ‘click’ is felt upon the needle piercing the SCTL, and a loss of resistance is described [1,2]. In the T4–T5 region, for example, the SCTL originates from the superior surface of the fifth rib (Fig. 2) [14]. The anterior and posterior layers diverge from the common origin of the SCTL on the rib [14]. The anterior and posterior layers of the SCTL are attached to the inferior surfaces of the fourth rib and transverse process of T4, respectively [14]. In addition, the morphology of the SCTL with some anatomical variations seems to differ depending on the location of the upper or lower thoracic spine [15]. Therefore, although the SCTL is the most important landmark for the PVB, it



**Fig. 1.** Anatomical targets of paraspinal blocks at the mid-thoracic region on sectional images of micro-computed tomography. (A) A cross-sectional image at the level of the transverse process. (B) A cross-sectional image of the intertransverse process region. (C) A sagittal-sectional image of the intertransverse process region. Arrows indicate the paraspinal block techniques. The arrowheads indicate the superior costotransverse ligament (SCTL). The asterisk indicates the costotransverse space between the rib (R) and transverse process (TP). The red dotted lines indicate the erector spinae fascial plane. PVB: paravertebral block, RLB: retrolaminar block, ESP: erector spinae plane block, ITP: intertransverse process block, SP: spinous process, L: vertebral lamina, P: pleura, CTJ: costotransverse joint, CVJ: costovertebral joint, ES: erector spinae muscles, IAP: inferior articular process, DRG: dorsal root ganglion, ICN: intercostal nerve.



**Fig. 2.** Paravertebral space and adjacent anatomical structures at the mid-thoracic region. (A) Illustrated diagram of a transverse sectional view of the intertransverse/intercostal region. (B) Micro-computed tomography image corresponding to illustration A [14]. (C) Illustrated diagram of a sagittal sectional view of the intertransverse process region. (D) Micro-computed tomography image corresponding to illustration C [14]. The arrow indicates the costotransverse foramen, and arrowheads indicate the anterior and posterior layer of the superior costotransverse ligament (SCTL). The asterisks indicate the costotransverse space between the rib (R) and transverse process (TP). ES: erector spinae muscle, IAP: inferior articular process, ITL: intertransverse ligament, DRG: dorsal root ganglion, DR: dorsal rami, VR: ventral rami, ICN: intercostal nerve, SG: sympathetic ganglion, P: pleura, TPVS: thoracic paravertebral space (bluish area), RS: retro-SCTL space (greenish area).

is occasionally difficult to identify using ultrasonography. The SCTL is located very close to the pleura; in one anatomical report, the mean distance between the pleura and the attachment of the SCTL was only 7.8 mm [14]. Furthermore, the posterior intercostal artery and vein within the TPVS are located close to the pleura. The unique anatomy of the TPVS could explain the risks associated with PVBs.

### Potential risks of block-related complications

Although the reported incidence of procedure-related complications following PVBs varies among studies, it appears to be low when ultrasonography is used [5]. However, a recent meta-analysis reported a similar incidence of pneumothorax, pleural puncture, and vascular puncture at 0.3% with ultrasound-guided PVBs [7], although this is likely an underestimation due to under-reporting. Indeed, the incidence of procedure-related complications was higher with PVB than with other regional techniques for breast surgery [7]. Previously reported incidences of pneumothorax, pleural puncture, and vascular puncture after a PVB using the classic landmark technique were 0.5%, 1.1%, and 3.8%, respectively [16]. Therefore, while ultrasonography might reduce the failure rate of the PVB, clinicians should be aware of these potential procedural risks.

### Spreading pattern of the injectate

Typically for PVBs, there is both an anteromedial spread of injectate within the TPVS and a lateral intercostal spread. A PVB with 20 ml of injectate has been shown to spread paravertebrally

and intercostally over approximately 3–4 segments in cadavers [17]. A single injection of a PVB with 25 ml of local anesthetic and multiple injections of PVB with 5 ml at each of the five levels provided a similar sensory block over 4–6 dermatomes in patients undergoing a unilateral mastectomy [18]. The ventral rami of the spinal nerve and sympathetic ganglion were shown to be involved in successful thoracic PVBs, and epidural spread via the intervertebral foramen is often observed [17].

The endothoracic fascia seems to be significantly involved in the variability of injectate spreading patterns following a thoracic PVB. The endothoracic fascia, which is the deep fascia of the thorax, is a fibroelastic structure lining the thoracic cage. It is interposed between the parietal pleura and the innermost intercostal muscle in the chest wall, and between the parietal pleura and the SCTL or transverse process in the TPVS [19]. The endothoracic fascia divides the TPVS into two potential fascial compartments: the anterior (extrapleural) and the posterior (subendothoracic) compartment [2,19]. The sympathetic ganglion is contained in the extrapleural compartment, whereas the spinal nerve is located in the subendothoracic compartment [2,19]. This anatomy was confirmed by electron microscopy in rats [20]. However, the endothoracic fascia appears to be difficult to observe using a dissection technique in human tissues because it is a very thin fascia that is indistinguishable from the parietal pleura [21]. An injection in the extrapleural compartment may produce extensive longitudinal, prevertebral, and contralateral diffusion of the injectate with a sympathetic blockade [19,20]. In contrast, injections in the subendothoracic compartment of the TPVS may result in a cloud-like spreading pattern, with only limited distribution over adjacent segments, but with a greater chance of epidural spread



[19,20]. The endothoracic fascia is superiorly continuous with the suprapleural membrane (Sibson's fascia) that is attached to the inner border of the first rib and costal cartilage anteriorly, the C7 transverse process posteriorly, and the mediastinal pleura medially [19]. Inferiorly, the endothoracic fascia is continuous with the abdominal transversalis fascia [21,22]. This continuity occurs dorsal to the diaphragm through the lumbocostal arches and aortic hiatus [19]. The transversalis fascia blends medially with the fascia of the anterior layer of the quadratus lumborum and psoas fascia [22]. Anatomically, an injection into the subendothoracic compartment of the TPVS at the lower thoracic levels can spread caudally via the medial and lateral arcuate ligaments to the retroperitoneal space in the abdomen [22]. This spread can affect peripheral nerves originating from the lumbar plexus [19–21].

### Clinical evidence

The PVB is the oldest paraspinal block technique, and thus there are numerous clinical reports of PVBs in patients with surgical and chronic pain. The PVB can also be used for surgical anesthesia. Historically, PVB was designed to replace spinal anesthesia and was frequently performed to control pain during abdominal surgery [1]. According to data taken from six randomized controlled trials, thoracic PVBs for surgical anesthesia are associated with lower pain intensity during the immediate postoperative period, less postoperative nausea and vomiting, a shorter length of hospital stay, and greater patient satisfaction than general anesthesia in patients undergoing breast surgery [23]. PVBs have shown similar postoperative pain control efficacy after thoracic surgery to thoracic epidural analgesia [24,25]. Moreover, contra-

indications to thoracic epidural analgesia do not preclude PVBs in most cases. For thoracic surgeries, such as thoracotomies, PVBs provide better postoperative analgesia and lower opioid consumption than ESP blocks and RLBs [26–28]. Although conflicting results have been reported for breast cancer surgery [29], the analgesic efficacy of PVBs was found to be superior to that of ESP and other truncal blocks [7]. The PVB was thus recommended as the first-choice regional analgesic technique for major breast surgery in recently published guidelines [30].

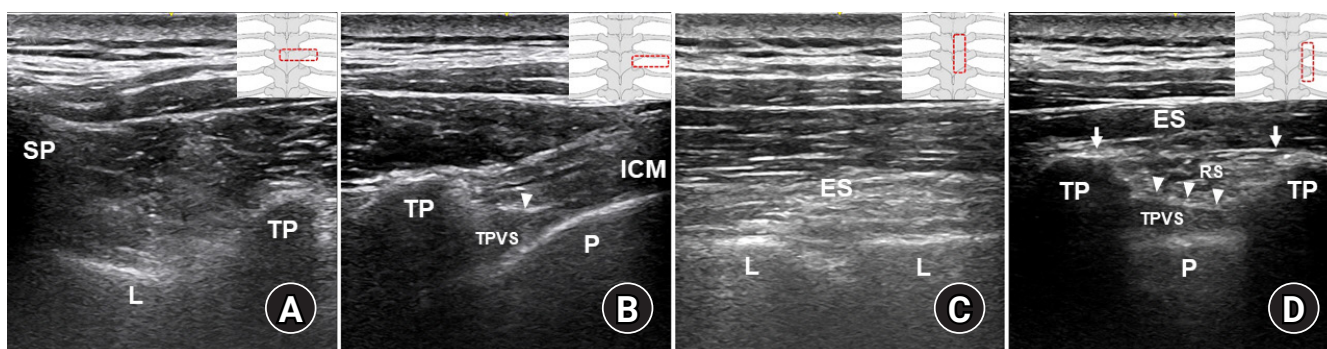
## Retrolaminar block

### Anatomical description

An RLB is anatomically described as an injection in the plane between the erector spinae muscles and the lamina (Fig. 1) [11].

### Anatomical considerations

The RLB, also known as the 'lamina technique,' was introduced much earlier than the ESP block. This technique was first described by Pfeiffer in 2006 as a landmark (blind) technique [31]. The main advantage of this technique is that it is a very simple procedure to perform, requiring either a single injection or the use of a catheter. Furthermore, it can be performed in the cervical and lumbar regions, and thus has a wide range of clinical indications. The target injection point for an RLB is the posterior surface of the vertebral lamina [32], while the ESP block targets the fascial plane deep to the erector spinae muscle at the tip of the transverse process (Fig. 3) [10], which is located more lateral-



**Fig. 3.** Ultrasound images of the paravertebral space and anatomical structures relevant to a paraspinal block at the mid-thoracic region. (A) A transverse scan to identify bony landmarks. (B) A transverse scan to perform a paravertebral block (PVB). (C) A parasagittal scan to perform a retrolaminar block (RLB). (D) A parasagittal scan of the intertransverse process (ITP) region. Illustrations in the right corner show the probe locations in each ultrasound image. Arrows indicate the erector spinae fascial plane (ESP), and arrowheads indicate the superior costotransverse ligament (SCTL). As shown in Fig. 3D, the erector spinae fascial plane is the target for an ESP block, the tissue complex posterior to the SCTL (retro-SCTL space) is the target for an ITP block, and the TPVS is directly targeted for the PVB. ES: erector spinae muscles, L: vertebral lamina, ICM: intercostal muscles, TP: transverse process, SP: spinous process, P: pleura, TPVS: thoracic paravertebral space, RS: retro-SCTL space.

ly than the target point of an RLB. Although the injection locations for these two techniques differ, there are anatomical similarities, because the anterior fascia of the erector spinae muscle group adheres to both the lamina and the transverse process.

### Spreading pattern of the injectate

Some anatomical studies have demonstrated that with an RLB, the injectate spreads to the TPVS, epidural space, intercostal space, and intervertebral foramina; however, the spreading pattern appears to be quite variable [33,34]. Compared with the conventional PVB, the spread of injectate to the TPVS is much more limited with an RLB [33]. The spinous process, lamina, and facet joint capsule can act as anatomical barriers between the retrolaminar space and the TPVS [34]. The lateral tip of the transverse process is directly and indirectly connected to the two layers of the thoracolumbar fascia [35]. The ESP block injectate is placed directly into the fascial space of the thoracolumbar fascia. For an RLB, however, the injectate is inserted into a plane continuous with the fascial space of the thoracolumbar fascia. Thus, in both techniques, the injectate can spread directly and indirectly into the posterior layer of the thoracolumbar fascia or the posterior fascia of the erector spinae [34]. However, cadaveric evaluation found the injectate of RLBs and ESP blocks to have distinct spreading patterns [34]. With the ESP block, which involves a direct injection into the fascial plane, the dye spreads more laterally, while with the RLB, it spreads vertically along the posterior surface of the lamina [34]. RLBs result in an intensely stained retrolaminar plane beneath the transversospinalis and erector spinae muscles, with wide vertical spread, which may indicate an adequate blockade of the dorsal rami at the affected spinal level [34].

### Clinical evidence

The RLB has been reported to be clinically effective in patients with rib fractures and those undergoing breast surgery [32,36,37]; however, clinical data regarding RLBs are more limited than the data available for the ESP block. In a previous report, the analgesic efficacy of the continuous RLB was found to be inferior to that of the continuous PVB in the first 24 h period after a mastectomy [38]. Furthermore, a single injection of an RLB was found to provide analgesia lasting only 2–3 h after breast surgery, which is a much shorter period than that reported for the PVB [39]. Additionally, in thoracoscopic surgery, PVBs provide better analgesia and result in less nausea than RLBs [28].

## Erector spinae plane block

### Anatomical description

The ESP block is anatomically described as an injection in the plane between the erector spinae muscles and the transverse process (Fig. 1) [11].

### Proposed mechanisms of action

The ESP block has gained popularity as a simpler and safer technique than the traditional PVB, given the option of injection through a catheter. However, the exact mechanism of action is still unclear. Some proposed mechanisms of action include analgesic effects mediated by elevated local anesthetic plasma concentrations due to systemic absorption, immunomodulatory analgesic effects via the lymphatic system, or analgesic effects mediated through nerve innervation of the thoracolumbar fascia [40]. However, these findings seem to be inconclusive and require further investigation [40]. The most controversial topic is whether the ESP block produces a neural blockade from the direct spread of the local anesthetic to the TPVS. Paravertebral spread was originally proposed as the primary mechanism of action of the ESP block [10]. However, anatomical study results are inconsistent. Some previous cadaveric studies have revealed limited or even no paravertebral spread with the ESP block, but more predominant posterior back muscle or fascia spread [34,41]. Nevertheless, the available evidence shows that paravertebral spread can and does occur. Magnetic resonance imaging of living subjects have demonstrated contrast medium spread into the paravertebral and even epidural spaces across multi-segmental levels with the ESP block [42,43].

### Limitations of cadaveric studies

Some limitations of cadaveric studies should be considered when interpreting these findings. The condition of the cadavers, such as their freeze-thaw status or whether they have been embalmed, can affect the results. Furthermore, owing to the nature of cadaveric studies, the sample size is limited and usually only descriptive results are reported. Additionally, postmortem changes in the muscle, fascia, and ligamentous tissue can significantly affect the diffusion of the injectate. More importantly, cadaveric studies cannot reflect delayed diffusion after an ESP block, as would occur with respiratory movement in living subjects.

## Clinical evidence

When the ESP block was first introduced, there was some controversy regarding its anatomical similarity to the RLB [44,45]. However, RLBs and ESP blocks show different spreading patterns in cadavers and different block efficacy in patients [34,46]. Although there are no clear clinical comparisons and more clinical data regarding RLBs are needed, the clinical efficacy of single-shot RLBs is controversial, while ESP blocks have been found to result in a significant reduction in postoperative pain [47–49]. Currently (5–6 years after the ESP block was first introduced), a large number of randomized controlled trials investigating the analgesic efficacy of ESP blocks in almost all types of surgeries performed on the human torso have been published [50]. Overall, the ESP block has provided better pain relief and lower opioid consumption after a variety of surgeries, such as breast surgery, laparoscopic cholecystectomy, and thoracotomy, than sham or no-block groups [47–54]. However, it is uncertain whether the ESP block can replace the conventional PVB, which has been found to afford better pain relief after thoracotomy and breast surgeries in several studies [7,27,53–55], although there were some conflicting results [29,54]. Furthermore, block reproducibility with consistent results is a major concern in clinical practice. Therefore, more controlled studies are needed to compare ESP blocks with robust multimodal analgesic regimens. Dermatome sensory blockade data on the ESP block should be evaluated according to the injected volume and spinal level. Considering the anatomical differences between the ESP block and PVB, it is reasonable to assume that these approaches differ in terms of their specific clinical indications and risk-benefit ratio. Thus, future clinical studies comparing ESP blocks with other truncal nerve blocks are warranted.

## Spreading pattern of the injectate

A significant amount of injectate spread following an ESP block injection has been observed in the back muscles and fascial layer in previous anatomical evaluations [34,41]. This spreading pattern clearly supports the multisegmental involvement of the dorsal rami of the spinal nerves with the ESP block. Certainly, this characteristic of the ESP block, which is similar to that of the RLB, can result in good analgesia during surgical procedures involving the spine or back [52,56]. However, to block the ventral rami of the spinal nerve or sympathetic ganglion, local anesthetics should be spread into the TPVS. The fascia structure is highly permeable to macromolecules, including local anesthetic agents [40]. At the microscopic level, gaps in its largely acellular architecture of interlinked collagen fibers readily permit rapid diffusion [40,57]. The

SCTL has a slit structure on both the medial and lateral ends, and its medial slit corresponds to the well-known anatomical ‘costo-transverse foramen’ (Fig. 4). Thus, the TPVS is not an anatomically isolated compartment or closed space, as it communicates with the outside posteriorly via the slits of the SCTL [14]. Additionally, some microroutes involving muscular branches of the dorsal rami and intercostal nerves and vessels or through the intercostal membrane could contribute to the spread of the injectate to the TPVS associated with the ESP block [40]. Indeed, there is considerable clinical evidence that although it has been reported sporadically or described as a side effect, that ESP blocks can involve the ventral rami and sympathetic nerves, yielding analgesia for visceral pain and complex regional pain syndrome, some sympathetically mediated symptoms (Harlequin syndrome, priapism, hypotension), and even motor blockade [58–65].

## Clinical considerations

Interfascial plane blocks are generally regarded as volume-dependent blocks [66]. The underlying principle is that a volume of local anesthetic is injected into a fascial plane remote from the intended site of action [9]. There are a few reports of local anesthetic systemic toxicity following ESP blocks with a large volume of local anesthetic [67,68]. However, the safe dose ranges of local anesthetics for ESP blocks have not been specifically evaluated based on serum concentrations. It is difficult to predict the volume of the injectate that will spread to the TPVS anteriorly or the back muscles and the fascial layer posteriorly with the ESP block. A previous cadaveric study showed that continually increasing the volume of injectate for ESP blocks does not guarantee an increase in the extent of paravertebral spread [69]. Therefore, for a safe and effective ESP block, clinical data regarding optimal dose-volume regimens that consider the patient condition, injection site, and types of local anesthetic should be gathered [70].

## Intertransverse process block

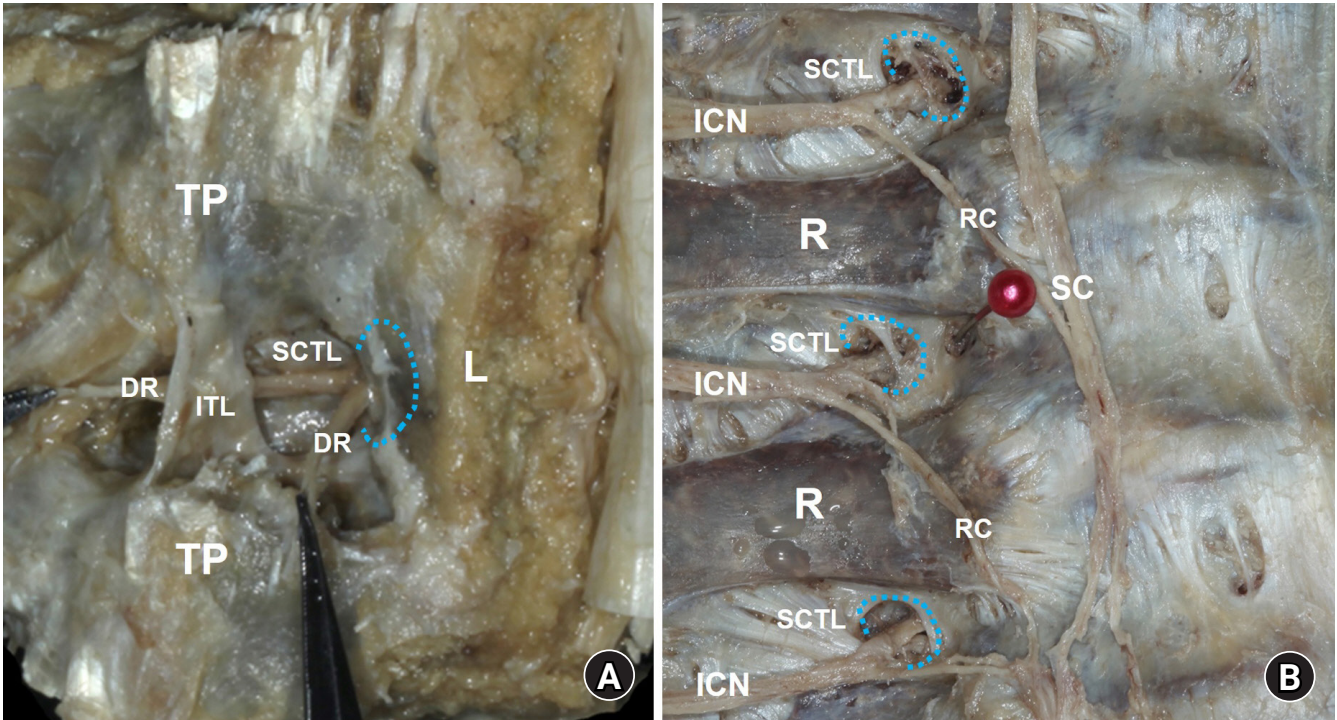
### Anatomical description

The ITP block is anatomically described as a block injected into the tissue between the two transverse processes, posterior to the SCTL, or halfway between the posterior aspect of the transverse process and the pleura (Fig. 1) [11].

### Anatomical considerations

The ITP block, recently named by international consensus [11],





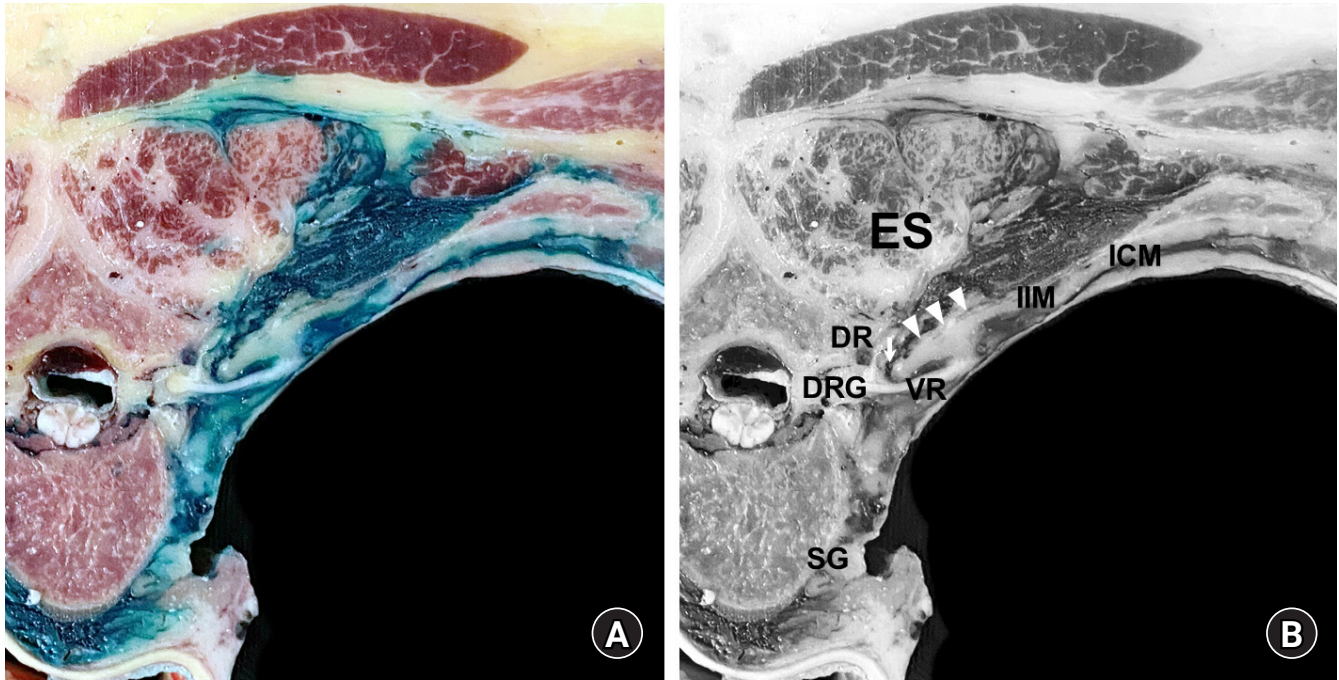
**Fig. 4.** Costovertebral foramina (CTF) at the mid-thoracic region. (A) The erector spinae muscles have been removed, and the dorsal rami of the spinal nerve (DR) emerge from the medial slit of the superior costotransverse ligament (SCTL), corresponding to the CTF (blue-dotted line) beneath the vertebral lamina (L). (B) In the intrathoracic view, the CTFs can be clearly visualized after the pleura and vessels have been removed. The ventral rami of the spinal nerve (intercostal nerve [ICN]) pass through the CTFs (blue-dotted line). TP: transverse process, ITL: intertransverse ligament, R: rib, RC: rami communicants, SC: sympathetic chain.

is a collective name for several reported block techniques, including the mid-point transverse process to pleura block [71], multiple injection costovertebral block [72], subtransverse process interligamentary block [73], and costovertebral foramen block [74]. The concept of the ITP block was first introduced by Costache et al. [71] in 2017 as a midpoint transverse process to the pleura block. The target site for the ITP block is tissue, which is clearly different from that of the fascial plane target for an ESP block or RLB. Thus, an ITP block is not an interfascial plane block. The complex area posterior to the SCTL was first described as the ‘intertransverse tissue complex’ (ITTC) and comprises the intertransverse ligament, fatty tissue, the intertransverse and levatores costarum muscles, and the SCTL, which borders the TPVS [72]. While the ITTC has been designated from an anatomical perspective, ultrasound images have not been able to show its intricacies in detail. The proposed term for the space posterior to the SCTL, the ‘retro-SCTL space’ [14], might clinically represent the appropriate target area of an anatomically intricate tissue complex for the ITP block. The erector spinae fascia, SCTL, the pleura that demarcates the erector spinae muscle compartment, the retro-SCTL space, and the TPVS are important landmarks used during an ultrasound-guided ITP block (Fig. 3) [75]. Recent mi-

cro-computed tomography images have provided a detailed three-dimensional anatomical depiction of the TPVS and retro-SCTL space using cadavers (Supplemental Video 1) [14,75].

### Spreading pattern of the injectate

In contrast to the ESP block or RLB, anatomical studies of ITP blocks have consistently demonstrated paravertebral spread with sympathetic involvement, which is a very similar pattern to that with the PVB (Fig. 5) [71,72,74,75]. The retro-SCTL space appears to directly communicate with the TPVS via the slit structure of the SCTL (the costovertebral foramen) and via the costovertebral space, which is the space between the transverse process and rib (Fig. 2) [14,75]. The costovertebral space is connected to the roof and base of the retro-SCTL space, and its base is incompletely covered by a part of the SCTL and radiate ligament [75]. Histological examination has revealed that the costovertebral space is mostly occupied by adipose and loose connective tissue [75]. In a cadaveric evaluation, the costovertebral foramen and costovertebral space were found to serve as anatomical conduits for anterior and intersegmental paravertebral spread of the ITP block, respectively [75]. Indeed, on real-time ultrasound images, anterior



**Fig. 5.** Dye spreading pattern following an intertransverse process (ITP) block. (A) A cross-sectional cut of a non-embalmed cadaver after a dye solution has been injected into the tissue complex posterior to the superior costotransverse ligament (SCTL), the retro-SCTL space, for an ITP block at the T4–T5 level [75]. (B) Anatomical structure annotations corresponding to Fig. 5A. The arrow indicates the costotransverse foramen (CTF; medial slit of the SCTL), and arrowheads indicate the SCTL. The dye was found to spread multidirectionally from the injection site (retro-SCTL space), into the paravertebral space through the CTF, intercostal space, and erector spinae (ES) compartment. The dye fully surrounded the dorsal rami (DR) and ventral rami (VR) of the spinal nerve and sympathetic ganglion (SG). DRG: dorsal root ganglion, IIM: intercostal membrane, ICM: intercostal muscles.

pleural displacement was observed with most ITP block injections [71,74,75]. However, some spreading of the injectate to the erector spinae fascia was also observed on real-time ultrasound images, indicating posterior spread [71,74,75]. Dye infiltration to the back muscles and fascia following the ITP block, which is similar to the spreading pattern of the ESP block, has been observed in most cadaveric studies [71,72,74,75]. Although this spread can contribute to the blockade of the dorsal rami of the spinal nerve, it can also result in the loss of injectate volume that can spread paravertebrally. A needle replacement technique has previously been proposed to minimize this posterior spread until adequate anterior spread is visualized by ultrasonography [74]. In terms of paravertebral spread, recent reports have suggested that as the ITP block involves injection into the retro-SCTL space, which has direct and close pathways to the TPVS, this could be anatomically more advantageous than the ESP block or RLB [71,72,74,75]. Local anesthetics follow a longer pathway to reach the TPVS, through both the erector spinae fascia and retro-SCTL space, with the RLB and ESP block. The bottom line shows that the ITP block has characteristics that fall somewhere between those of the PVB and ESP block.

### Clinical evidence

Indeed, despite the limited sample sizes of the studies, ITP blocks have been shown to have excellent analgesic efficacy and provide a strong sensory block in patients undergoing breast surgery or thoracotomy [71–74]. However, more data are required concerning the effectiveness of the ITP block compared to the ESP block or RLB. The clinical potential and efficacy of ITP blocks should be evaluated in further clinical studies and compared to those of thoracic paraspinal or truncal nerve blocks.

### Conclusions

A precise anatomical understanding of the TPVS is essential for a successful and safe performance of thoracic paraspinal blocks. Despite some potential risks, the PVB is a well-established technique with a wealth of available clinical data and comparable analgesic efficacy to epidural blocks. Thus, education and training regarding thoracic PVB performance in clinical practice should continue. ESP blocks and RLBs, which are more superficial blocks, do not approach the pleura and neurovascular structures,



and their procedure-related risks are lower compared to the PVB. Furthermore, the ESP block and RLB can be performed in difficult situations or in the cervical/lumbar regions for a wide range of clinical indications. However, it is uncertain whether the ESP block has the same analgesic efficacy as the conventional PVB. The ITP block targets the retro-SCTL space, which has more direct and closer pathways to the TPVS and appears to be anatomically more advantageous than the ESP block or RLB. Further clinical studies are needed to confirm this anatomical finding for ITP blocks.

Each type of thoracic paraspinal block has a different anatomical basis, resulting in different spreading patterns of the injectate. Consequently, the intrinsic characteristics of the neural blockade differ according to the technique. Understanding the proposed mechanisms of action of each paraspinal block could assist clinicians in further investigating and refining block performance, with the ultimate goal of optimizing analgesic efficacy and improving patient outcomes.

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## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## Supplementary Material

Supplemental Video 1. Serial three-dimensional images at the T4–T5 level are shown in the cross and sagittal sections.

## References

- Richardson J, Lönnqvist PA. Thoracic paravertebral block. *Br J Anaesth* 1998; 81: 230-8.
- Karmakar MK. Thoracic paravertebral block. *Anesthesiology* 2001; 95: 771-80.
- Krediet AC, Moayeri N, van Geffen GJ, Bruhn J, Renes S, Bigeleisen PE, et al. Different approaches to ultrasound-guided thoracic paravertebral block: an illustrated review. *Anesthesiology* 2015; 123: 459-74.
- Boezaart AP, Lucas SD, Elliott CE. Paravertebral block: cervical, thoracic, lumbar, and sacral. *Curr Opin Anaesthesiol* 2009; 22: 637-43.
- Pace MM, Sharma B, Anderson-Dam J, Fleischmann K, Warren L, Stefanovich P. Ultrasound-guided thoracic paravertebral blockade: a retrospective study of the incidence of complications. *Anesth Analg* 2016; 122: 1186-91.
- Kus A, Gurkan Y, Gul Akgul A, Solak M, Tokar K. Pleural puncture and intrathoracic catheter placement during ultrasound guided paravertebral block. *J Cardiothorac Vasc Anesth* 2013; 27: e11-2.
- Singh NP, Makkar JK, Kuberan A, Guffey R, Uppal V. Efficacy of regional anesthesia techniques for postoperative analgesia in patients undergoing major oncologic breast surgeries: a systematic review and network meta-analysis of randomized controlled trials. *Can J Anaesth* 2022; 69: 527-49.
- Chitnis SS, Tang R, Mariano ER. The role of regional analgesia in personalized postoperative pain management. *Korean J Anesthesiol* 2020; 73: 363-71.
- Elsharkawy H, Pawa A, Mariano ER. Interfascial plane blocks: back to basics. *Reg Anesth Pain Med* 2018; 43: 341-6.
- Forero M, Adhikary SD, Lopez H, Tsui C, Chin KJ. The erector spinae plane block: a novel analgesic technique in thoracic neuropathic pain. *Reg Anesth Pain Med* 2016; 41: 621-7.
- El-Boghdadly K, Wolmarans M, Stengel AD, Albrecht E, Chin KJ, Elsharkawy H, et al. Standardizing nomenclature in regional anesthesia: an ASRA-ESRA Delphi consensus study of abdominal wall, paraspinal, and chest wall blocks. *Reg Anesth Pain Med* 2021; 46: 571-80.
- Xu JL. Paraneuraxial nerve blocks: a well-defined novel terminology that is clinically essential for regional anesthesia. *J Clin Anesth* 2017; 43: 14.
- Standring S. Gray's anatomy: the anatomical basis of clinical practice. 42nd ed. London, Elsevier Health Sciences. 2020, pp 732-939.
- Cho TH, Kim SH, O J, Kwon HJ, Kim KW, Yang HM. Anatomy of the thoracic paravertebral space: 3D micro-CT findings and their clinical implications for nerve blockade. *Reg Anesth Pain Med* 2021; 46: 699-703.
- Ibrahim AF, Darwish HH. The costotransverse ligaments in human: a detailed anatomical study. *Clin Anat* 2005; 18: 340-5.
- Lönnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. *Anaesthesia* 1995; 50: 813-5.
- Cowie B, McGlade D, Ivanusic J, Barrington MJ. Ultrasound-guided thoracic paravertebral blockade: a cadaveric study. *Anesth Analg* 2010; 110: 1735-9.
- Uppal V, Sondekoppam RV, Sodhi P, Johnston D, Ganapathy S.



- Single-injection versus multiple-injection technique of ultrasound-guided paravertebral blocks: a randomized controlled study comparing dermatomal spread. *Reg Anesth Pain Med* 2017; 42: 575-81.
19. Karmakar MK, Chung DC. Variability of a thoracic paravertebral block. Are we ignoring the endothoracic fascia? *Reg Anesth Pain Med* 2000; 25: 325-7.
  20. Stopar Pintaric T, Veranic P, Hadzic A, Karmakar M, Cvetko E. Electron-microscopic imaging of endothoracic fascia in the thoracic paravertebral space in rats. *Reg Anesth Pain Med* 2012; 37: 215-8.
  21. Bouman EA, Sieben JM, Balthasar AJR, Joosten EA, Gramke HF, van Kleef M, et al. Boundaries of the thoracic paravertebral space: potential risks and benefits of the thoracic paravertebral block from an anatomical perspective. *Surg Radiol Anat* 2017; 39: 1117-25.
  22. Saito T, Den S, Tanuma K, Tanuma Y, Carney E, Carlsson C. Anatomical bases for paravertebral anesthetic block: fluid communication between the thoracic and lumbar paravertebral regions. *Surg Radiol Anat* 1999; 21: 359-63.
  23. Thavaneswaran P, Rudkin GE, Cooter RD, Moyes DG, Perera CL, Maddern GJ. Brief reports: paravertebral block for anesthesia: a systematic review. *Anesth Analg* 2010; 110: 1740-4.
  24. Yeung JH, Gates S, Naidu BV, Wilson MJ, Gao Smith F. Paravertebral block versus thoracic epidural for patients undergoing thoracotomy. *Cochrane Database Syst Rev* 2016; 2: CD009121.
  25. Ding X, Jin S, Niu X, Ren H, Fu S, Li Q. A comparison of the analgesia efficacy and side effects of paravertebral compared with epidural blockade for thoracotomy: an updated meta-analysis. *PLoS One* 2014; 9: e96233.
  26. Xiong C, Han C, Zhao D, Peng W, Xu D, Lan Z. Postoperative analgesic effects of paravertebral block versus erector spinae plane block for thoracic and breast surgery: a meta-analysis. *PLoS One* 2021; 16: e0256611.
  27. Turhan Ö, Sivriköz N, Sungur Z, Duman S, Özkan B, Şentürk M. Thoracic paravertebral block achieves better pain control than erector spinae plane block and intercostal nerve block in thoracoscopic surgery: a randomized study. *J Cardiothorac Vasc Anesth* 2021; 35: 2920-7.
  28. Wang Q, Wei S, Li S, Yu J, Zhang G, Ni C, et al. Comparison of the analgesic effect of ultrasound-guided paravertebral block and ultrasound-guided retrolaminar block in Uniportal video-assisted thoracoscopic surgery: a prospective, randomized study. *BMC Cancer* 2021; 21: 1229.
  29. Weng WT, Wang CJ, Li CY, Wen HW, Liu YC. Erector spinae plane block similar to paravertebral block for perioperative pain control in breast surgery: a meta-analysis study. *Pain Physician* 2021; 24: 203-13.
  30. Jacobs A, Lemoine A, Joshi GP, Van de Velde M, Bonnet F; PROSPECT Working Group collaborators#. PROSPECT guideline for oncological breast surgery: a systematic review and procedure-specific postoperative pain management recommendations. *Anaesthesia* 2020; 75: 664-73.
  31. Pfeiffer G, Oppitz N, Schöne S, Richter-Heine I, Höhne M, Koltermann C. Analgesia of the axilla using a paravertebral catheter in the lamina technique. *Anaesthesist* 2006; 55: 423-7.
  32. Voscopoulos C, Palaniappan D, Zeballos J, Ko H, Janfaza D, Vlassakov K. The ultrasound-guided retrolaminar block. *Can J Anaesth* 2013; 60: 888-95.
  33. Sabouri AS, Crawford L, Bick SK, Nozari A, Anderson TA. Is a retrolaminar approach to the thoracic paravertebral space possible?: a human cadaveric study. *Reg Anesth Pain Med* 2018; 43: 864-8.
  34. Yang HM, Choi YJ, Kwon HJ, O J, Cho TH, Kim SH. Comparison of injectate spread and nerve involvement between retrolaminar and erector spinae plane blocks in the thoracic region: a cadaveric study. *Anaesthesia* 2018; 73: 1244-50.
  35. Willard FH, Vleeming A, Schuenke MD, Danneels L, Schleip R. The thoracolumbar fascia: anatomy, function and clinical considerations. *J Anat* 2012; 221: 507-36.
  36. Jüttner T, Werdehausen R, Hermanns H, Monaca E, Danzeisen O, Pannen BH, et al. The paravertebral lamina technique: a new regional anesthesia approach for breast surgery. *J Clin Anesth* 2011; 23: 443-50.
  37. Zeballos JL, Voscopoulos C, Kapottos M, Janfaza D, Vlassakov K. Ultrasound-guided retrolaminar paravertebral block. *Anaesthesia* 2013; 68: 649-51.
  38. Murouchi T, Yamakage M. Retrolaminar block: analgesic efficacy and safety evaluation. *J Anesth* 2016; 30: 1003-7.
  39. Onishi E, Murakami M, Nishino R, Ohba R, Yamauchi M. Analgesic effect of double-level retrolaminar paravertebral block for breast cancer surgery in the early postoperative period: a placebo-controlled, randomized clinical trial. *Tohoku J Exp Med* 2018; 245: 179-85.
  40. Chin KJ, El-Boghdadly K. Mechanisms of action of the erector spinae plane (ESP) block: a narrative review. *Can J Anaesth* 2021; 68: 387-408.
  41. Ivanusic J, Konishi Y, Barrington MJ. A cadaveric study investigating the mechanism of action of erector spinae blockade. *Reg Anesth Pain Med* 2018; 43: 567-71.
  42. Schwartzmann A, Peng P, Maciel MA, Forero M. Mechanism of the erector spinae plane block: insights from a magnetic resonance imaging study. *Can J Anaesth* 2018; 65: 1165-6.
  43. Schwartzmann A, Peng P, Maciel MA, Alcarraz P, Gonzalez X,

- Forero M. A magnetic resonance imaging study of local anesthetic spread in patients receiving an erector spinae plane block. *Can J Anaesth* 2020; 67: 942-8.
44. Ueshima H, Otake H. Similarities between the retrolaminar and erector spinae plane blocks. *Reg Anesth Pain Med* 2017; 42: 123-4.
  45. Murouchi T. Consideration of block nomenclature: erector spinae plane block or retrolaminar block? *Reg Anesth Pain Med* 2017; 42: 124.
  46. Onishi E, Toda N, Kameyama Y, Yamauchi M. Comparison of clinical efficacy and anatomical investigation between retrolaminar block and erector spinae plane block. *Biomed Res Int* 2019; 2019: 2578396.
  47. Tulgar S, Kapakli MS, Senturk O, Selvi O, Serifsoy TE, Ozer Z. Evaluation of ultrasound-guided erector spinae plane block for postoperative analgesia in laparoscopic cholecystectomy: a prospective, randomized, controlled clinical trial. *J Clin Anesth* 2018; 49: 101-6.
  48. Gürkan Y, Aksu C, Kuş A, Yörükoğlu UH, Kılıç CT. Ultrasound guided erector spinae plane block reduces postoperative opioid consumption following breast surgery: a randomized controlled study. *J Clin Anesth* 2018; 50: 65-8.
  49. Krishna SN, Chauhan S, Bhoi D, Kaushal B, Hasija S, Sangdup T, et al. Bilateral erector spinae plane block for acute post-surgical pain in adult cardiac surgical patients: a randomized controlled trial. *J Cardiothorac Vasc Anesth* 2019; 33: 368-75.
  50. Jiao B, Chen H, Chen M, Lu P, Liu J, Chen C. Opioid-sparing effects of ultrasound-guided erector spinae plane block for adult patients undergoing surgery: a systematic review and meta-analysis. *Pain Pract* 2022; 22: 391-404.
  51. Zhang Y, Liu T, Zhou Y, Yu Y, Chen G. Analgesic efficacy and safety of erector spinae plane block in breast cancer surgery: a systematic review and meta-analysis. *BMC Anesthesiol* 2021; 21: 59.
  52. Liang X, Zhou W, Fan Y. Erector spinae plane block for spinal surgery: a systematic review and meta-analysis. *Korean J Pain* 2021; 34: 487-500.
  53. Kot P, Rodriguez P, Granell M, Cano B, Rovira L, Morales J, et al. The erector spinae plane block: a narrative review. *Korean J Anesthesiol* 2019; 72: 209-20.
  54. Saadawi M, Layera S, Aliste J, Bravo D, Leurcharusmee P, Tran Q. Erector spinae plane block: a narrative review with systematic analysis of the evidence pertaining to clinical indications and alternative truncal blocks. *J Clin Anesth* 2021; 68: 110063.
  55. Swisher MW, Wallace AM, Sztain JF, Said ET, Khatibi B, Abanobi M, et al. Erector spinae plane versus paravertebral nerve blocks for postoperative analgesia after breast surgery: a randomized clinical trial. *Reg Anesth Pain Med* 2020; 45: 260-6.
  56. Oh SK, Lim BG, Won YJ, Lee DK, Kim SS. Analgesic efficacy of erector spinae plane block in lumbar spine surgery: a systematic review and meta-analysis. *J Clin Anesth* 2022; 78: 110647.
  57. Yang HM, Kim SH. Injectate spread in interfascial plane block: a microscopic finding. *Reg Anesth Pain Med* 2019. Advance Access published on Jul 5, 2019. doi: 10.1136/rapm-2019-100693.
  58. Bang S, Choi J, Kim ED. A high thoracic erector spinae plane block used for sympathetic block in patients with upper extremity complex regional pain syndrome. *J Clin Anesth* 2020; 60: 99-100.
  59. Elkoundi A, Eloukkal Z, Bensghir M, Belyamani L, Lalaoui SJ. Erector spinae plane block for hyperalgesic acute pancreatitis. *Pain Med* 2019; 20: 1055-6.
  60. Aydin ME, Ahiskalioglu A, Tekin E, Ozkaya F, Ahiskalioglu EO, Bayramoglu A. Relief of refractory renal colic in emergency department: a novel indication for ultrasound guided erector spinae plane block. *Am J Emerg Med* 2019; 37: 794. e1-3.
  61. Sullivan TR, Kanda P, Gagne S, Costache I. Harlequin syndrome associated with erector spinae plane block. *Anesthesiology* 2019; 131: 665.
  62. Elkoundi A, Eloukkal Z, Bensghir M, Belyamani L. Priapism following erector spinae plane block for the treatment of a complex regional pain syndrome. *Am J Emerg Med* 2019; 37: 796. e3-4.
  63. Pak A, Singh P. Epidural-like effects with bilateral erector spinae plane catheters after abdominal surgery: a case report. *A A Pract* 2020; 14: 137-9.
  64. Selvi O, Tulgar S. Ultrasound guided erector spinae plane block as a cause of unintended motor block. *Rev Esp Anesthesiol Reanim (Engl Ed)* 2018; 65: 589-92.
  65. De Cassai A, Fasolo A, Geraldini F, Munari M. Motor block following bilateral ESP block. *J Clin Anesth* 2020; 60: 23.
  66. Hamilton DL. Local anesthetic systemic toxicity following erector spinae plane block: sometimes less is more. *Korean J Anesthesiol* 2021; 74: 361-2.
  67. Yawata S, Imamachi N, Sakura S, Yamamoto H, Saito Y. Local anesthetic systemic toxicity of levobupivacaine in erector spinae plane block. *Korean J Anesthesiol* 2021; 74: 271-2.
  68. Karaca O, Pinar HU. Is high dose lumbar erector spinae plane block safe? *J Clin Anesth* 2020; 62: 109721.
  69. Choi YJ, Kwon HJ, O J, Cho TH, Won JY, Yang HM, et al. Influence of injectate volume on paravertebral spread in erector spinae plane block: an endoscopic and anatomical evaluation. *PLoS One* 2019; 14: e0224487.
  70. Tulgar S, Ahiskalioglu A, Balaban O. Reply to Dr. Ueshima: the relationship of local anesthetic volume and dermatomal spread of sensorial block in erector spinae plane blocks: a new dilemma.

- J Clin Anesth 2019; 52: 57.
71. Costache I, de Neumann L, Ramnanan CJ, Goodwin SL, Pawa A, Abdallah FW, et al. The mid-point transverse process to pleura (MTP) block: a new end-point for thoracic paravertebral block. *Anaesthesia* 2017; 72: 1230-6.
  72. Nielsen MV, Moriggl B, Hoermann R, Nielsen TD, Bendtsen TE, Børglum J. Are single-injection erector spinae plane block and multiple-injection costotransverse block equivalent to thoracic paravertebral block? *Acta Anaesthesiol Scand* 2019; 63: 1231-8.
  73. Kilicaslan A, Sarkilar G, Altınok T, Tulgar S. A novel ultrasound-guided technique in peri-paravertebral area: subtransverse process interligamentary (STIL) plane block: the game has not ended yet. *J Clin Anesth* 2020; 60: 76-7.
  74. Shibata Y, Kampitak W, Tansatit T. The novel costotransverse foramen block technique: distribution characteristics of injectate compared with erector spinae plane block. *Pain Physician* 2020; 23: E305-14.
  75. Cho TH, Kwon HJ, O J, Cho J, Kim SH, Yang HM. The pathway of injectate spread during thoracic intertransverse process (ITP) block: micro-computed tomography findings and anatomical evaluations. *J Clin Anesth* 2022; 77: 110646.



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## Remimazolam – current knowledge on a new intravenous benzodiazepine anesthetic agent

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Intravenous anesthetic agents such as midazolam, propofol, and ketamine are routinely used to provide anesthesia and sedation. They have been shown to effectively induce and maintain amnesia, sedation, and hypnosis in various patient groups and clinical settings. However, all anesthetic agents have the potential to cause unwanted side effects such as hemodynamic instability, respiratory depression, or slow recovery due to prolonged post-procedural sedation. Remimazolam, a recently approved benzodiazepine for general anesthesia and procedural sedation in Korea, has been successfully used for these purposes. To date, inconclusive knowledge has been obtained regarding the use of remimazolam in different patient populations and under various surgical conditions. With respect to the specific pharmacokinetic and pharmacodynamic characteristics of remimazolam, the use of remimazolam is expected to increase providing safe general anesthesia and sedation. This review aims to provide an overview of the basic and clinical pharmacology of remimazolam and to compare it with midazolam and propofol.

**Keywords:** Amnesia; Anesthesia; Benzodiazepine; Conscious sedation; Hypnosis; Remimazolam.

### Introduction

Remimazolam is a rapidly metabolized benzodiazepine (BZD) that has been approved for general anesthesia and procedural sedation in Korea since 2021. It shows the typical pharmacodynamic profile of other BZDs (e.g., midazolam), but has high organ-independent elimination clearance. It is rapidly metabolized by nonspecific esterases [predominantly carboxylesterase 1A (CES 1A)], mainly localized in the human liver, to CNS7054, a so-called inactive metabolite with reduced binding affinity with a 300 to 400 times reduced binding affinity at the  $\gamma$ -aminobutyric acid (GABA) type A receptor. After administration, plasma concentrations of remimazolam predictably and rapidly decrease, and with adequate dosing, there is no prolonged sedative effect. Though it has been approved in Korea for general anesthesia, further clinical experience with remimazolam as well as evidence-based approaches for dosing and drug handling are needed for its safe and efficient use in various patient populations and clinical conditions. Therefore, the aim of this review article is to provide an overview of the specific pharmacodynamic and pharmacokinetic characteristics of remimazolam relevant to its clinical application as a modern intravenous sedative and anesthetic agent.



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## Basic knowledge on intravenous anesthetic agents

### Mechanism of action of intravenous anesthetic agents

While the introduction of general anesthesia was a revolutionary achievement in medical history, the mechanism of action of anesthetic agents is still not fully understood. The concept that anesthetic agents produce neuro-depression in specific areas of the central nervous system by enhancing the effect of inhibitory neurotransmitters (especially GABA), reducing the effect of excitatory neurotransmitters, and suppressing specific neuronal network activity necessary for consciousness and arousal has been generally accepted [1,2]. The GABA receptor system is the main inhibitory receptor population in the human central nervous system and the main target receptor for intravenous anesthetic agents that induce general anesthesia [1]. Most intravenous anesthetic agents, such as barbiturates, BZDs, propofol, and etomidate, bind to GABA type A receptors, except for ketamine, which mainly acts via the N-methyl-D-aspartate (NMDA) receptor along with other receptor types. All intravenous anesthetic agents can induce amnesia, hypnosis, sedation, unconsciousness, and immobility (muscle-suppression), although immobility is achieved to a greater extent with inhalational anesthetic agents. Intravenous anesthetic agents may also induce cardiovascular depression, respiratory depression, or pain during injection.

### An ideal intravenous anesthetic agent and soft drug

An ideal intravenous anesthetic agent (Table 1) has not yet been

developed. All the available intravenous anesthetic agents can cause undesirable side effects. Therefore, balanced anesthesia using a combination of different anesthetic agents at the lowest possible doses to achieve adequate anesthesia has been used in the past to minimize side effects in daily practice. Modern anesthetic agents must therefore be effective, efficient, and well tolerated. To improve usability, new intravenous anesthetic agents should also offer a drug effect that is predictable, with a rapid onset and offset. Drug development programs are searching for intravenous anesthetic agents that are specifically structured to undergo rapid biotransformation into inactive metabolites. This type of drug is called a “soft drug,” and remifentanyl is a well-known prototype. Remimazolam, which is the newest “soft drug,” has been developed based on the midazolam molecular structure (Figs. 1 and 2) and is a structural analog with an added ester side chain. After

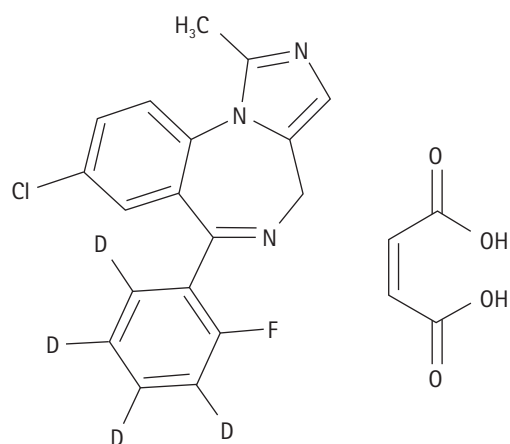
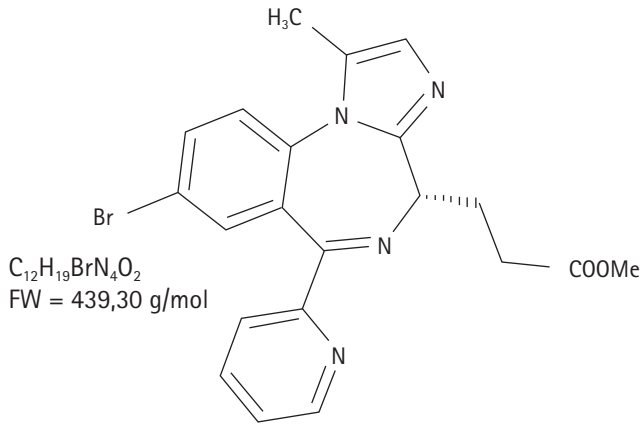


Fig. 1. Chemical structure of midazolam.

Table 1. Ideal Intravenous Anesthetic Agent

Physical and chemical properties	Pharmacology
Chemically stable	Painless injection
Water soluble	Low incidence of thrombophlebitis
No additives/No reconstitution required	Harmless on extravasation and intraarterial injection
Long shelf-life	Low incidence of adverse reactions
Compatible with other intravenous fluids or drugs	Smooth onset of anesthesia
Bacteriostatic	No associated unwanted movements
	Anticonvulsant, antiemetic, and analgesic effects
	No associated respiratory depression or bronchodilation
	No cardiovascular depression or stimulation
	Predictable recovery
	Rapid conversion to non-active metabolites
	No hepatic or renal impairment
	No suppression of corticosteroid synthesis
	No association with emergence phenomenon
	No teratogenic effects
	Not much accumulation in body tissues, maintenance of general anesthesia possible



**Fig. 2.** Chemical structure of remimazolam.

discontinuing the administration of a soft drug, the effects rapidly disappear, as the parent compound is quickly converted to inactive or much less active metabolites [3]. Anesthetic soft drugs can be further characterized by pharmacologic efficiency, which is an easy dosing scheme with a superior care-to-treatment-cost ratio, rapid restoration of protective reflexes, rapid return of spontaneous ventilation, and reduced need for postoperative care monitoring [3].

Midazolam, a well-known BDZ, is metabolized by hepatic cytochrome P450 enzymes and glucuronide conjugation [4]. However, in contrast to remimazolam, midazolam metabolites are active. The sedative or anesthetic effect of midazolam and its metabolites can be prolonged due to its organ dependency and much lower drug clearance rate, especially after prolonged drug administration or in patients with advanced age or reduced hepatic or renal function. Midazolam, in contrast to remimazolam, cannot be called a soft drug. To date, the use of midazolam for anesthesia and sedation has been limited mainly to postoperative intensive care unit sedation. Midazolam is no longer used for the maintenance of intravenous anesthesia.

## Remimazolam

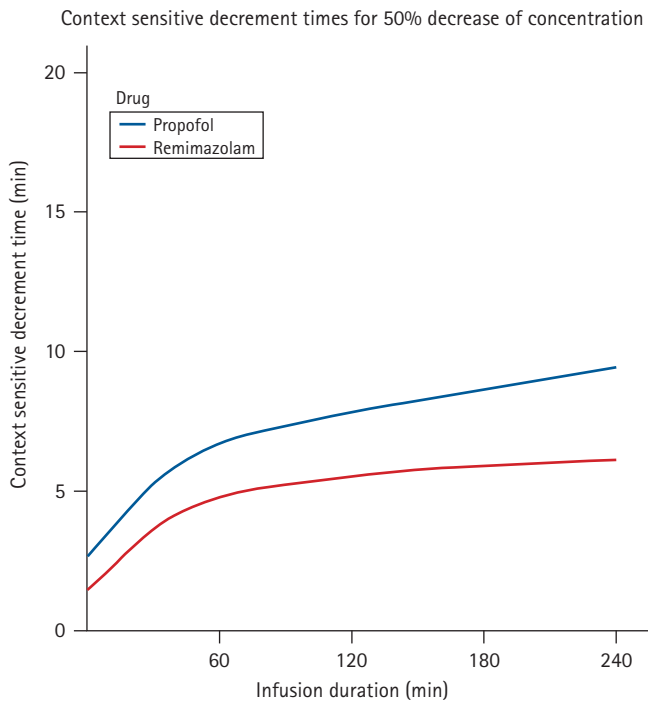
### Basic pharmacology of remimazolam

Depending on the plasma and effect site concentrations (biophase) of remimazolam, the following effects can be reliably achieved: amnesia, sedation and hypnosis, unconsciousness, and some degree of immobility. In comparison to midazolam, remimazolam does not cause prolonged sedative effects after discontinuation because it is rapidly metabolized by nonspecific tissue esterases to CNS7054, the only active metabolite with an affinity for the GABA type A receptor that is 300 times lower and with no

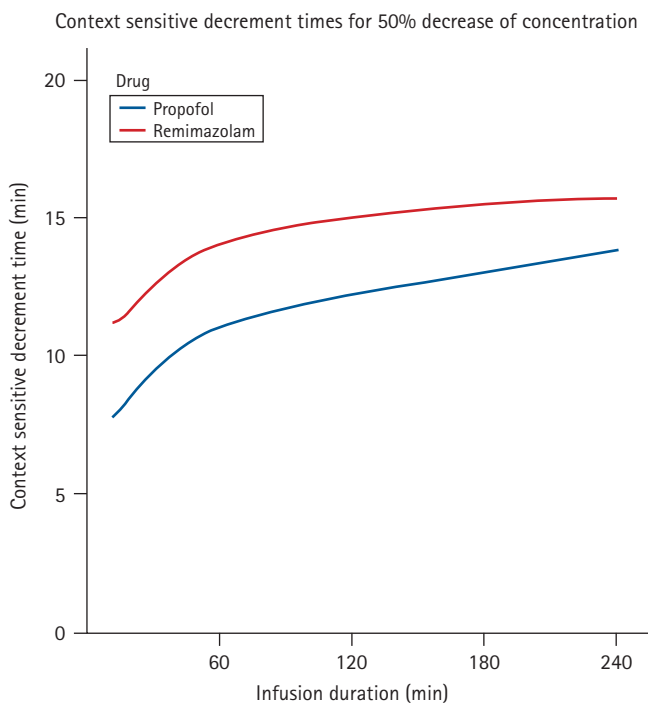
clinically relevant effect at the receptor site [5]. Remimazolam is a “soft drug” with the pharmacodynamic characteristics of a BZD. Remimazolam shows some characteristics of an ideal intravenous anesthetic agent. It is water-soluble, has a high clearance rate that is organ-independent, and shows more benign hemodynamic and respiratory side effects than propofol.

The pharmacokinetics of remimazolam have been described using non-compartmental and compartmental modeling approaches as well as a recirculatory model [6–8]. In these pharmacokinetic models, total body clearance was found to be independent of body weight, which was remarkable. In a clinical trial, Lu et al. [9] estimated that a body-weight-independent single dose of 11.43 mg of remimazolam achieves a 90% ( $ED_{90}$ ) probability for adequate sedation during colonoscopy. This study illustrates body-weight-independent and simple dosing concepts for remimazolam. Total body clearance values have been estimated at  $70.3 \pm 13.9$  L/h by Antonik et al. [8]  $66.7 \pm 2.59$  L/h by Wiltshire et al. [7], and  $69 \pm 7.2$  L/h by Schuttler et al. [6]. In contrast, the total body clearance of midazolam has been measured at  $22.6 \pm 8.36$  L/h by Wiltshire et al. [7]. Thus, the clearance of midazolam appears to be nearly one-third the total body clearance of remimazolam. The total body clearance for propofol has been measured at  $102 \pm 18$  L/h by Gepts et al. [10] in a rather historic but still used dataset, incorporated as the “Marsh model” [11] in commercially available target-controlled infusion (TCI) systems for propofol. Therefore, the estimated total body clearance rate of propofol is approximately 25–30% higher than that of remimazolam, but the clearance of propofol is organ-dependent and can be reduced in hepatic disease. In contrast, Stöhr et al. [12] showed that neither hepatic nor renal dysfunction impairs the clearance of remimazolam. A total volume of distribution at steady state ( $V_{dss}$ ) of approximately 35 L has been described for remimazolam [6,8], whereas for propofol, the  $V_{dss}$  has been estimated at 400 L [10], which is approximately 10 times the  $V_{dss}$  of remimazolam. A smaller  $V_{dss}$  speeds up drug elimination and patient recovery, as it indicates that less drug has accumulated in the body during administration, and so less has to be cleared after discontinuation. Based on pharmacokinetic simulations, context-sensitive decrement times of a 50% decrease in the plasma and effect site concentrations of remimazolam are very comparable to the simulated times for propofol (Figs. 3 and 4). In these simulations, the pharmacokinetic dataset of Gepts/Marsh et al. [11] for propofol and the pharmacokinetic dataset of Schuttler et al. [6] for remimazolam were used. The decrement time is shorter for remimazolam when we look at the decrease in plasma concentration, but it is approximately 3 to 4 min longer when we look at the decrease in the effect site concentration. This is more consistent with the clin-





**Fig. 3.** Simulation of context-sensitive decrement times of plasma concentrations for remimazolam and propofol (remimazolam  $k_{e0} = 0.25 \text{ min}^{-1}$ ; propofol  $k_{e0} = 0.26 \text{ min}^{-1}$ ).



**Fig. 4.** Simulation of the context-sensitive decrement times of effect concentrations for remimazolam and propofol (remimazolam  $k_{e0} = 0.25 \text{ min}^{-1}$ ; propofol  $k_{e0} = 0.26 \text{ min}^{-1}$ ).

ical finding that recovery times after remimazolam anesthesia tend to be approximately 1–5 min longer when directly compared to propofol [13].

The transfer constant  $k_{e0}$  (1/min) describes the speed of drug exchange between the central compartment and the effect compartment or the biophase. A  $k_{e0}$  of approximately  $0.25 \text{ min}^{-1}$  has been estimated for remimazolam using the modified observer's assessment of alertness and sedation (MOAA/S) scale as a parameter of the electroencephalogram (EEG) in volunteers of both sexes by Wiltshire et al. [7]. A  $k_{e0}$  value of 0.33 has been described by Eisenried et al. [14] in young male healthy volunteers using the beta ratio of the EEG as a pharmacodynamic parameter. A larger  $k_{e0}$  value would speed up substance exchange between the effect compartment and central compartment and thus shorten the induction and recovery times. From a scientific point of view, insufficient data have been published to date regarding the exact estimation of the  $k_{e0}$  value of remimazolam for the bispectral index (BIS). This is the most clinically relevant EEG parameter when remimazolam is administered to induce and maintain general anesthesia or sedation.

Interaction modeling between opioids and remimazolam during general anesthesia has only been described for remifentanyl in a publication by Zhou et al. [15], in which the BIS was the pharmacodynamic effect parameter. This published interaction model for remimazolam and remifentanyl during general anesthesia is inconclusive, as the interaction only shows a relevant effect and a weak interaction up to a remifentanyl dosing of  $0.5 \mu\text{g}/\text{kg}/\text{min}$ , and with higher dosages of remifentanyl, the interaction is further reduced. This might be explained by the study designs of the re-evaluated trials, as the whole range of clinically relevant remifentanyl and remimazolam concentrations were not studied [15]. Even more relevant for the clinical use of remimazolam is its anesthetic drug potency compared to that of propofol, which is described by the half-maximal effective concentration ( $EC_{50}$ ).  $EC_{50}$  is the plasma concentration at the time when 50% of the maximal effect for a pharmacodynamic parameter (e.g., the BIS) is achieved. In the study conducted by Wiltshire et al. [7], a decrease in the maximum BIS of 50% was achieved with a remimazolam effect site concentration of  $0.259 \mu\text{g}/\text{ml}$ , whereas for propofol, the  $EC_{50}$  value for the BIS was estimated as  $1.78 \pm 0.67 \mu\text{g}/\text{ml}$  in a publication by Mourisse et al. [16]. Considering these published  $EC_{50}$  values, remimazolam is much more potent than propofol in terms of the effect-site concentrations estimated for the same effect on the BIS. This may explain the slightly prolonged recovery times of remimazolam compared to propofol, as a decrease of the effect site concentration of propofol by 50% reduces the anesthetic effect more than a reduction in the effect site

concentration of remimazolam by 50%.

In summary, although the most accurate pharmacokinetic parameters of remimazolam have been described, this is not the case for the pharmacodynamic parameters, such as  $EC_{50}$  and the transfer constant  $k_{e0}$ . Further studies are needed to validate these important pharmacological parameters of remimazolam.

### Clinical pharmacology of remimazolam

The hemodynamic stability of remimazolam, especially when compared to propofol, is remarkable. Most intravenous anesthetic agents besides ketamine exhibit dose-dependent cardiovascular depressive effects. These cardiovascular effects can be explained by a dose-dependent decrease in systemic vascular resistance as well as a dose-dependent decrease in cardiac contractility. The effects of remimazolam on intracellular calcium homeostasis in endothelial and neuronal cells have not yet been fully elucidated. Urabe et al. [17] studied the effect of remimazolam on the intracellular concentration of calcium. They described how remimazolam can increase the calcium concentration in endothelial and neuronal cells via the G-protein coupled receptors (GPCRs)-inositol 1,4,5-triphosphate ( $IP_3$ ) pathway. They discussed how the effect is reversible, whereas, when propofol is administered, this effect is different and irreversible. This might be the first step to explaining the different hemodynamic effects of remimazolam compared to propofol, possibly modulated by different effects on the intracellular calcium homeostasis of endothelial cells.

Decreased blood pressure with a mean arterial pressure below 65 mmHg for > 1 min is associated with an increased incidence of postoperative myocardial injury or acute kidney injury [18]. As remimazolam is a BZD, better hemodynamic stability than propofol can be expected. Frölich et al. compared the hemodynamic effects of propofol, midazolam, and dexmedetomidine. They found that dexmedetomidine and propofol reduced the arterial blood pressure in a dose-dependent manner. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were maintained in the midazolam group during induction of mild-to-moderate sedation in American Society of Anesthesiologists Physical Status (ASA PS) I human volunteers of both sexes; a significant decrease in the SBP and DBP occurred with the use of propofol [19]. Lim et al. compared the cardiovascular effects of the co-administration of midazolam (0.03 mg/kg) and a reduced dose of propofol (0.8 mg/kg) to a propofol dose of 1.2 mg/kg, each combined with remifentanyl for induction of anesthesia in ASA PS I to II patients of both sexes aged > 65 years. The co-administration of midazolam and a lower dose of propofol reduced the time to loss of consciousness, and the decrease in mean arterial blood pressure before, immedi-

ately after, and 3 min after intubation was significantly smaller [20]. The hemodynamic effects of remimazolam has the similar characteristics with midazolam. Moreover, remimazolam shows rapid on-set and off-set. Therefore, remimazolam is associated with the better hemodynamic stability than other intravenous anesthetic agents, including propofol.

The concentration of intravenous anesthetic agents and the anesthetic effects over time can be more accurately controlled with the use of a TCI system than with a manually controlled infusion system. Several research groups have investigated and described pharmacokinetic and pharmacodynamic models of remimazolam. Sufficient pharmacokinetic data have been published to further develop and test a TCI system for remimazolam in the near future. Insufficient data have been published describing the concentration-effect relationship of remimazolam on typical EEG parameters such as the BIS during general anesthesia and during co-administration with an opioid in patients [6,14,15]. Further clinical investigations are necessary to clearly define the pharmacodynamic interactions between remimazolam and different opioids in a clinical setting. The parameter " $k_{e0}$ " is important for calculating the speed at which the effect-site concentrations of remimazolam will increase or decrease. This parameter is necessary for a TCI system to directly model and target effect site concentrations and to increase the adjustability of the drug effect over time, especially to shorten recovery times by adequate dosing.

### Remimazolam for anesthetic induction and maintenance

For anesthesia induction and maintenance, remimazolam should be compared with propofol. Propofol has the following disadvantages when used for anesthetic induction and maintenance: 1) pain on injection, 2) decrease in blood pressure, 3) decrease in heart rate, 4) respiratory depression, and 5) propofol infusion syndrome (very rare). In the following, we present clinical trial results comparing remimazolam and propofol for the induction and maintenance of general anesthesia.

Dai et al. [21] evaluated the safety and efficacy of remimazolam for anesthetic induction compared with propofol at 2 mg/kg in 190 patients with ASA PS I or II. A bolus dose of sufentanil (0.3 to 0.5  $\mu$ g/kg) was administered 1 min before anesthetic induction. Anesthesia was successfully induced with remimazolam at 0.2 mg/kg (group R1), 0.3 mg/kg (group R2), and 0.4 mg/kg (group R3) in 89%, 94%, and 100% of patients within 1 min, respectively. Successful induction rates were not significantly different between the R2, R3, and propofol groups. Dai et al. [21] also compared the hypotension rate for the three induction doses of remimazolam (0.2 mg/kg, 0.3 mg/kg, and 0.4 mg/kg) to that for the induction

dose of propofol (group P) at 2 mg/kg. Hypotension during induction, defined as a mean arterial blood pressure < 65 mmHg or a systolic blood pressure decrease to < 70% of baseline values, occurred in 13% of patients in group R1 and 24% of patients in group R2. The incidence of hypotension was significantly less in groups R1 and R2 compared to group P (44%). This study has the limitation that the anesthetic drug effect over time was not exactly comparable between the three remimazolam groups and the propofol group. Sufentanil dosing was not standardized. Nevertheless, in this trial, remimazolam showed superior hemodynamic stability during anesthetic induction even though co-administered with sufentanil. Pain on injection was not reported in this trial for all three remimazolam groups; in contrast, it was reported in 27% of patients who had received propofol.

Zhang et al. [22] compared an induction dose of remimazolam (0.2 mg/kg) for anesthesia induction and 1.0 mg/kg/h for anesthesia maintenance to an induction dose of propofol (2 to 2.5 mg/kg) and a propofol maintenance dose of 3–6 mg/kg/h in patients with ASA PS I or II undergoing hysteroscopy. Analgesia was achieved with remifentanyl using a TCI with an effect-site target concentration of 1.5 µg/ml in both groups. Remifentanyl infusion was initiated after induction with remimazolam or propofol. Based on their definitions of adverse events, the authors reported less significantly low peripheral oxygen saturation values ≤ 95%, lower injection pain (2.4% vs. 80.5%), and less postoperative dizziness (0 vs. 24.4%) when remimazolam was used instead of propofol. They concluded that remimazolam is “a safer alternative to anesthesia during hysteroscopy.” However, although awakening times were longer in the remimazolam groups (199 ± 80 s vs. 60 ± 12 s) in this trial, the post-anesthetic care unit length of stay was shorter in the remimazolam group (5.44 ± 1 min vs. 6.3 ± 1.9 min). The depth of anesthesia was monitored using the MOAA/S scale. Furuta et al. [23] presented a case report of successful induction and maintenance of general anesthesia with remimazolam during total mastectomy in a female patient aged 81 years with severe aortic valve stenosis. They concluded that general anesthesia using remimazolam preserved cardiac output in this patient and therefore, remimazolam might be a safe alternative for patients with severe aortic valve stenosis to avoid a further and critical decrease in

cardiac contractility.

Liu et al. [24] compared two groups of 30 patients each that were induced with remimazolam 0.3 mg/kg at a constant infusion rate of 1.8 mg/kg/h or propofol as a TCI with a target plasma concentration of 2.5 µg/ml scheduled for valve replacement cardiac surgery. All patients received a sufentanil dose of 1 µg/kg at an infusion rate of 0.1 µg/kg/min. After 7 min, the patients were relaxed, and after 10 min or after the BIS decreased below 60, they were intubated. The primary outcome was the maximum change in heart rate compared to baseline, though the maximum change in mean arterial blood pressure was also evaluated. This study did not find a significant difference of heart rate change between the groups; however, in the remimazolam group, a significantly smaller decrease in mean arterial blood pressure during induction was noted. They concluded that remimazolam may be a safe and effective alternative to propofol for anesthetic induction in patients with cardiac valve disease.

As remimazolam is a BZD, the specific reversal agent flumazenil is available and can be used in clinical practice to further accelerate recovery times or specifically treat prolonged postoperative sedation. This is a valuable advantage compared to propofol because clinicians can easily discriminate between prolonged sedation and other postoperative pathologies, such as postoperative stroke, which would also impact the speed of postoperative recovery to full awareness. However, the routine use of flumazenil for the reversal of remimazolam should be prospectively evaluated for possible side effects and safety in future studies. The main differences between remimazolam and propofol are summarized in Table 2.

## Precipitation

Sasaki et al. [25] reported the precipitation of remimazolam after a bolus administration of 0.2 mg/kg with Ringer's acetate solution. Yoshida et al. [26] also reported occlusion of an intravenous line running Ringer's acetate solution when remimazolam was used at a concentration of 2 mg/ml. The solubility of remimazolam is higher at low pH than at high pH, and its solubility is higher in normal saline than in Ringer's solution. Therefore, precipitation

**Table 2.** Comparison between Remimazolam and Propofol

		Remimazolam	Propofol
Anesthetic induction	Speed	Fast	Fast
	Pain at administration	No	Yes
Anesthetic maintenance	Hypotension	Less frequent, severe	More frequent, severe
Emergence from anesthesia	Speed	Fast	Fast
	Reverse agent	Flumazenil	-



can occur when it is co-administered with Ringer's solution. The risk of precipitation increases when a solution with a high remimazolam concentration and a low infusion rate of the maintenance fluid is used. This should be avoided.

### Further evaluation of remimazolam

To precisely titrate remimazolam to a chosen pharmacodynamic effect, accurate pharmacokinetic and pharmacodynamic models are essential. To date, interaction modeling between opioids and remimazolam during general anesthesia has only been described for remifentanyl in a publication by Zhou et al. [15], for which the BIS was used as a pharmacodynamic effect parameter. Further randomized controlled trials that precisely describe the pharmacodynamic interaction of remimazolam with remifentanyl, sufentanyl, and fentanyl are necessary for feasible and rational dosing strategies to be developed for various clinical settings and patient populations. The development of a TCI system for remimazolam targeting plasma and effect-site concentrations would further improve exact dosing. The availability of a TCI system could also help reduce recovery times, as the time to reach an estimated awakening concentration of remimazolam can continuously be calculated and displayed on a modern TCI smart pump system. The use of flumazenil to quickly antagonize any residual sedative or anesthetic effects of remimazolam should also be further investigated. Flumazenil will certainly result in shorter recovery times and may also reduce the incidence of postoperative cognitive deficit (POCD) or cognitive decline shortly after surgery. Shi et al. [27] showed that remimazolam had a protective effect in a rat model of cerebral ischemia/reperfusion. Other harmful or protective side effects of general anesthetics, such as recurrence rates of cancer at the site of resection or effects on metastatic disease burden, the incidence of postoperative nausea and vomiting, and the incidence and severity of POCD should be further investigated.

### Conclusion

It has previously been shown that remimazolam is non-inferior to midazolam in terms of providing adequate sedation, and when co-administered with opioids, is non-inferior to propofol for induction and maintenance of general anesthesia [8,13]. The hemodynamic and respiratory stability of remimazolam compared to propofol is notable, but further well-designed randomized controlled clinical trials are needed to confirm and support these findings. Awakening times can be slightly prolonged directly compared to propofol; however, current knowledge suggests that the difference is only in the range of 1 to 5 min, which might not

be clinically relevant in daily practice [13]. Additionally, a significant advantage of remimazolam is that prolonged recovery can be specifically treated with flumazenil. The risk of precipitation in the infusion line should be recognized, and Ringer's solution should not be used together with remimazolam as the maintenance fluid. Remimazolam is the first new intravenous anesthetic agent that has been successfully introduced into clinical practice in more than four decades, primarily given its superior hemodynamic safety profile compared to propofol. Remimazolam is a soft drug with a pharmacological profile that should enable it to at least partially replace propofol as a standard intravenous anesthetic agent for general anesthesia in the future.

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### Conflicts of Interest

Jörg Fechner worked as a medical adviser for PAION in Aachen, Germany and as a consultant for HANAPharm in Seoul, Korea. Seong-Hyop Kim has no competing interests to declare.

### Author Contributions

Seong-Hyop Kim (Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing)

Jörg Fechner (Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing)

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## References

- Shin TJ, Kim PJ, Choi B. How general anesthetics work: from the perspective of reorganized connections within the brain. *Korean J Anesthesiol* 2022; 75: 124-38.
- Son Y. Molecular mechanisms of general anesthesia. *Korean J Anesthesiol* 2010; 59: 3-8.
- Birgenheier NM, Stuart AR, Egan TD. Soft drugs in anesthesia: remifentanyl as prototype to modern anesthetic drug development. *Curr Opin Anaesthesiol* 2020; 33: 499-505.
- Wandel C, Böcker R, Böhler H, Browne A, Rügheimer E, Martin E. Midazolam is metabolized by at least three different cytochrome P450 enzymes. *Br J Anaesth* 1994; 73: 658-61.
- Kilpatrick GJ, McIntyre MS, Cox RF, Stafford JA, Pacofsky GJ, Lovell GG, et al. CNS 7056: a novel ultra-short-acting Benzodiazepine. *Anesthesiology* 2007; 107: 60-6.
- Schüttler J, Eisenried A, Lerch M, Fechner J, Jeleazcov C, Ihmsen H. Pharmacokinetics and pharmacodynamics of remimazolam (CNS 7056) after continuous infusion in healthy male volunteers: Part I. Pharmacokinetics and clinical pharmacodynamics. *Anesthesiology* 2020; 132: 636-51.
- Wiltshire HR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part II. Population pharmacokinetic and pharmacodynamic modeling and simulation. *Anesth Analg* 2012; 115: 284-96.
- Antonik LJ, Goldwater DR, Kilpatrick GJ, Tilbrook GS, Borkett KM. A placebo- and midazolam-controlled phase I single ascending-dose study evaluating the safety, pharmacokinetics, and pharmacodynamics of remimazolam (CNS 7056): Part I. Safety, efficacy, and basic pharmacokinetics. *Anesth Analg* 2012; 115: 274-83.
- Lu Z, Zhou N, Li Y, Yang L, Hao W. Up-down determination of the 90% effective dose (ED90) of remimazolam besylate for anesthesia induction. *Ann Palliat Med* 2022; 11: 568-73.
- Gepts E, Camu F, Cockshott ID, Douglas EJ. Disposition of propofol administered as constant rate intravenous infusions in humans. *Anesth Analg* 1987; 66: 1256-63.
- Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. *Br J Anaesth* 1991; 67: 41-8.
- Stöhr T, Colin PJ, Ossig J, Pesic M, Borkett K, Winkle P, et al. Pharmacokinetic properties of remimazolam in subjects with hepatic or renal impairment. *Br J Anaesth* 2021; 127: 415-23.
- Doi M, Morita K, Takeda J, Sakamoto A, Yamakage M, Suzuki T. Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIb/III trial. *J Anesth* 2020; 34: 543-53.
- Eisenried A, Schüttler J, Lerch M, Ihmsen H, Jeleazcov C. Pharmacokinetics and pharmacodynamics of remimazolam (CNS 7056) after continuous infusion in healthy male volunteers: Part II. pharmacodynamics of electroencephalogram effects. *Anesthesiology* 2020; 132: 652-66.
- Zhou J, Leonowens C, Ivaturi VD, Lohmer LL, Curd L, Ossig J, et al. Population pharmacokinetic/pharmacodynamic modeling for remimazolam in the induction and maintenance of general anesthesia in healthy subjects and in surgical subjects. *J Clin Anesth* 2020; 66: 109899.
- Mourisse J, Lerou J, Struys M, Zwarts M, Booij L. Multi-level approach to anaesthetic effects produced by sevoflurane or propofol in humans: 1. BIS and blink reflex. *Br J Anaesth* 2007; 98: 737-45.
- Urabe T, Miyoshi H, Narasaki S, Yanase Y, Uchida K, Noguchi S, et al. Characterization of intracellular calcium mobilization induced by remimazolam, a newly approved intravenous anesthetic. *PLoS One* 2022; 17: e0263395.
- Salmasi V, Maheshwari K, Yang D, Mascha EJ, Singh A, Sessler DI, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: a retrospective cohort analysis. *Anesthesiology* 2017; 126: 47-65.
- Frölich MA, Arabshahi A, Katholi C, Prasain J, Barnes S. Hemodynamic characteristics of midazolam, propofol, and dexmedetomidine in healthy volunteers. *J Clin Anesth* 2011; 23: 218-23.
- Lim YS, Kang DH, Kim SH, Jang TH, Kim KH, Ryu SJ, et al. The cardiovascular effects of midazolam co-induction to propofol for induction in aged patients. *Korean J Anesthesiol* 2012; 62: 536-42.
- Dai G, Pei L, Duan F, Liao M, Zhang Y, Zhu M, et al. Safety and efficacy of remimazolam compared with propofol in induction of general anesthesia. *Minerva Anestesiol* 2021; 87: 1073-9.
- Zhang X, Li S, Liu J. Efficacy and safety of remimazolam besylate versus propofol during hysteroscopy: single-centre randomized controlled trial. *BMC Anesthesiol* 2021; 21: 156.
- Furuta M, Ito H, Yamazaki M. Anaesthetic management using remimazolam in a patient with severe aortic stenosis: a case report. *BMC Anesthesiol* 2021; 21: 202.
- Liu T, Lai T, Chen J, Lu Y, He F, Chen Y, et al. Effect of remimazolam induction on hemodynamics in patients undergoing valve replacement surgery: a randomized, double-blind, controlled trial. *Pharmacol Res Perspect* 2021; 9: e00851.
- Sasaki H, Hoshijima H, Mizuta K. Ringer's acetate solution-in-

- duced precipitation of remimazolam. *Br J Anaesth* 2021; 126: e87-9.
26. Yoshida K, Tanaka S, Watanabe K. A case of intravenous line occlusion when using Acetated Ringer's solution and remimazolam. *J Clin Anesth* 2021; 70: 110190.
27. Shi M, Chen J, Liu T, Dai W, Zhou Z, Chen L, et al. Protective effects of remimazolam on cerebral ischemia/reperfusion injury in rats by inhibiting of NLRP3 inflammasome-dependent pyroptosis. *Drug Des Devel Ther* 2022; 16: 413-23.



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# Comparison of the clinical performance of the i-gel™, LMA Supreme™, and Ambu AuraGain™ in adult patients during general anesthesia: a prospective and randomized study

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**Background:** Supraglottic airway devices (SADs) are routinely used for securing the airway. In this study, the clinical performance of three SADs in adult patients under general anesthesia was compared.

**Methods:** American Society of Anesthesiologists physical status I–III subjects were randomly assigned to the i-gel™ (I), LMA Supreme™ (L), or Ambu AuraGain™ (A) group (30 per group). The primary objective of this study was to compare insertion times. Additionally, the ease of insertion, number of attempts, oropharyngeal leak pressure (OLP), airway maneuver requirement, difficulty with gastric tube placement, and complications were assessed.

**Results:** Demographic data did not differ between the groups. Group I ( $16.9 \pm 4.9$  s) had a significantly shorter time of insertion than Group L ( $19.6 \pm 5.2$  s) and Group A ( $22.1 \pm 5.7$  s) ( $P = 0.001$ ). The OLP for Group A ( $29.8 \pm 3.0$  cmH<sub>2</sub>O) was higher than those for Group L ( $24.1 \pm 6.3$  cmH<sub>2</sub>O) and Group I ( $9.4 \pm 6.1$  cmH<sub>2</sub>O) ( $P < 0.001$ ). The number of insertion attempts ( $P = 0.232$ ), ease of insertion ( $P = 0.630$ ), airway maneuver requirement ( $P = 0.585$ ), difficulty with gastric tube placement ( $P = 0.364$ ), and complications ( $P = 0.873$ ) were not significantly different between the groups.

**Conclusions:** All three devices are convenient and effective for airway management in adults under general anesthesia. However, the shorter insertion time required for the i-gel may make it more suitable for resuscitation and emergencies, while aspiration risk may be reduced with the Ambu AuraGain, given its high OLP.

**Keywords:** Airway management; General anesthesia; Elective surgical procedures; Laryngeal masks; Pressure; Ventilation.

## Introduction

For more than a decade, anesthesia has been traditionally administered by conventional mask anesthesia using the Goldmann dental mask and endotracheal intubation (ETI) [1]. Since Dr. Archie Brain introduced the laryngeal mask airway (LMA) in 1981, supraglottic airway devices (SADs) have begun to replace ETI for resuscitation and difficult intubation as well as for general anesthesia [2,3]. SADs are able to maintain stable hemody-

namics while requiring less anesthesia than ETI [3].

Over the years, many newer devices have evolved for clinical use, including the i-gel, LMA Supreme, and Ambu AuraGain. Among these second-generation devices, the i-gel airway (Intersurgical Ltd., UK) has a soft, flexible, gel-like texture and is made of a thermoplastic elastomer non-inflatable cuff to create a seal with the peri-laryngeal structures [1,4-6].

The LMA Supreme (Teleflex Medical, Co., Ireland), which has many similarities to the i-gel, is another disposable second-generation SAD that is made of silicone with an inflatable cuff and a curved, anatomically shaped semi-rigid airway tube that is elliptical in cross section [7,8].

The Ambu AuraGain (Ambu A/S, Denmark) is a newer, second-generation SAD that was launched in June 2014 [1]. It is also a disposable device made of polyvinyl chloride and has a preformed curve that follows the human airway [9-11].

These recently-introduced second-generation SADs have a gastric channel to minimize the risk of aspiration resulting from gastric insufflation. Hence, they can be used in elective laparoscopic surgeries as well as for difficult intubations and resuscitations. Although these devices have been extensively studied individually, no study has compared all three devices collectively in elective surgeries. Therefore, we designed this study to evaluate the clinical performance of the i-gel, LMA Supreme, and Ambu AuraGain in adult non-obese patients under general anesthesia. The primary objective of our study was to determine and compare the insertion times of these three SADs. The ease of insertion, number of insertion attempts, oropharyngeal leak pressure (OLP), airway maneuver requirement, gastric tube placement difficulty, and any other complications were also assessed.

## Materials and Methods

This study was approved by the Institutional Review Board (97<sup>th</sup> ECM II B/P28). A total of 90 male and female patients aged 18-65 years with an American Society of Anesthesiologists (ASA) physical status I-III undergoing elective surgery lasting < 2 h under general anesthesia at the Department of Anesthesiology, King George Medical University, Lucknow (Ref. no. ECR/262/Inst/UP/2013/RR-16) were included. The study was also registered under the Clinical Trial Registry of India (Registration no. CTRI/2020/01/022633). Informed and written consent was obtained from all study participants. This study was conducted in accordance with the ethical principles of the Helsinki Declaration-2013 and followed good clinical practice guidelines.

Patients with any of the following were excluded from the

study: risk of aspiration, body mass index (BMI) > 35 kg/m<sup>2</sup>, unstable vital signs, anticipated difficult airway, high possibility of respiratory complications (asthma, chronic obstructive pulmonary disease, or recent pneumonia), history of obstructive sleep apnea, and history of gastroesophageal reflux disease.

Thirty subjects each were randomly allocated to the i-gel (I), LMA Supreme (L), or Ambu AuraGain (A) group using computer-generated software. Based on the ASA guidelines, all patients fasted for at least 8 h before the surgery and were premedicated with oral alprazolam 0.25 mg and ranitidine (150 mg) on the night before surgery.

Upon arrival to the operating room, noninvasive blood pressure, pulse oximetry (SpO<sub>2</sub>), electrocardiogram, and end-tidal carbon dioxide monitoring were initiated according to the ASA standards. All patients received intravenous (IV) ondansetron 0.1 mg/kg and IV midazolam 0.01 mg/kg. Preoxygenation was performed for 3 min with 100% O<sub>2</sub> at 8 L/min of fresh gas flow (FGF). Anesthesia was induced by IV fentanyl (2 µg/kg) and IV propofol 1.5 mg/kg. After the eyelash reflex disappeared, the subjects were paralyzed with a loading dose of IV vecuronium (0.1 mg/kg).

Mask ventilation of the lungs was performed through a face-mask with O<sub>2</sub> at 6 L/min of FGF for 3 min. After lubricating with water-soluble gel and determining the size of the device (depending on the patient's weight and according to the manufacturer's instructions), the device was inserted in accordance with the manufacturers' recommendations by one of the three study investigators, each of which had previously inserted more than 400 SADs in clinical practice, with a minimum of 30 prior insertions for each device. After device insertion, the cuff was inflated and the intra-cuff pressure was then standardized to 60 cmH<sub>2</sub>O (based on the manufacturers' recommendations) in Groups L and A. An appropriately sized Ryle's tube was then inserted through the gastric port of the device. A visible chest rise and end-tidal carbon dioxide waveform with gentle squeezing of the bag was used to confirm the appropriate placement of the SAD.

Patients were then connected to the anesthesia delivery system and mechanical ventilation was initiated with the tidal volume set at 8 ml/kg and the respiratory rate between 14 and 18 breaths/min. An FGF mixture of 3 L/min (oxygen 2 L/min and nitrous oxide 1 L/min) was maintained on 2% sevoflurane and IV vecuronium (0.01 mg/kg to maintain end-tidal carbon dioxide between 35 and 40 mmHg). An unblinded observer who was not part of the study performed the data collection.

The device insertion time was calculated from the time of picking the device till the appearance of the square wave end-tidal carbon dioxide upstroke. Other outcomes measured included the

OLP, the ease of insertion, first attempt rate, overall success rate, airway maneuver requirement for successful ventilation, and any associated postoperative complications.

The OLP was determined by an audible leak over the patient's mouth upon closing the expiratory valve at 30 cmH<sub>2</sub>O with a gas flow of 3 L/min. If there was no audible leak, a stethoscope was placed over the trachea to listen for the leak. The OLP was measured 15 min after device insertion.

The ease of insertion was evaluated according to the resistance to insertion of the SAD on a four-point rank scale between 1 and 4 (1 = no resistance, 2 = mild resistance, 3 = moderate resistance, 4 = unable to pass the device). The number of attempts was also recorded. Device insertion was considered successful if the device was inserted in the first or second attempt after any airway maneuvers. The attempt was considered a failure if more than two attempts were needed and if the airway was secured using a tracheal tube. Maneuvers for successful ventilation included inserting the device further, head extension, and jaw thrust. An inadequate oxygenation/ventilation situation (inability to generate 6–8 ml/kg tidal volume during positive pressure ventilation, a rise in end tidal carbon dioxide > 50 mmHg despite airway maneuvers or device adjustments, or an SpO<sub>2</sub> < 90%) during surgery was also considered a device failure, and ETI was performed.

After the surgical procedure, sevoflurane was discontinued and IV neostigmine (50 µg/kg) and glycopyrrolate (10 µg/kg) were administered to antagonize the residual neuromuscular block. The SAD was removed when the patient was fully awake and checked for any complications, including coughing, bronchospasm, desaturation, blood staining, and the presence of tongue, teeth, or lip injury. All patients were observed for 1 h postoperatively. Any sore throat, dysphagia, dysphonia, or numbness of the lip was evaluated immediately in the postoperative care unit after surgery.

### Statistical analysis

All statistical analyses were performed using SPSS (IBM, SPSS Inc., USA) version 21.1 statistical analysis software. Continuous data were analyzed using the Student's t-test. For categorical data, the chi-square test was used. Since there were three groups, ANOVA was used for the analysis. For all analyses, statistical significance was set at  $P < 0.05$ . The sample size was calculated using the time of insertion as the primary objective (to detect a difference of 4 s), with a standard deviation of 4.2 [12], a power of 0.9, and an alpha value of 0.05 (two-sided). The results indicated that each group needed a minimum of 26 subjects. Taking into consid-

eration a dropout rate of 10%, 30 patients were enrolled in each group.

## Results

Ninety-six patients were assessed for eligibility, six of which were excluded (two had high blood pressures and four had loose teeth). Thus, 90 patients were randomly allocated into Groups I, L, and A (Fig. 1).

In this study, the demographic variables of age, sex, body weight, height, BMI, Mallampati score, and ASA physical status classification were comparable among the groups, with no statistically significant differences ( $P > 0.05$ ), as shown in Table 1.

Various aspects related to device insertion, such as the size, number of attempts, insertion time, OLP, ease of insertion, device failure, airway maneuver requirements, and difficulty with gastric tube placement, are listed in Table 2. Group I ( $16.9 \pm 4.9$  s) had a significantly shorter insertion time than Group L ( $19.6 \pm 5.2$  s) and Group A ( $22.1 \pm 5.7$  s) ( $P = 0.001$ ). The OLP at 15 min for Group A ( $29.8 \pm 3.0$  cmH<sub>2</sub>O) was higher than that for Group L ( $24.1 \pm 6.3$  cmH<sub>2</sub>O) and Group I ( $9.4 \pm 6.1$  cmH<sub>2</sub>O) ( $P < 0.001$ ).

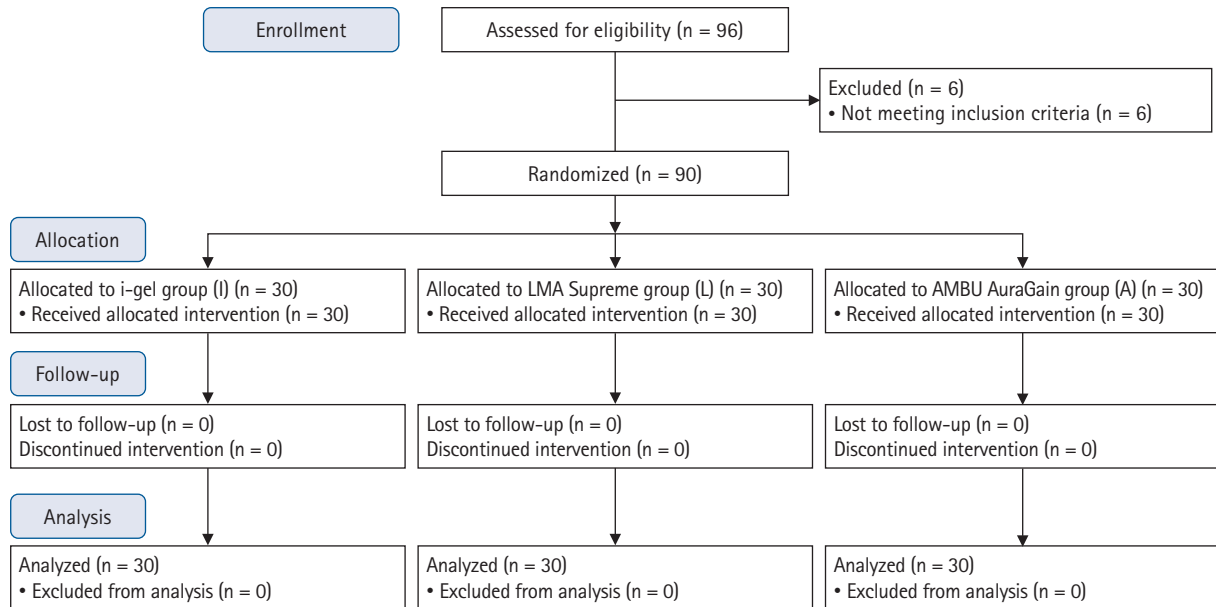
The adverse events and complications among the three groups were comparable and not statistically significantly different, as shown in Table 3.

## Discussion

In this study, we compared the clinical performance of three SADs in non-obese patients under general anesthesia. While previous studies have evaluated these devices individually or compared two of them, there is a paucity of studies that have compared all three of these devices in a single study.

In our study, we found that the i-gel, LMA Supreme, and Ambu AuraGain are effective and convenient in non-obese patients under general anesthesia. Insertion time, which is an important determinant during emergencies and for resuscitation, was considered the primary objective in this study. Longer insertion times may cause more interruption during chest compressions and increase the chances of neurological and respiratory morbidity during resuscitation attempts. In addition, increased apnea time may lead to an increase in blood CO<sub>2</sub> levels and may jeopardize the acid-base balance. Avoiding any possible delay in airway management is an important aspect to consider for the clinical research of SADs. Among the three SADs, the i-gel had the shortest insertion time. This device has previously been shown to have a comparably shorter insertion time, both in a study of adult patients undergoing laparoscopic cholecystectomy by Sabuncu et al.





**Fig. 1.** CONSORT flow diagram. Ninety patients were randomly allocated into the i-gel™, LMA Supreme™, or Ambu AuraGain™ group (30 per group).

**Table 1.** Demographic Data and Preoperative Assessment of the Study Groups

	Group I (n = 30)	Group L (n = 30)	Group A (n = 30)	P value
Age (yr)	40.2 ± 11.6	42.0 ± 11.5	40.6 ± 15.7	0.852
Sex (F/M)	24/6	25/5	24/6	0.130
Height (cm)	155.7 ± 9.8	156.0 ± 8.5	159.8 ± 8.5	0.157
Weight (kg)	58.9 ± 6.3	59.7 ± 5.2	59.1 ± 5.5	0.866
BMI (kg/m <sup>2</sup> )	24.6 ± 4.2	24.8 ± 3.9	23.3 ± 3.4	0.302
Mallampati score (I/II/III)	0/28/2	7/20/3	5/23/2	0.086
ASA PS (I/II/III)	18/12/0	11/12/7	12/13/5	0.070

Values are presented as mean ± SD or number. Group I: i-gel, Group L: LMA Supreme, Group A: Ambu AuraGain. BMI: body mass index, ASA PS: American Society of Anesthesiologists physical status classification.

**Table 2.** Comparisons of Various Parameters between the Study Groups

	Group I (n = 30)	Group L (n = 30)	Group A (n = 30)	P value
Size of device (size 3/4)	24/6	25/5	23/7	0.812
Number of attempts (1/2)	29/1	25/5	26/4	0.232
Insertion time (s)	16.9 ± 4.9	19.6 ± 5.2	22.1 ± 5.7	0.001
OLP (cmH <sub>2</sub> O)	9.4 ± 6.1	24.1 ± 6.3	29.8 ± 3.0	< 0.001
Ease of insertion (1/2/3/4)*	25/3/2/0	24/3/3/0	23/6/1/0	0.630
Failed insertion/device failure during surgery	0/0	0/0	0/0	1.000
Airway maneuver requirement	2	1	3	0.585
Gastric tube insertion difficulty	1	0	0	0.364

Values are presented as number or mean ± SD. Group I: i-gel, Group L: LMA Supreme, Group A: Ambu AuraGain. OLP: oropharyngeal leak pressure. \*Ease of insertion was graded as 1 = no resistance, 2 = minimal resistance, 3 = moderate resistance, and 4 = unable to place the device.

**Table 3.** Adverse Events (Inadequate Oxygenation/Ventilation) and Complications

	Group I (n = 30)	Group L (n = 30)	Group A (n = 30)	P value
Adverse events (inadequate oxygenation/ventilation)*	0	0	0	1.000
Intraoperative complications				0.873
Blood staining	0	1	0	
Nausea	3	3	4	
Sore throat	4	4	3	

Values are presented as number. Group I: i-gel, Group L: LMA Supreme, Group A: Ambu AuraGain. \*Inadequate oxygenation/ventilation consists of an inability to generate 6–8 ml/kg tidal volume during positive pressure ventilation, a rise in end-tidal carbon dioxide > 50 mmHg despite airway maneuvers/device adjustments, or SpO<sub>2</sub> < 90%.

[12] and in a study of geriatric patients by In et al. [3]. This could be explained by the absence of an inflatable cuff, since additional time is required to inflate the cuff to provide optimal cuff pressure for both the LMA Supreme and Ambu AuraGain devices. To limit the bias associated with device familiarity in this study, only clinicians who had successfully inserted each of the SADs a minimum of 30 times before the study were permitted to perform the device insertions.

Similar to our study, Wong et al. [10] found that the insertion time was longer for the Ambu AuraGain than for the LMA Supreme. In our study, a mean difference of 2.5 s in insertion time was found between the LMA Supreme (19.6 s) and Ambu AuraGain (22.1 s). In another study, Shariffuddin et al. [13] found that the Ambu AuraGain took a mean 6 s longer to obtain the first capnograph trace compared to the LMA Supreme. The authors of that study attributed this to the structural differences between the two devices, since the Ambu AuraGain has a less pliable firm tip and bulky posterior curvature with a larger cuff to provide better sealing pressures [13], while the LMA Supreme has a hard tube wall pre-shaped according to the anatomical curve, and the radian design makes the front end of the ventilation tube and the laryngeal vestibule form an effective orientation, enabling quicker insertion [14].

Regarding ease of insertion, no resistance was observed in 80% (72/90) of our study population, and close to 90% (80/90) of the patients in our study had successful insertions in the first attempt. The first-attempt success rate was found to be comparable among the groups. Our results are consistent with those of Teoh et al. [15], who found that 47 (94%) LMA Supremes and 48 (96%) i-gels were successfully inserted on the first attempt. This could be due to the lower Mallampati scores (I, II) and normal airways in our patient population (83/90) and the clinicians' considerable experience.

We had no device insertion failures, in contrast to the seven observed by Shariffuddin et al. [13], and we had a high first-pass success rate among all three groups. Both of these differences can be explained by the use of neuromuscular blocking agents in our

study, which may have provided better muscle relaxation and thereby facilitated easier insertion. Regarding the airway maneuver parameter, the majority of cases (93.3%) did not require any airway maneuvers; however, six cases (6.7%) required airway maneuvers for the device to be inserted further. The Ambu AuraGain required more airway maneuvers than the i-gel or the LMA Supreme.

In our study, the Ambu AuraGain achieved the highest OLP among the three SADs, followed by the LMA Supreme and the i-gel. OLP is a significant characteristic feature that determines the efficiency of a supraglottic device. It defines the sealing capability between the device and supraglottic mucosa. The better sealing pressures observed in Group A in our study reconfirm previous findings by Lopez et al. [7] and Wong et al. [10]. The wider airway tube and prominent posterior cuff design of the Ambu AuraGain provides a tighter and more consistent perilaryngeal seal, as explained in previous studies [7]. The higher OLP with the Ambu AuraGain makes it more suitable for positive pressure ventilation along with reduced aspiration risks.

Despite the low OLP in the i-gel group in our study, none of our study patients experienced inadequate oxygenation/ventilation. This could be explained by the better chest compliance in our patient population (since we excluded patients with obesity, restrictive lung disease, and any pulmonary pathology) and the structure of the i-gel device, which is fabricated with a thermoplastic elastomer (styrene ethylene butadiene styrene) to provide improved sealing pressures when its warmed up to body temperature. The low OLP observed in the i-gel study group could also have been a consequence of the fact that we had to reuse some i-gel devices after sterilization because of the unavailability of the device due to the COVID-19 pandemic lockdown in our setup. Two size 4 i-gels were reused for six patients in our study. Before reuse, we ensured that no device was visibly physically damaged. Previous studies [16,17] have confirmed that there is no difference in leak volumes and leak fraction (defined as the leak volume divided by the inspired tidal volume) between the i-gel and endo-

tracheal tubes in non-obese patients.

Difficulties with gastric drain insertion was comparable among the groups, although it was most difficult with the i-gel device. Teoh et al. [15] suggested that the likely reason for this difficulty is the smaller size of the aperture for the gastric access port with the i-gel. In a study conducted by Joshi et al. [18], gastric drain insertion was reported to be easier with the Ambu AuraGain due to the reduced friction in the inner surface of its polyvinyl material and its short and wide gastric channel [11]. Fernandes et al. [19] also reported that the placement of gastric tubes in the i-gel was more difficult due to the narrow tract of the i-gel.

The postoperative complications among the groups were comparable, with no statistically significant difference among them. Nausea was seen in 11% (10/90) and sore throat was present in 12% (11/90) of the patient population. In previous studies, the incidence of postoperative sore throat varied from 3–10% for the Ambu AuraGain and 0–38% for the LMA Supreme [7,13]. The incidence of sore throat was lower in our study, which can be explained by our better lubrication and shorter duration of surgery (< 2 h). There was no nerve damage or trauma to any of the perilyngeal structures of the oral cavity. Blood staining occurred in only one patient. L'Hermite et al. [20] compared the incidence of sore throat following the insertion of three SADs (LMA Unique, LMA Supreme, and i-gel) and reported that the incidence of sore throat was similar among the three devices.

Despite the effective measures taken, this study had some limitations. First, our study only included subjects who were not obese and had normal BMIs, and blinding was not possible. Additionally, hemodynamic monitoring was not performed, though it could have improved the study. Fiberoptic bronchoscopy was not used to assess the anatomical position of the seal, as it was logistically not feasible to perform bronchoscopy in all cases. Finally, we reused the i-gel devices for six of our patients, which could have affected our results.

In conclusion, our study demonstrated that all three devices are convenient and effective for airway management in non-obese adults under general anesthesia. However, the shorter insertion time required for the i-gel may make it more suitable for resuscitation and emergencies, while the maximum OLP associated with the Ambu AuraGain may make it more useful for reducing aspiration risk.

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## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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## References

- Hernandez MR, Klock PA Jr, Ovassapian A. Evolution of the extraglottic airway: a review of its history, applications, and practical tips for success. *Anesth Analg* 2012; 114: 349-68.
- Brain AI. The development of the Laryngeal Mask--a brief history of the invention, early clinical studies and experimental work from which the Laryngeal Mask evolved. *Eur J Anaesthesiol Suppl* 1991; 4: 5-17.
- In CB, Cho SA, Lee SJ, Sung TY, Cho CK. Comparison of the clinical performance of airway management with the i-gel® and laryngeal mask airway Supreme™ in geriatric patients: a prospective and randomized study. *Korean J Anesthesiol* 2019; 72: 39-46.
- Duckett J, Fell P, Han K, Kimber C, Taylor C. Introduction of the I-gel supraglottic airway device for prehospital airway management in a UK ambulance service. *Emerg Med J* 2014; 31: 505-7.
- Theiler L, Gutzmann M, Kleine-Brueggene M, Urwyler N,

- Kaempfen B, Greif R. i-gel™ supraglottic airway in clinical practice: a prospective observational multicentre study. *Br J Anaesth* 2012; 109: 990-5.
6. Shin WJ, Cheong YS, Yang HS, Nishiyama T. The supraglottic airway I-gel in comparison with ProSeal laryngeal mask airway and classic laryngeal mask airway in anaesthetized patients. *Eur J Anaesthesiol* 2010; 27: 598-601.
  7. Lopez AM, Agusti M, Gambus P, Pons M, Anglada T, Valero R. A randomized comparison of the Ambu AuraGain versus the LMA supreme in patients undergoing gynaecologic laparoscopic surgery. *J Clin Monit Comput* 2017; 31: 1255-62.
  8. Fletcher AJ, Santhirapala R, Young PJ. Introducing the LMA Supreme into clinical practice: use by experienced and inexperienced LMA users. *Br J Anaesth* 2008; 101(Issue eLetters Supplement).
  9. Sudheesh K, Chethana GM, Chaithali H, Nethra SS, Devikarani D, Shwetha G. A new second-generation supraglottic airway device (Ambu® AuraGain•) versus intubating laryngeal mask airway as conduits for blind intubation: a prospective, randomised trial. *Indian J Anaesth* 2019; 63: 558-64.
  10. Wong DT, Ooi A, Singh KP, Dallaire A, Meliana V, Lau J, et al. Comparison of oropharyngeal leak pressure between the Ambu® AuraGain™ and the LMA® Supreme™ supraglottic airways: a randomized-controlled trial. *Can J Anaesth* 2018; 65: 797-805.
  11. Jagannathan N, Hajduk J, Sohn L, Huang A, Sawardekar A, Gebhardt ER, et al. A randomised comparison of the Ambu® AuraGain™ and the LMA® supreme in infants and children. *Anaesthesia* 2016; 71: 205-12.
  12. Sabuncu U, Kusderci HS, Oterkus M, Abdullayev R, Demir A, Uludag O, et al. AuraGain and i-gel laryngeal masks in general anesthesia for laparoscopic cholecystectomy. Performance characteristics and effects on hemodynamics. *Saudi Med J* 2018; 39: 1082-9.
  13. Shariffuddin II, Teoh WH, Tang E, Hashim N, Loh PS. Ambu® AuraGain™ versus LMA Supreme™ Second Seal™: a randomised controlled trial comparing oropharyngeal leak pressures and gastric drain functionality in spontaneously breathing patients. *Anaesth Intensive Care* 2017; 45: 244-50.
  14. Wang F, Zhang R. Application of the LMA-Supreme™ and i-gel™ laryngeal masks during pelvic operations in adults. *Asian J Surg* 2016; 39: 1-5.
  15. Teoh WH, Lee KM, Suhitharan T, Yahaya Z, Teo MM, Sia AT. Comparison of the LMA Supreme vs the i-gel in paralysed patients undergoing gynaecological laparoscopic surgery with controlled ventilation. *Anaesthesia* 2010; 65: 1173-9.
  16. Lai CJ, Liu CM, Wu CY, Tsai FF, Tseng PH, Fan SZ. I-gel is a suitable alternative to endotracheal tubes in the laparoscopic pneumoperitoneum and Trendelenburg position. *BMC Anesthesiol* 2017; 17: 3.
  17. Dhanda A, Singh S, Bhalotra AR, Chavali S. Clinical comparison of i-gel supraglottic airway device and cuffed endotracheal tube for pressure-controlled ventilation during routine surgical procedures. *Turk J Anaesthesiol Reanim* 2017; 45: 270-6.
  18. Joshi R, Rudingwa P, Kundra P, Panneerselvam S, Mishra SK. Comparison of Ambu AuraGain™ and LMA® ProSeal in children under controlled ventilation. *Indian J Anaesth* 2018; 62: 455-60.
  19. Fernández Díez A, Pérez Villafañe A, Bermejo González JC, Marcos Vidal JM. Supreme laryngeal mask airway vs the I-gel supraglottic airway in patients under general anesthesia and mechanical ventilation with no neuromuscular block: a randomized clinical trial. *Rev Esp Anesthesiol Reanim* 2009; 56: 474-8.
  20. L'Hermite J, Dubout E, Bouvet S, Bracoud LH, Cuvillon P, Coussey JE, et al. Sore throat following three adult supraglottic airway devices: a randomised controlled trial. *Eur J Anaesthesiol* 2017; 34: 417-24.



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# Comparison between the coronal diameters of the cervical spinal canal and spinal cord measured using computed tomography and magnetic resonance imaging in Korean patients

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**Background:** If the proportion of the spinal cord in the epidural space can be determined under C-arm fluoroscopy during cervical epidural block, a safe entry point for the epidural needle can be established. The aim of this study was the measurement of the cord to canal transverse diameter ratio of each cervical spines.

**Methods:** We retrospectively evaluated the imaging data of 100 patients who underwent both cervical computed tomography (CT) and cervical magnetic resonance imaging (MRI) at our hospital. We measured the diameters of the spinal canal and spinal cord from the 3rd cervical vertebra to the 1st thoracic vertebra (T1) at each level by using the patients' cervical CT and MRI images. The spinal cord and spinal canal diameters were measured in the transverse plane of the cervical MRI and CT images, respectively.

**Results:** The spinal cord to spinal canal diameter ratio was the highest at the 4th and 5th cervical vertebrae ( $0.64 \pm 0.07$ ) and the lowest at T1 ( $0.55 \pm 0.06$ , 99% CI [0.535, 0.565]).

**Conclusions:** Our findings suggest that the cord to canal transverse diameter ratio could be used as a reference to reduce direct spinal cord injuries during cervical epidural block under C-arm fluoroscopy. In the C-arm fluoroscopic image, if an imaginary line connecting the left and right innermost lines of the pedicles of T1 is drawn and if the needle is inserted into the outer one-fifth of the left and right sides, the risk of puncturing the spinal cord would be relatively reduced.

**Keywords:** Cervical cord; Cervical vertebrae; Epidural injections; Fluoroscopy; Safety management; Spinal canal; Spinal cord injuries; Three-dimensional imaging.



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## Introduction

Cervical epidural nerve block is commonly used for the treatment of neck pain and radiating pain in the upper extremities due to cervical disc herniation or postherpetic neuralgia [1-5]. The interlaminar and transforaminal approaches are commonly used for cervical epidural nerve block. Compared to the interlaminar approach, the transforaminal approach enables more effective injection of drugs that reduce inflammation and nerve edema to the target lesions. However, the transforaminal approach might result in serious complications, such as spinal radicular artery damage or spinal cord infarction, during particulate steroid injection or epidural needle positioning [6-8]. Therefore, the cervical interlaminar approach with nonparticulate steroid injection is recommended

[9,10]. However, this approach could also result in serious complications, such as quadriplegia due to inadvertent intramedullary injection or spinal cord injury, even when performed under C-arm fluoroscopy [11,12].

Therefore, we aimed to identify a safe needle insertion point that can avoid cervical cord punctures as far as possible when performing cervical epidural block using the interlaminar approach under C-arm fluoroscopy. To date, most studies have suggested measuring the cervical cord diameter and cervical cord to canal ratio in the sagittal plane to predict the risk of cervical cord injury after trauma [13–16]. To our knowledge, this is the first study to investigate the utility of the cervical cord to canal diameter ratio for a safer interlaminar approach, which represents the cervical cord to epidural space diameter in the coronal plane.

Cervical interlaminar epidural block is usually performed in the prone position under C-arm fluoroscopy. We presumed that if the ratio of the cervical cord to epidural diameter in the posteroanterior (PA) view under C-arm fluoroscopy could be calculated, the percentage of spinal cord punctures could be reduced by positioning the epidural needle at more lateral and safer levels. The epidural space diameter could be measured as the innermost distance between the left and right pedicles under the C-arm fluoroscopy PA view, but the C-arm image is a magnified image. Therefore, we postulated that the transverse diameter of the epidural space under C-arm fluoroscopy could be measured via computed tomography (CT) because bony structures can be clearly visualized under CT, and the transverse diameter of the cervical cord could be measured via magnetic resonance imaging (MRI) at the same point. Accordingly, the primary outcome of this study was the measurement of the cord to canal transverse diameter ratio, i.e., the cord to epidural space transverse diameter ratio of each cervical vertebral level from the 3rd cervical vertebra (C3) to the 1st thoracic vertebra (T1). We also aimed to determine the differences in the cord to canal transverse diameter ratio according to the age, sex, height, and body weight of the included patients.

## Materials and Methods

This study was approved by the Institutional Review Board of Daegu Catholic University Hospital (CR-21-045). This study was conducted in accordance with the ethical principles of the Helsinki Declaration-2013 and followed good clinical practice guidelines. The study included 100 patients (50 men and 50 women aged 20 to 70 years old) who visited our hospital and underwent both cervical CT and MRI simultaneously and whose medical records from December 1, 2020, through study completion, an average of two years were investigated retrospectively (Table 1). We

**Table 1.** Demographic Characteristics

Variable			
Sex (M/F)		50 (50)/50 (50)	
Age (yr)	53.43 ± 12.26	< 60	66 (66.0)
		≥ 60	34 (34.0)
Height (cm)	163.54 ± 9.29	< 165	51 (51.0)
		≥ 165	49 (49.0)
Weight (kg)	65.72 ± 13.47	< 65	53 (53.0)
		≥ 65	47 (47.0)
Body mass index (kg/m <sup>2</sup> )	24.38 ± 3.30	< 25	63 (63.0)
		≥ 25	37 (37.0)

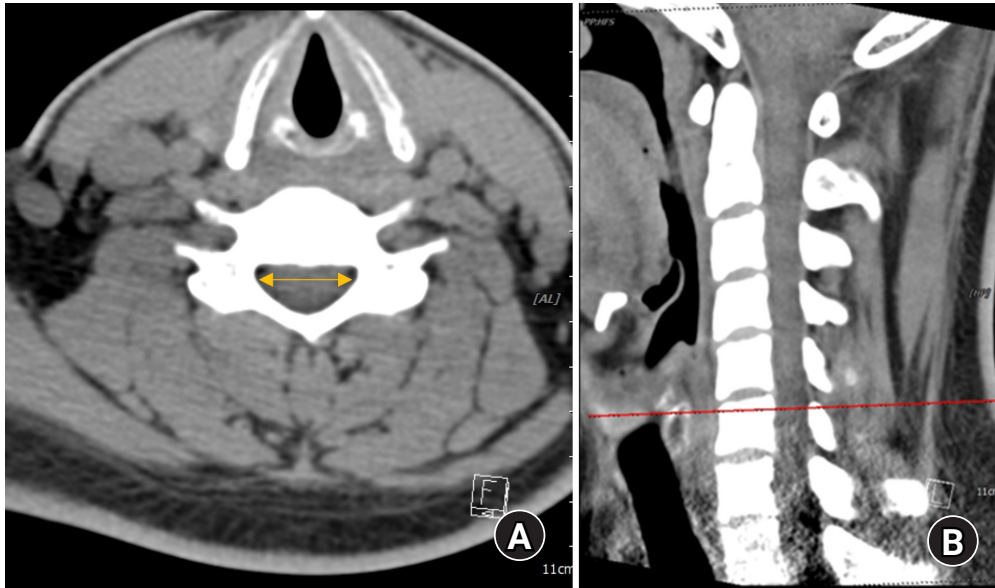
Values are presented as number (%) or mean ± SD.

excluded patients who had a history of cervical spine surgery or cervical cord edema, whose CT or MRI images did not include all the cervical vertebrae from C3 to T1, and who had at least one missing medical detail such as diagnosis, age, height, or weight.

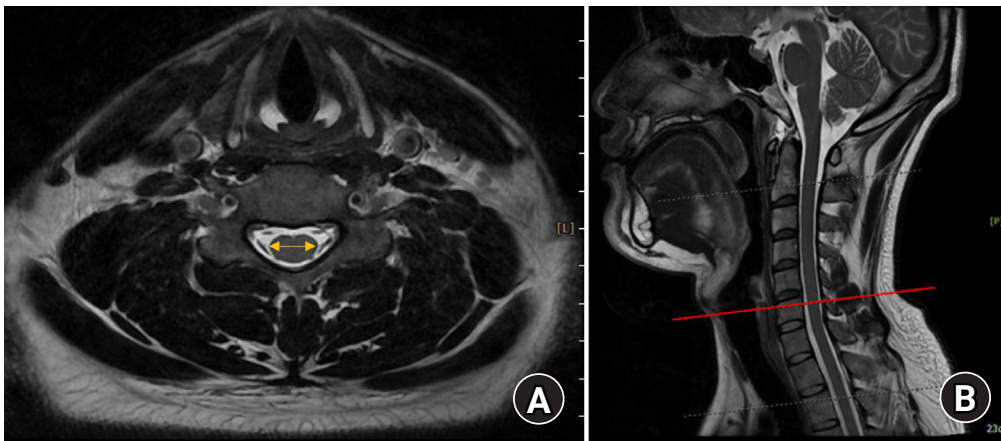
The spinal canal diameter, i.e., the epidural transverse diameter, was measured as the distance between the innermost border of the left and right pedicles at each upper pedicular level from C3 to T1 on transverse CT images by using a picture archiving and communication system (PACS; INFINTT PACS G3, INFINTT Healthcare, Korea) (Fig. 1). The spinal cord transverse diameter was measured between the left and right outermost distances of the cord at each upper pedicular level, which were almost the same locations used for measuring the spinal canal diameter, from C3 to T1 on transverse MRI images by using the PACS (Fig. 2). All measurements were performed three times by an anesthesiologist, and the average values were used as data in the analyses.

Summary for general characteristics were performed using descriptive analysis, the values of mean and standard deviation (SD) presented for quantitative variables, and the values of frequency and percent for qualitative variables. Comparison result for spinal canal transverse diameter, spinal cord transverse diameter, and ratio of the cord to canal transverse diameter were analyzed using repeated measure one factor analysis. Comparison result for spinal canal transverse diameter, spinal cord transverse diameter, and ratio of the cord to canal transverse diameter by demographic characteristics and interaction effects were analyzed using repeated measure two factor analysis. Multiple comparison result was performed by contrast under Bonferroni correction. The data analysis was performed by a medical statistician. All statistical analyses were performed using the IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., USA). And all tests were two-sided and a P value of less than 0.05 considered to indicate statistical significance.

The sample size was calculated on the basis of the findings of a



**Fig. 1.** (A) Cervical canal diameter measured using a CT image. (B) Landmarks used to measure the cervical canal diameter. CT: computed tomography.



**Fig. 2.** (A) Cervical cord diameter measured using a MRI. (B) Landmarks used to measure the cervical cord diameter. MRI: magnetic resonance image.

previous study [13] in which the ratio of the anteroposterior (AP) diameter of the spinal cord to the size of the spinal bony canal was  $51.5 \pm 5.7\%$  and  $46.5 \pm 6.1\%$  at C3 and the 7th cervical vertebra (C7), respectively. Accordingly, the number of patients required for a type I error of 0.05 and a power of 80% was 100.

## Results

The transverse diameter of the spinal canal measured on CT was  $20.4 \pm 1.54$  mm at C3, and it was longer than that measured at T1 ( $17.87 \pm 1.47$  mm). The diameter was the longest ( $20.7 \pm 1.56$  mm) at the 5th cervical vertebra (C5), and the diameters gradually shortened at the lower cervical vertebrae (Table 2). The

transverse diameter of the spinal cord measured on MRI was the longest at C5 ( $13.25 \pm 0.95$  mm) and the shortest at T1 ( $9.80 \pm 0.76$  mm) (Table 3). The cord to canal transverse diameter ratios, namely the cord to epidural space transverse diameter ratio of each cervical vertebral level, were the highest at the 4th cervical vertebra (C4) and C5 ( $0.64 \pm 0.07$ ) and the lowest at T1 ( $0.55 \pm 0.06$ , 95% CI [0.538, 0.562], 99% CI [0.535, 0.565]). The cord to canal transverse diameter ratios were significantly lower at T1 than at C3, C4, C5, 6th cervical vertebra (C6), and C7. The cord to canal transverse diameter ratios were also significantly lower at C7 ( $0.57 \pm 0.07$ , 95% CI [0.556, 0.584], 99% CI [0.552, 0.588]) than at C3, C4, C5, and C6 (Table 4, Fig. 3). However, no significant difference was observed according to sex, age, height, weight,

**Table 2.** Spinal Canal Transverse Diameter (Width) at Each Upper Pedicular Level in the Coronal Plane Measured Using CT

		C3	C4	C5	C6	C7	T1	P value		
								Spinal level	G	Spinal level*G
Total		20.4 ± 1.54	20.46 ± 1.53	20.7 ± 1.56	20.63 ± 1.46	19.77 ± 1.57	17.87 ± 1.47	< 0.001*		
								C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	-	-
Sex	M	20.69 ± 1.68	20.67 ± 1.78	21.04 ± 1.73	21.01 ± 1.63	20.27 ± 1.5	18.53 ± 1.42	< 0.001*		0.008*
	F	20.11 ± 1.35	20.26 ± 1.22	20.37 ± 1.3	20.26 ± 1.16	19.29 ± 1.51	17.21 ± 1.22	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.002	C3, C4, C5, C6, C7 > T1 <sup>†</sup>
Age	< 60	20.67 ± 1.58	20.68 ± 1.49	21.02 ± 1.32	20.84 ± 1.34	19.94 ± 1.4	18.03 ± 1.54	< 0.001*		
	≥ 60	19.86 ± 1.33	20.01 ± 1.53	20.08 ± 1.82	20.21 ± 1.61	19.44 ± 1.85	17.54 ± 1.29	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.013	0.525
Height	< 165	19.98 ± 1.31	20.12 ± 1.24	20.22 ± 1.55	20.15 ± 1.19	19.3 ± 1.57	17.25 ± 1.26	< 0.001*		
	≥ 165	20.83 ± 1.65	20.81 ± 1.73	21.19 ± 1.43	21.12 ± 1.55	20.26 ± 1.44	18.5 ± 1.42	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.000	0.397
Weight	< 65	20.04 ± 1.31	20.32 ± 1.32	20.37 ± 1.55	20.51 ± 1.45	19.57 ± 1.66	17.5 ± 1.47	< 0.001*		
	≥ 65	20.81 ± 1.7	20.62 ± 1.74	21.09 ± 1.5	20.77 ± 1.47	20.01 ± 1.45	18.29 ± 1.38	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.033	0.123
BMI	< 25	20.24 ± 1.58	20.41 ± 1.64	20.65 ± 1.43	20.71 ± 1.38	19.78 ± 1.65	17.73 ± 1.58	< 0.001*		
	≥ 25	20.66 ± 1.46	20.54 ± 1.35	20.79 ± 1.78	20.5 ± 1.59	19.76 ± 1.45	18.09 ± 1.26	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.617	0.164

Values are presented as mean ± SD. P values are obtained via repeated-measures one-factor or two-factor analysis. BMI: body mass index, CT: computed tomography, G: group. \*Statistically significant at P < 0.05, <sup>†</sup>Multiple comparison result by contrast.

**Table 3.** Spinal Cord Transverse Diameter (Width) at Each Upper Pedicular Level in the Coronal Plane Measured Using MRI

		C3	C4	C5	C6	C7	T1	P value		
								Spinal level	G	Spinal level*G
Total		12.3 ± 0.86	13.06 ± 1.02	13.25 ± 0.95	12.78 ± 0.99	11.26 ± 1.03	9.80 ± 0.76	< 0.001*		
								C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	-	-
Sex	M	12.20 ± 0.90	12.96 ± 1.08	13.22 ± 0.92	12.69 ± 1.08	11.28 ± 1.16	9.83 ± 0.86	< 0.001*		
	F	12.42 ± 0.81	13.19 ± 0.94	13.29 ± 1.00	12.89 ± 0.87	11.22 ± 0.86	9.76 ± 0.64	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.581	0.202
Age	< 60	12.21 ± 0.93	12.94 ± 1.12	13.17 ± 1.01	12.63 ± 1.02	11.20 ± 1.06	9.73 ± 0.77	< 0.001*		
	≥ 60	12.45 ± 0.72	13.29 ± 0.79	13.39 ± 0.83	13.06 ± 0.88	11.36 ± 0.97	9.91 ± 0.74	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.142	0.585
Height	< 165	12.35 ± 0.84	13.10 ± 1.04	13.20 ± 1.00	12.83 ± 0.85	11.18 ± 0.78	9.76 ± 0.62	< 0.001*		
	≥ 165	12.25 ± 0.89	13.02 ± 1.01	13.30 ± 0.91	12.74 ± 1.11	11.33 ± 1.23	9.83 ± 0.88	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.953	0.449
Weight	< 65	12.39 ± 0.85	13.23 ± 1.04	13.41 ± 1.03	12.97 ± 0.94	11.37 ± 0.98	9.88 ± 0.77	< 0.001*		
	≥ 65	12.20 ± 0.87	12.89 ± 0.98	13.09 ± 0.84	12.59 ± 1.01	11.13 ± 1.07	9.71 ± 0.75	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.113	0.737
BMI	< 25	12.35 ± 0.86	13.15 ± 0.99	13.34 ± 0.96	12.87 ± 0.93	11.35 ± 1.00	9.88 ± 0.78	< 0.001*		
	≥ 25	12.20 ± 0.86	12.91 ± 1.08	13.09 ± 0.94	12.61 ± 1.08	11.08 ± 1.07	9.64 ± 0.70	C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.199	0.986

Values are presented as mean ± SD. P values are obtained via repeated-measures one-factor or two-factor analysis. BMI: body mass index, G: group, MRI: magnetic resonance image. \*Statistically significant at P < 0.05, <sup>†</sup>Multiple comparison result by contrast.

and the body mass index.

## Discussion

On comparing the transverse diameters of the spinal canal and spinal cord by using CT and MRI, the cord to canal diameter ratio was the highest at C4 and C5 and the lowest at T1. In this study, the T1 level was close to the C7 to T1 interlaminar foramen because the diameters of the spinal canal and spinal cord

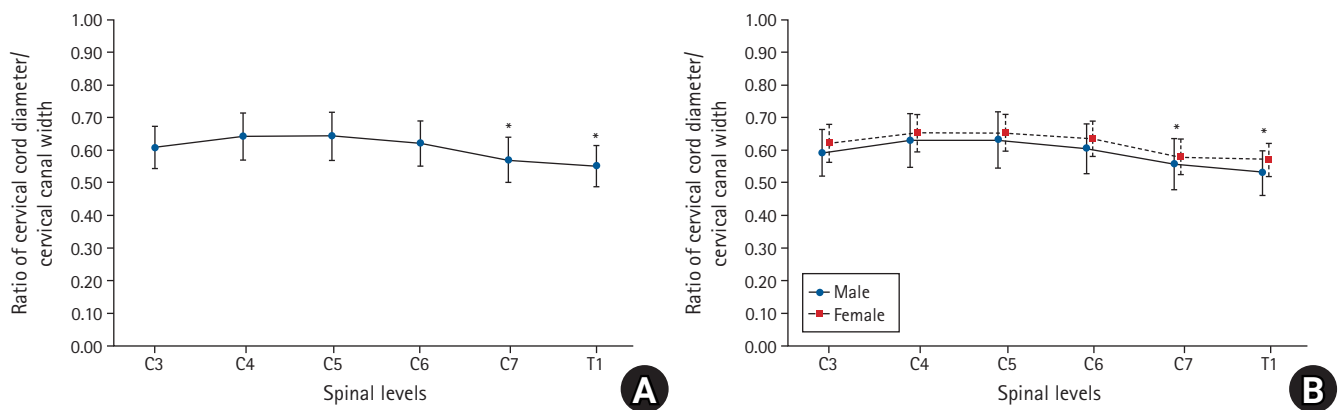
were measured at the upper pedicular levels. If epidural block was performed under C-arm fluoroscopy, the T1 level would be the safest injection site to reduce spinal cord injuries during cervical epidural block, as shown in previous reports [12]. Considering that the cord to canal transverse diameter ratio increases as we move to the upper cervical vertebrae, performing an epidural nerve block at levels higher than C6–7 and C7–T1 would increase the probability of spinal cord injury. Assuming the spinal cord was located in the middle of the vertebral body in the



**Table 4.** Ratio of the Transverse Diameter (Width) of the Spinal Cord/Spinal Canal at Each Vertebral Level

		C3	C4	C5	C6	C7	T1	P value			
								Spinal level	G	Spinal level*G	
Total		0.61 ± 0.07	0.64 ± 0.07	0.64 ± 0.07	0.62 ± 0.07	0.57 ± 0.07	0.55 ± 0.06	< 0.001*			
									C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	-	-
Sex	M	0.59 ± 0.07	0.63 ± 0.08	0.63 ± 0.09	0.61 ± 0.08	0.56 ± 0.08	0.53 ± 0.07	< 0.001*			
	F	0.62 ± 0.06	0.65 ± 0.06	0.65 ± 0.06	0.64 ± 0.05	0.58 ± 0.05	0.57 ± 0.05		C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.028	0.616
Age	< 60	0.6 ± 0.07	0.63 ± 0.07	0.63 ± 0.06	0.61 ± 0.07	0.56 ± 0.07	0.54 ± 0.06	< 0.001*			
	≥ 60	0.63 ± 0.06	0.67 ± 0.07	0.67 ± 0.09	0.65 ± 0.06	0.58 ± 0.07	0.57 ± 0.06		C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.010	0.480
Height	< 165	0.62 ± 0.06	0.65 ± 0.06	0.66 ± 0.08	0.64 ± 0.06	0.58 ± 0.06	0.57 ± 0.05	< 0.001*			
	≥ 165	0.59 ± 0.07	0.63 ± 0.08	0.63 ± 0.07	0.61 ± 0.07	0.56 ± 0.08	0.53 ± 0.07		C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.030	0.734
Weight	< 65	0.62 ± 0.06	0.65 ± 0.07	0.66 ± 0.08	0.63 ± 0.07	0.58 ± 0.07	0.57 ± 0.06	< 0.001*			
	≥ 65	0.59 ± 0.07	0.63 ± 0.08	0.62 ± 0.06	0.61 ± 0.07	0.56 ± 0.07	0.53 ± 0.06		C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.028	0.713
BMI	< 25	0.62 ± 0.06	0.65 ± 0.07	0.65 ± 0.06	0.62 ± 0.06	0.57 ± 0.07	0.56 ± 0.06	< 0.001*			
	≥ 25	0.59 ± 0.07	0.63 ± 0.07	0.63 ± 0.09	0.62 ± 0.08	0.57 ± 0.07	0.53 ± 0.06		C3, C4, C5, C6 > C7 > T1 <sup>†</sup>	0.228	0.471

Values are presented as mean ± SD. P values are obtained via repeated-measures one-factor or two-factor analysis. BMI: body mass index, G: group. \*Statistically significant at P < 0.05, <sup>†</sup>Multiple comparison result by contrast.



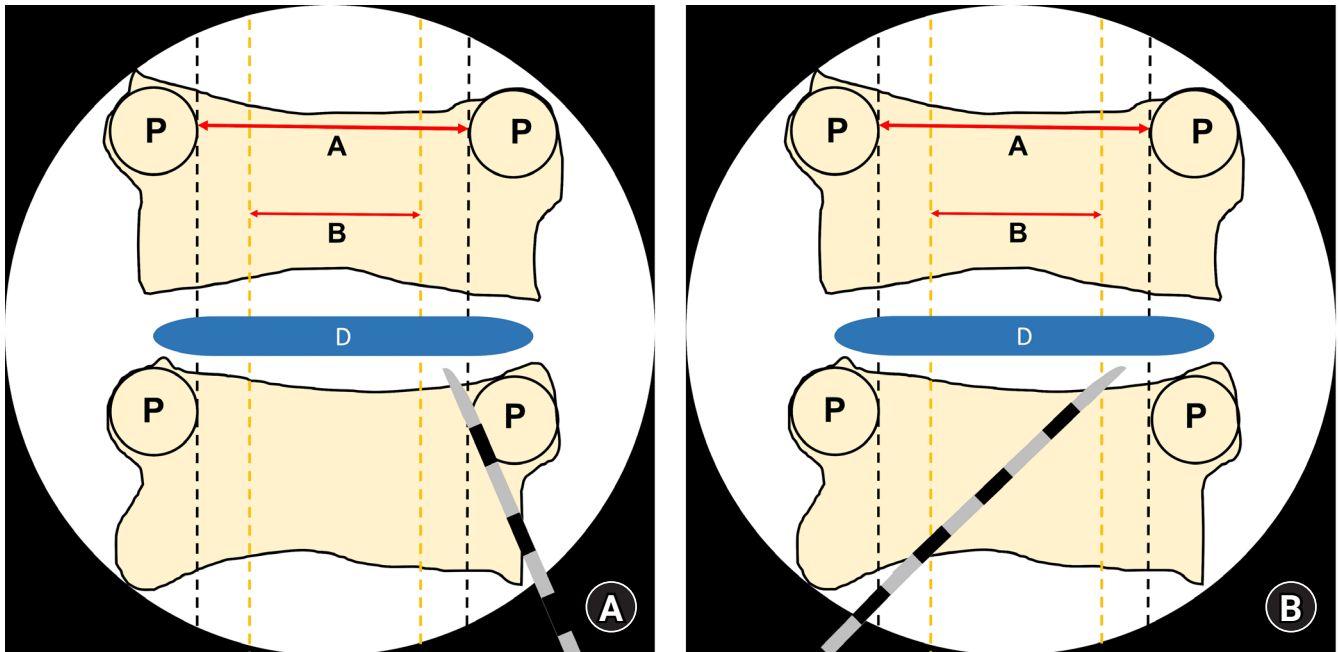
**Fig. 3.** Graphs showing the ratio of the cervical cord/cervical canal diameter at each level. (A) The cord to canal diameter ratios were significantly lower at C7 and T1 than at C3, C4, C5, and C6. (B) There was no significant difference according to sex. \*Statistically significant at P < 0.05.

coronal plane and epidural block was performed at the T1 level, we could postulate that the risk of direct spinal cord puncture by the epidural needle would be reduced if the needle was inserted in the outer one-fifth region when an imaginary line was drawn between the innermost site of the pedicle under C-arm fluoroscopy, because the cord to canal diameter ratio at this site was the lowest (Fig. 4). In other words, assuming that the transverse diameter of the spinal canal is 1, the mean value, 95% CI, and 99% CI values of the cord to canal transverse diameter ratio are less than 0.6. This means that the outer sum of the cord is over 0.4; therefore, the possibility of having spinal cord in the outer one-fifth region of the transverse spinal canal on both sides is extremely low.

If cervical interlaminar epidural nerve block was performed by inserting the needle to the outside as much as possible, it would

result in effective left or right unilateral block. Although this is an imaginary line, if the operator performs the cervical epidural nerve block along this virtual line, direct damage to the spinal cord caused by the needle could be reduced or prevented. However, the present study describes the location where the cord cannot be directly pierced with a needle as much as possible using images, and it is not a study that was actually conducted on patients. When positioning the needle on the outer one-fifth of the cervical canal under the C-arm AP image during the cervical epidural block, it should be considered that the ligamentum flavum is thinner as it goes outward rather than in the center, and if the needle is pierced too deeply, it can cause root injury.

Complications that may occur during cervical epidural nerve block include rare and serious ones like spinal cord injury, epidural hematoma, and epidural abscess, as well as minor ones



**Fig. 4.** Schematic figure showing the imaginary lines that are observed using C-arm fluoroscopy during the cervical epidural block. The epidural needles are placed in the outer one-fifth of the cervical canal width by paramedian (A) and modified paramedian (B) approaches. The cervical cord will be in the inner three-fifth of the cervical canal width. A: cervical cord width, B: cervical epidural width, D: intervertebral disc, P: pedicle.

like post-dural puncture headache and paresthesia [17]. All the reported cases of spinal cord injury during cervical epidural nerve block occurred under deep sedation [12,18]. Therefore, performing the procedure under arousal or under appropriate sedation is recommended so that the patient's response can be immediately confirmed during the procedure and potential injuries can be avoided or reduced. In addition, because the ligamentum flavum of the cervical spine has a fusion defect rate ranging from 51% to 74% depending on the level of the cervical spine, the possibility exists that the operator might not feel the loss of resistance when performing an epidural block using the midline approach [19].

Stanley et al. [20] reported that the spinal canal AP diameters measured in the sagittal plane were shorter at C3, C4, and C5 than at other levels. The cross-sectional area of the spinal canal was the smallest at C4 and C7. Inoue et al. [15] used CT myelography and reported that the spinal canal AP diameter and spinal cord AP diameter in the sagittal plane decreased gradually from the C3 to C6 levels. Similarly, the transverse diameters measured from the axial image in the present study gradually decreased from cranial to caudal levels. On average, the spinal canal AP diameters range from 15.33 to 20.46 mm from C1 to C7 in the sagittal plane, with the longest diameter at C1 and the shortest at C4 [21,22]. Moreover, the sagittal canal diameters are shorter in females than in males by approximately 1 mm [21]. Ishikawa et al. [14] reported

that the mean spinal cord areas in the coronal plane were the widest at C4 and in the 20s, but it decreased with age. Nakashima et al. [13] reported that the spinal canal diameter did not correlate with the spinal cord diameter, but correlated with the AP diameter of the dura mater in the sagittal plane. They also reported that the AP diameter of the spinal cord was approximately 50% of that of the spinal canal and the AP diameter of the spinal cord was approximately 60% of that of the dural sac in the sagittal plane. In the present study, the ratio of the transverse diameter of the spinal cord to that of the epidural space obtained from the axial images was in the range of 0.55 to 0.64, showing similar results to the previous study that measured the AP diameters in the sagittal plane.

This study also has a few limitations. Although CT is very useful for visualizing bony structures, it does not allow the measurement of the exact diameter of the spinal cord. Therefore, in this study, the diameter of the spinal canal was measured using CT, and the diameter of the spinal cord was measured using MRI, which helped accurately visualize the structure of the spinal cord. Consequently, although the measurement location was set to each pedicle, some errors may have been introduced because the measurement point was not identical in CT and MRI. However, since the images were acquired at intervals of 1 mm, the difference was insignificant. In addition, CT or MRI cross-sections were not always obtained perpendicular to the cross-sectional

area during diameter measurements. Nevertheless, since we measured transverse but not AP diameters, the diameters of the spinal cord and spinal canal should be identical even if the image slice was not cut vertically, and hence, this variation did not affect the length measurements. Finally, the MRI or CT of a patient is taken in the supine position, while an actual epidural block is performed in the prone position with neck flexion. Furthermore, in the prone position with neck flexion, the cervical cord moves to the ventral side and is tented; therefore, it may not exactly match the cord to canal diameter ratio measured in this study and that in the actual epidural block. In the sagittal plane, as the cervical cord moves to the anterior space in the prone position with neck flexion, the length of the posterior epidural space can be significantly increased. However, in the coronal plane, even if the cord moves to the anterior space, there is no significant difference in the cord width; consequently, there may be no significant change in the cord to canal transverse diameter ratio according to the position.

In conclusion, we measured the transverse diameters of the cervical spinal canal and spinal cord and calculated the spinal cord to spinal canal diameter ratios at various cervical vertebrae and found that the ratios were the smallest at T1 and the largest at C4 and C5. By using our data as reference, cervical epidural nerve block under C-arm fluoroscopy could be performed after considering the location of the imaginary spinal cord in order to potentially avoid serious side effects such as direct spinal cord punctures.

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## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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 Kyung Wook Jeong (Data curation; Formal analysis; Investigation; Methodology; Visualization)  
 Taeha Ryu (Data curation; Project administration; Software)  
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## References

1. Shakir A, Ma V, Mehta B. Comparison of pain score reduction using triamcinolone vs. dexamethasone in cervical transforaminal epidural steroid injections. *Am J Phys Med Rehabil* 2013; 92: 768-75.
2. Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic cervical interlaminar epidural injections in managing chronic pain of cervical postsurgery syndrome: preliminary results of a randomized, double-blind, active control trial. *Pain Physician* 2012; 15: 13-25.
3. Manchikanti L, Pampati V, Falco FJ, Hirsch JA. An updated assessment of utilization of interventional pain management techniques in the Medicare population: 2000 - 2013. *Pain Physician* 2015; 18: E115-27.
4. Crette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St-Pierre A, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med* 1997; 336: 1634-40.
5. Shakir A, Kimbrough DA, Mehta B. Postherpetic neuralgia involving the right C5 dermatome treated with a cervical transforaminal epidural steroid injection: a case report. *Arch Phys Med Rehabil* 2007; 88: 255-8.
6. Brouwers PJ, Kottink EJ, Simon MA, Prevo RL. A cervical anterior spinal artery syndrome after diagnostic blockade of the right C6-nerve root. *Pain* 2001; 91: 397-9.
7. Rozin L, Rozin R, Koehler SA, Shakir A, Ladham S, Barmada M, et al. Death during transforaminal epidural steroid nerve root block (C7) due to perforation of the left vertebral artery. *Am J Forensic Med Pathol* 2003; 24: 351-5.
8. Williams KN, Jackowski A, Evans PJ. Epidural haematoma requiring surgical decompression following repeated cervical epidural steroid injections for chronic pain. *Pain* 1990; 42: 197-9.
9. Manchikanti L, Hirsch JA. Neurological complications associated with epidural steroid injections. *Curr Pain Headache Rep* 2015; 19: 482.

10. Rathmell JP, Benzon HT, Dreyfuss P, Huntoon M, Wallace M, Baker R, et al. Safeguards to prevent neurologic complications after epidural steroid injections: consensus opinions from a multidisciplinary working group and national organizations. *Anesthesiology* 2015; 122: 974-84.
11. Hodges SD, Castleberg RL, Miller T, Ward R, Thornburg C. Cervical epidural steroid injection with intrinsic spinal cord damage. Two case reports. *Spine (Phila Pa 1976)* 1998; 23: 2137-42.
12. Maddela R, Wahezi SE, Sparr S, Brook A. Hemiparesis and facial sensory loss following cervical epidural steroid injection. *Pain Physician* 2014; 17: E761-7.
13. Nakashima H, Yukawa Y, Suda K, Yamagata M, Ueta T, Kato E. Relatively large cervical spinal cord for spinal canal is a risk factor for development of cervical spinal cord compression: a cross-sectional study of 1211 subjects. *Spine (Phila Pa 1976)* 2016; 41: E342-8.
14. Ishikawa M, Matsumoto M, Fujimura Y, Chiba K, Toyama Y. Changes of cervical spinal cord and cervical spinal canal with age in asymptomatic subjects. *Spinal Cord* 2003; 41: 159-63.
15. Inoue H, Ohmori K, Takatsu T, Teramoto T, Ishida Y, Suzuki K. Morphological analysis of the cervical spinal canal, dural tube and spinal cord in normal individuals using CT myelography. *Neuroradiology* 1996; 38: 148-51.
16. Koike H, Hatta Y, Tonomura H, Nonomura M, Takatori R, Nagae M, et al. Can a relatively large spinal cord for the dural sac influence severity of paralysis in elderly patients with cervical spinal cord injury caused by minor trauma? *Medicine (Baltimore)* 2020; 99: e20929.
17. Chang A, Wang D. Complications of fluoroscopically guided cervical interlaminar epidural steroid injections. *Curr Pain Headache Rep* 2020; 24: 63.
18. Lieberman R, Dreyfuss P, Baker R. Fluoroscopically guided interlaminar cervical epidural injections. *Arch Phys Med Rehabil* 2003; 84: 1568-9.
19. Lirk P, Kolbitsch C, Putz G, Colvin J, Colvin HP, Lorenz I, et al. Cervical and high thoracic ligamentum flavum frequently fails to fuse in the midline. *Anesthesiology* 2003; 99: 1387-90.
20. Stanley JH, Schabel SI, Frey GD, Hungerford GD. Quantitative analysis of the cervical spinal canal by computed tomography. *Neuroradiology* 1986; 28: 139-43.
21. Gupta SK, Roy RC, Srivastava A. Sagittal diameter of the cervical canal in normal Indian adults. *Clin Radiol* 1982; 33: 681-5.
22. Zhang L, Chen HB, Wang Y, Zhang LY, Liu JC, Wang ZG. Cervical spinal canal narrowing and cervical neurological injuries. *Chin J Traumatol* 2012; 15: 36-41.



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# Video laryngoscope versus USB borescope-aided endotracheal intubation in adults with anticipated difficult airway: a prospective randomized controlled study

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**Background:** Video laryngoscopes are approved equipment for difficult airway intubations. The borescope, which was introduced during the coronavirus disease 2019 (COVID-19) era, is placed over a direct laryngoscope blade to provide an economical video laryngoscope. In the current study, we investigated the use of an endotracheal tube mounted over a USB borescope versus a video laryngoscope in patients with suspected difficult airways.

**Methods:** After obtaining informed consent, 120 adult patients with suspected difficult airways undergoing elective surgery were included in this study. Patients were randomized into the USB borescope and video laryngoscope groups. The primary outcome was time to successful intubation. The secondary outcomes included hemodynamic changes, anesthetist's satisfaction, and the incidence of complications.

**Results:** Intubation time was comparable between the two groups (video laryngoscope: 30.63 s and borescope: 28.35 s;  $P = 0.166$ ). However, the view was clearer ( $P = 0.026$ ) and the incidence of fogging was lower ( $P = 0.015$ ) with the video laryngoscope compared to the borescope. Conversely, anesthetist's satisfaction frequency was higher with the borescope than with the video laryngoscope ( $P < 0.001$ ).

**Conclusions:** The video laryngoscope provided a better view and less fogging with an intubation time that was comparable to that of the borescope; however, the higher cost of the video laryngoscope limits its availability. Therefore, the borescope is a low-cost, readily available device that can be used for intubating patients with potentially difficult airways.

**Keywords:** Airway management; General anesthesia; Intratracheal intubation; Intubation; Laryngoscopy; Trachea.



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## Introduction

Securing the airway with endotracheal intubation has always been one of the most challenging aspects of anesthesia, with an incidence of failed intubation reaching up to six out of every 13,380 patients [1]. Airway difficulty can be assessed using various bedside tests, such as mouth opening, the Mallampati classification of oral opening [2], thyromental distance, and neck circumference [3], among others, including the El-Ganzouri risk index (mouth opening, thyromental distance, Mallampati class, neck movement, prognathism, weight, and history of difficult intubation) [4-6].

Various algorithms have been developed for difficult airway intubations. For example, the Difficult Airway Society algorithm uses a stepwise approach [7]. Difficult airway intubation equipment and skilled personnel should be available whenever difficulties are anticipated. This equipment can be as simple as different blade and tube sizes, stylets, bougies, and intubating laryngeal masks or as sophisticated as video laryngoscopes and fiberoptic bronchoscopes [8]. While the efficacy of video laryngoscope and fiberoptic bronchoscope in the management of challenging airways has been shown, their cost and bulky size limit their availability and the number of skilled personnel trained to use them [9,10]. Therefore, the need for an airway equipment that is available in every operating room to aid whenever unanticipated difficult intubation is encountered is always present.

The introduction of the video laryngoscope has changed how difficult airways are managed. Except for patients with limited mouth opening, for which the flexible fiberoptic bronchoscope is still superior, the video laryngoscope has replaced the fiberoptic bronchoscope for patients with anticipated and unanticipated difficult airways [11].

However, although it has been found to be cost-effective for organ inspection [12], the use of the USB borescope to confirm and aid in endotracheal intubation has only been studied in intubation simulator models and cadavers [13], and only a few case reports have suggested its applicability to confirm intubation [14].

In this study, the video laryngoscope was compared with the conventional laryngoscope aided by a USB borescope in the intubation of adult patients with suspected difficult airways. To our knowledge, this is the first randomized clinical trial to investigate this topic.

## Materials and Methods

The institutional research ethics committee of Cairo University El-Kasr Alainy Hospital approved this study (IRB number: N-15-2021/MSC). The trial was registered at clinicaltrials.gov (reference number: NCT 05158088). The study was conducted from December 2021 to April 2022 in accordance with the Helsinki Declaration-2013. All patients who were screened and met the eligibility criteria were invited to participate in the trial, and all the enrolled patients provided written informed consent. Consent was requested from patients upon arrival to the operating suite for surgery or on the ward if they were admitted the night before surgery.

## Patients

Patients with an El-Ganzouri score  $\geq 4$  [4] undergoing elective

surgery under general anesthesia between October 2021 and March 2022 met the inclusion criteria. The exclusion criteria were as follows: presence of pulmonary diseases, uncontrolled hypertension, ischemic heart disease, cervical spinal fracture, limited mouth opening, tumors or polyps in the upper airway, and a history of difficult intubation, difficult bag-mask ventilation, or difficult bag-mask ventilation after induction of anesthesia.

Using a computer-generated table, patients were randomly allocated to either the video laryngoscope or the USB borescope group. Patient identifiers were attached to the opened envelopes and secured by a dedicated person, independent of the randomization proceedings. To account for potential dropouts, we recruited 120 patients (60 patients per group).

## Procedures

Information on the age, sex, American Society of Anesthesiologists physical status, and body mass index were collected during the pre-anesthetic visit by an anesthetist not involved in this study. The anesthetist also assessed the airway and measured the common predictive indices for difficult intubation (mouth opening, thyromental distance, modified Mallampati score, neck movement, prognathism, body weight, and history of difficult intubation) according to the El-Ganzouri Risk Index score for difficult intubation [3]. The intubations were performed by an anesthetist with at least one year of intubation experience, with prior experience using a video laryngoscope and at least two practice intubations on a manikin using a borescope.

After the patients arrived in the operating room, they were connected to standard monitoring devices (electrocardiogram, non-invasive blood pressure, and pulse oximetry). A baseline reading was taken, and they received O<sub>2</sub> at 100% for at least 3 min using a face mask. Anesthesia induction consisted of intravenous fentanyl 1.5 µg/kg and propofol 2 mg/kg based on the estimated lean body weight. Manual mask ventilation and inflation of the lungs were attempted through a face mask using sevoflurane in O<sub>2</sub> before the muscle relaxant was injected. Once the bag-mask ventilation was verified, atracurium 0.5 mg/kg was administered.

For patients allocated into the USB borescope group, a properly-sized endotracheal tube was placed over the USB borescope (T Takmly 5.5-HD, China semi-rigid waterproof borescope with an external diameter of 5.5 mm), with the tip of the borescope receding behind the tip of the endotracheal tube by approximately 1 cm, which was coated externally with a water-soluble sterile lubricant. A properly sized laryngoscope blade was inserted into the patient's mouth using the operator's left hand and advanced inward to the oropharynx while elevating the tongue. The USB bo-

rescope was placed into the oral cavity using the operator's right hand and, while being tracked on a mobile phone, it was advanced to the glottic opening. If needed, the USB borescope was rotated and/or external laryngeal manipulation was performed to align it with the vocal cord. A properly sized endotracheal tube was then inserted ([Supplementary Video 1](#)).

For patients allocated into the video laryngoscope group, a video laryngoscope (Insighters Insight iS3, China) was placed, a properly size blade was then inserted, and the video laryngoscope gently was introduced, the epiglottis was lifted until the glottis opening was observed. A properly sized endotracheal tube was then inserted.

Correct placement of the endotracheal tube was further confirmed by the presence of an end-tidal carbon dioxide waveform and auscultation. Successful intubation attempts were defined as tracheal tube placement confirmed by a persistent end-tidal carbon dioxide waveform and auscultation of clear and equal bilateral breath sounds with an absence of air sounds over the epigastrium. The patients were then mechanically ventilated, with the end-tidal carbon dioxide levels maintained between 30 and 35 mmHg, and 1% isoflurane in oxygen maintained at 50%.

To ensure patient safety, a maximum of two intubation attempts were conducted. Intubation was considered a failure if desaturation ( $\text{SpO}_2$  90%) occurred or if the attempt took more than 90 s. In such cases, the attempted intubation was abandoned and bag-mask ventilation was reinitiated. An additional dose of propofol (0.5–1 mg/kg) was then administered and the insertion of a laryngeal mask was attempted. In the case of failure, fiberoptic intubation was then performed.

Complications associated with tracheal intubation, such as hypoxia ( $\text{SpO}_2 < 92\%$ ), esophageal intubation, lip or dental injury, mucosal bleeding, and postoperative sore throat, were assessed in the anesthesia recovery area. A senior anesthetist who was not involved in the study performed these assessments.

The anesthetist's overall satisfaction with the intubation experience was assessed and scored as good, satisfactory, or poor based on visualization of the glottis and the need for manipulations to aid in the intubation. The anesthetists also evaluated their overall experience with the video laryngoscope or borescope (3 for good, 2 for satisfactory, and 1 for poor overall experience). The intubation time was recorded as the time from the introduction of the laryngoscope into the oral cavity to the appearance of the end-tidal carbon dioxide waveform. Successful intubation on the first attempt, number of attempts, clarity of the view (Cormack-Lehane grade), presence of fogging during the procedure, and incidence of loss of airway (e.g., esophageal intu-

bation), were noted. Heart rate (HR), systolic and diastolic blood pressure, mean arterial blood pressure (MAP), and  $\text{SpO}_2$  were documented before induction (baseline), immediately after induction, immediately after intubation, and 5 min after intubation.

Both the borescope and the video laryngoscope were disinfected using a gauze soaked in alcohol at a concentration of 70–90%. They were wiped for 5 min and then rinsed with saline.

## Outcomes

The primary outcome was the time of intubation in seconds, assessed as the time from the introduction of the laryngoscope into the oral cavity to the appearance of the end-tidal carbon dioxide waveform.

The secondary outcomes included vital changes during and after intubation, clarity of the view, presence of fogging, incidence of complications, level of experience needed to handle the equipment (all had a minimum of one year of experience in anesthesia, having performed > 100 successful intubation procedures), number of attempts necessary for correct endotracheal intubation, and the anesthetists' overall intubation experience.

## Statistical analysis

In a previous study, the mean intubation time using a video laryngoscope was  $77.43 \pm 35.55$  s. We calculated the sample size that could detect a mean difference of 25% between the study groups. MedCalc Software version 14 (MedCalc Software Bvba, Belgium) was used to calculate the sample size. A minimum of 106 patients (53 per group) were estimated to have a study power of 80% and an alpha error of 0.05. We increased the target number to 120 patients (60 per group) to account for possible drop-outs.

All measurement indices were expressed as the mean  $\pm$  SD or number (%). After the normality of the data distribution was analyzed, normally distributed data were compared using the independent sample t-test. Unpaired quantitative variables were evaluated using the Student's t-test and analysis of variance. The Mann-Whitney *U* test was used for intergroup comparisons, and the Wilcoxon signed-rank test was used to compare different time points within the same group. Intergroup comparisons of categorical variables were performed using the chi-squared test. The *P* value was set at < 0.05. All data were statistically analyzed by statisticians using SPSS software (version 16.0; IBM Corp., USA).

## Results

After written informed consent was obtained, 130 patients were initially screened for suitability and 120 who met the inclusion criteria were randomly assigned to the video laryngoscope and borescope groups. All enrolled patients were followed up successfully, and no patients were lost to follow-up. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram for this trial is shown in Fig. 1.

The patients' demographic and operative data were comparable between the two groups (Table 1). The time of intubation (primary outcome) was also comparable between the two groups ( $P = 0.166$ ).

The view was clearer (Cormack-Lehane grade) with the video laryngoscope than with the borescope ( $P = 0.026$ ). However, the anesthetist's satisfaction with the intubation experience was better with the borescope than with the video laryngoscope, and there was a lower incidence of fogging with the video laryngoscope ( $P = 0.015$ ). However, the incidence of complications, level of experience needed to handle the equipment, and number of trials to correct endotracheal intubation were comparable between the two groups (Table 2). There were no major adverse events related to the use of the intubation techniques in either group apart from mucosal bleeding (borescope group = 2 cases; video laryngoscope group = 4 cases) ( $P = 0.679$ ), and there was no need for more advanced airway equipment, such as fiberoptic

intubation, or intubation failure for any patient in the study.

The HR and MAP were comparable between the two groups except for the time immediately after intubation ( $P = 0.039$ ) and 5 min after intubation ( $P = 0.021$ ), where the HR was significantly higher in the video laryngoscope group than in the borescope group (Table 3).

## Discussion

In the current study, the time of intubation between the video la-

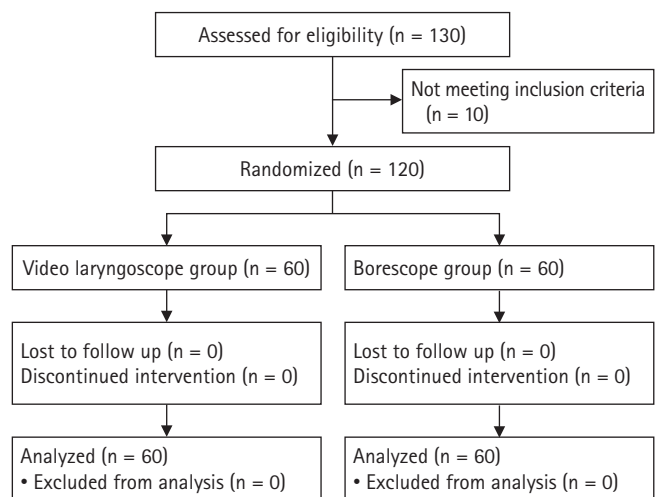


Fig. 1. CONSORT flow diagram.

Table 1. Patients' Demographic and Surgical Characteristics

Parameter	Video laryngoscope (n = 60)	Borescope (n = 60)	P value
Sex (Male)	28 (46.7)	33 (55.0)	0.361
ASA (I/II)	46 (76.7)/14 (23.3)	48 (80.0)/12 (20.0)	0.658
Age (yr)	42.30 ± 14.49	44.80 ± 9.68	0.269
BMI (kg/m <sup>2</sup> )	29.26 ± 3.47	28.20 ± 3.93	0.120
El-Ganzouri score	4.57 ± 0.56	4.87 ± 1.00	0.045*
Anesthetist experience (yr)	2.87 ± 1.56	3.37 ± 1.70	0.095

Values are presented as mean ± SD or frequency (%). ASA: American Society of Anesthesiologists classification, BMI: body mass index. \*Statistically significant difference ( $P < 0.05$ ).

Table 2. Comparison of Outcomes between the Two Groups

Parameter	Video laryngoscope (n = 60)	Borescope (n = 60)	P value
Cormack-Lehane grade (1/2a/2b/3)	40 (66.7)/16 (26.7)/2 (3.3)/2 (3.3)	25 (41.7)/23 (38.3)/8 (13.3)/4 (6.7)	0.026*
Time of intubation (s)	30.6 ± 7.9	28.3 ± 9.9	0.166
Anesthetist's satisfaction (1/2/3)	18 (30)/17 (28.3)/25 (41.6)	6 (10)/8 (13.3)/46 (76.6)	< 0.001*
Fogging	2 (3.3)	10 (16.7)	0.015*
Number of trials (1/2)	52 (86.7)/8 (13.3)	55 (91.7)/5 (8.3)	0.378
Complications	4 (6.7)	2 (3.3)	0.679

Values are presented as mean ± SD or frequency (%). \*Statistically significant difference ( $P < 0.05$ ).



**Table 3.** Comparison of HR and MAP between the Two Groups

Parameter		Video laryngoscope (n = 60)	Borescope (n = 60)	P value
HR (/min)	T0	86.4 ± 15.6	85.3 ± 15.0	0.692
	T1	87.6 ± 13.6	86.6 ± 16.3	0.707
	T2	91.4 ± 11.5	92.3 ± 15.3	0.707
	T3	94.4 ± 12.8	89.6 ± 12.0	0.039*
	T4	85.9 ± 12.7	80.9 ± 10.6	0.021*
MAP (mmHg)	T0	95.9 ± 17.7	93.1 ± 14.7	0.351
	T1	85 ± 14.6	82.0 ± 13.1	0.244
	T2	98.8 ± 18.1	96.0 ± 14.2	0.351
	T3	97.6 ± 17.6	96.1 ± 14.0	0.628
	T4	81.9 ± 13.7	85.5 ± 13.3	0.152

Values are presented as mean ± SD. MAP: mean arterial blood pressure, HR: heart rate, T0: baseline, T1: after induction, T2: during intubation trial, T3: immediately after intubation, T4: 5 min after intubation. \*Statistically significant difference ( $P < 0.05$ ).

ryngoscope and borescope groups was not statistically significant. However, the Cormack-Lehane grade was statistically significantly better with the video laryngoscope, and there was a lower incidence of fogging. However, the number of trials and incidence of complications were not statistically significantly different between the groups. Considering how complex and expensive the video laryngoscope is, this lack of statistical significance provides favorable support for the borescope as an inexpensive and safe device to use for intubating patients with an anticipated difficult airway.

Previous studies assessing the effectiveness of the video laryngoscope in the intubation of patients with suspected difficult airways have shown a higher success rate with the video laryngoscope from the first attempt than with the direct laryngoscope, yet the intubation time was found to be longer, with an average of 46 s in the video laryngoscope group versus 33 s in the direct laryngoscope group [15]. In a Cochrane systematic review comparing video laryngoscopy and direct laryngoscopy, video laryngoscopy was found to result in a statistically significant reduction in the number of failed intubation trials in participants with an anticipated difficult airway (though not in those without an anticipated difficult airway), and the Cormack-Lehane view was better with the video laryngoscope. However, the review found insufficient data regarding the incidence of complications, such as hypoxia and laryngeal and airway trauma [16]. Additionally, with the video laryngoscope, reduced movement in the cervical spine has been reported during intubation of patients with an unsecured cervical spine [17].

There is an increasing need for intubation equipment, such as video laryngoscopes, that cause less particle dispersion and thus result in a lower incidence of airborne infections, especially in the coronavirus disease 2019 (COVID-19) era [18]. We believe that these benefits are anticipated with the borescope.

The use of the borescope started with the COVID-19 pandemic, and it has been tested and compared to the video laryngoscope in terms of the time to intubation. However, to the best of our knowledge, it has not been tested except in one study that was performed and tested on mannequins [19].

A previous case report has also shown that, given the direct visualization during intubation, the borescope could be used to confirm intubation when capnography fails to show any trace [14]. Other previous studies have shown that the borescope can be mounted over a direct laryngoscope to create a low-cost video laryngoscope [20,21]. In the current study, the tube was mounted over the borescope and a direct laryngoscope was used to lift the tongue, providing a better view and allowing for the tube to be manipulated to improve the view and confirm intubation above the carina level.

Although the view was clearer with the video laryngoscope, as evidenced by the lower incidence of fogging than with the borescope, anesthetists' satisfaction was higher with the borescope than with the video laryngoscope. This could be explained by the advantages of the borescope over the video laryngoscope as an economical, pocket-sized device that requires no battery charging or sophisticated software. Moreover, the fact that the borescope (but not the video laryngoscope) can be navigated behind the vocal cords could increase the anesthetist's confidence regarding correct endotracheal tube placement, in addition to the benefit of examining the airway until the tracheal carina.

One limitation of this study was the anesthetists' initial unfamiliarity with the borescope. However, we overcame this by demonstrating the procedure and requiring the anesthetist to perform two trials on mannequins prior to the performing any intubations on patients. This led to better orientation with the borescope.

In conclusion, the video laryngoscope provided a better view and less fogging than the borescope with comparable intubation time; however, the high price associated with the video laryngoscope limits its availability. Therefore, the borescope is a low-cost, readily available device that can be used for intubating patients with potentially difficult airways. Further studies are needed to confirm the effectiveness of the borescope in other aspects of intubation in emergency settings.

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## Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

## Author Contributions

Mohamed Elshazly (Data curation; Investigation; Methodology; Project administration; Supervision; Writing – review & editing)  
Mark Medhat (Conceptualization; Methodology; Writing – original draft)  
Sahar Marzouk (Supervision; Writing – review & editing)  
Enas M. Samir (Conceptualization; Writing – review & editing)

## Supplementary Material

Supplemental Video 1. A demonstrative video of endotracheal intubation using USB borescope.

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## References

1. Samssoon GL, Young JR. Difficult tracheal intubation: a retrospective study. *Anaesthesia* 1987; 42: 487-90.
2. Mallampati SR. Clinical sign to predict difficult tracheal intubation (hypothesis). *Can Anaesth Soc J* 1983; 30: 316-7.

3. Gonzalez H, Minville V, Delanoue K, Mazerolles M, Concina D, Fourcade O. The importance of increased neck circumference to intubation difficulties in obese patients. *Anesth Analg* 2008; 106: 1132-6.
4. el-Ganzouri AR, McCarthy RJ, Tuman KJ, Tanck EN, Ivankovich AD. Preoperative airway assessment: predictive value of a multivariate risk index. *Anesth Analg* 1996; 82: 1197-204.
5. Shiga T, Wajima Z, Inoue T, Sakamoto A. Predicting difficult intubation in apparently normal patients: a meta-analysis of bedside screening test performance. *Anesthesiology* 2005; 103: 429-37.
6. Vannucci A, Cavallone LF. Bedside predictors of difficult intubation: a systematic review. *Minerva Anestesiol* 2016; 82: 69-83.
7. Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. *Br J Anaesth* 2015; 115: 827-48.
8. Muallem M, Baraka A. Aids for facilitation of difficult tracheal intubation review and recent advances. *Middle East J Anaesthesiol* 2012; 21: 785-91.
9. Gill RL, Jeffrey AS, McNarry AF, Liew GH. The availability of advanced airway equipment and experience with videolaryngoscopy in the UK: two UK surveys. *Anesthesiol Res Pract* 2015; 2015: 152014.
10. Dawson AJ, Marsland C, Baker P, Anderson BJ. Fiberoptic intubation skills among anaesthetists in New Zealand. *Anaesth Intensive Care* 2005; 33: 777-83.
11. Avidan A, Shapira Y, Cohen A, Weissman C, Levin PD. Difficult airway management practice changes after introduction of the GlideScope videolaryngoscope: A retrospective cohort study. *Eur J Anaesthesiol* 2020; 37: 443-50.
12. Moon Y, Oh J, Hyun J, Kim Y, Choi J, Namgoong J, et al. Cost-effective smartphone-based articulable endoscope systems for developing countries: instrument validation study. *JMIR Mhealth Uhealth* 2020; 8: e17057.
13. Sanri E, Akoglu EU, Karacabey S, Verimli U, Akoglu H, Sehirli U, et al. Diagnostic utilities of tracheal ultrasound and USB-endoscope for the confirmation of endotracheal tube placement: a cadaver study. *Am J Emerg Med* 2018; 36: 1943-6.
14. Karippacheril JG, Umesh G, Nanda S. Assessment and confirmation of tracheal intubation when capnography fails: a novel use for an USB camera. *J Clin Monit Comput* 2013; 27: 531-3.
15. Aziz MF, Dillman D, Fu R, Brambrink AM. Comparative effectiveness of the C-MAC video laryngoscope versus direct laryngoscopy in the setting of the predicted difficult airway. *Anesthesiology* 2012; 116: 629-36.
16. Lewis SR, Butler AR, Parker J, Cook TM, Schofield-Robinson OJ,

- Smith AF. Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation: a Cochrane Systematic Review. *Br J Anaesth* 2017; 119: 369-83.
17. Kill C, Risse J, Wallot P, Seidl P, Steinfeldt T, Wulf H. Videolaryngoscopy with glidescope reduces cervical spine movement in patients with unsecured cervical spine. *J Emerg Med* 2013; 44: 750-6.
  18. Adánez Martínez MG, Leal Costa C, García López JA, Torres Ganfornina M, Ramos Morcillo AJ, Hernández Ruipérez T, et al. Perception of level of knowledge, skills, and safety before and after training to perform videolaryngoscopy with the Intubox barrier system for airway management in patients with COVID-19. *Emergencias* 2021; 33: 93-9.
  19. Findik M, Kayipmaz AE, Kavalci C, Sencelikel TS, Muratoglu M, Akcebe A, et al. Why USB-endoscope laryngoscopy is as effective as video laryngoscopy. *Clin Invest Med* 2020; 43: E55-9.
  20. Saha S. A do-it-yourself video laryngoscope for endotracheal intubation of COVID-19 positive patient. *Indian J Anaesth* 2020; 64: 904-5.
  21. Saoraya J, Musikatavorn K, Sereeyotin J. Low-cost videolaryngoscope in response to COVID-19 pandemic. *West J Emerg Med* 2020; 21: 817-8.

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# Microvascular reactivity as a predictor of major adverse events in patients with on-pump cardiac surgery

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**Background:** Microcirculatory disturbances are typically most severe during cardiopulmonary bypass (CPB), which occurs during cardiac surgeries. If microvascular reactivity compensates for microcirculatory disturbances during CPB, tissue hypoxemia can be minimized. The primary aim of this study was to assess whether microvascular reactivity during CPB could predict major adverse events (MAE) after cardiac surgery.

**Methods:** This prospective observational study included 115 patients who underwent elective on-pump cardiac surgeries. A vascular occlusion test (VOT) with near-infrared spectroscopy was performed five times for each patient: before the induction of general anesthesia, 30 min after the induction of general anesthesia, 30 min after applying CPB, 10 min after protamine injection, and post-sternal closure. The postoperative MAE was recorded. The area under the receiver operating characteristic (AUROC) curve analysis was performed for the prediction of MAE using the recovery slope.

**Results:** Of the 109 patients, MAE occurred in 32 (29.4%). The AUROC curve for the recovery slope during CPB was 0.701 ( $P < 0.001$ ; 95% CI [0.606, 0.785]). If the recovery slope during CPB was  $< 1.08\%/s$ , MAE were predicted with a sensitivity of 62.5% and specificity of 72.7%.

**Conclusions:** Our study demonstrated that the recovery slope of the VOT during CPB could predict MAE after cardiac surgery. These results support the idea that disturbances in microcirculation induced by CPB can predict the development of poor clinical outcomes, thereby demonstrating the potential role of microvascular reactivity as an early predictor of MAE after cardiac surgery.

**Keywords:** Cardiac surgical procedures; Cardiopulmonary bypass; Hemodynamics; Microcirculation; Near-infrared spectroscopy; Postoperative complications.

## Introduction

Within the body's circulatory system, the desynchronization between macrocirculation and microcirculation, such that the restoration of systemic circulation does not ensure the restoration of microcirculatory perfusion and oxygenation of the tissues, is called 'mi-



circulatory shock' [1,2]. Numerous studies have shown that microcirculatory shock is significantly associated with poor clinical outcomes in patients with sepsis [3–5]. However, most studies related to microcirculation in cardiac surgeries are insufficient to conclusively establish the associations between microcirculatory dysfunction and clinical outcomes. Notably, some studies have shown a correlation between microcirculatory dysfunction and major adverse events (MAE) such as stroke [6], myocardial infarction (MI) [7], heart failure [8], acute kidney injury (AKI) [9], gastrointestinal (GI) bleeding [10], and acute respiratory distress syndrome (ARDS) [11].

Ample studies have been conducted on microcirculation in patients undergoing cardiac surgeries and sepsis patients, because they are at an increased risk of microcirculatory shock [12,13]. The patients undergoing cardiac surgeries are typically older adults with comorbidities. Cardiac surgery causes systemic inflammation and endothelial dysfunction induced by the production of free radicals and inflammatory mediators, complement activation, and ischemia/reperfusion injuries [4,14]. Excessive transfusions, fluids, and vasopressors can negatively affect microcirculation [15,16].

Cardiopulmonary bypass (CPB)-induced microcirculatory perfusion disturbances have been demonstrated in several studies [13,17]. The observed microcirculatory perfusion disturbance was largely absent in the patients undergoing off-pump surgeries [17]. Another study showed that microcirculatory alterations decreased with time but persisted for > 24 h post on-pump cardiac surgeries [13]. Interestingly, the extent of the microvascular changes seems related to tissue ischemia and correlated with the peak lactate levels post-surgery. This data suggests that impaired microvascular perfusion contributes to organ dysfunction following CPB. The preservation of microcirculatory perfusion may thus improve clinical outcomes.

Therefore, several studies have investigated whether microcirculatory shock in cardiac surgeries correlates with the postoperative outcomes using a vascular occlusion test (VOT) with near-infrared spectroscopy (NIRS) [18–21]. Some studies have found that the recovery slope of VOT (representing the microvascular reactivity) in the intensive care unit (ICU) post-surgery was associated with postoperative outcomes [19,20]. However, predicting the postoperative outcomes as early as possible is beneficial for adopting intraoperative preventive strategies.

We hypothesized that if the microvascular reactivity is preserved during CPB, tissue hypoxemia can be minimized. In contrast, in the patients with disturbed microvascular reactivity during CPB, tissue hypoxemia develops, which may lead to poor clinical outcomes. The primary aim of this study was to assess

whether the microvascular reactivity during CPB can predict MAE post-cardiac surgery. Additionally, the association of these microcirculatory parameters with other postoperative clinical outcomes, including the Sequential Organ Failure Assessment (SOFA) score, Acute Physiologic and Chronic Health Evaluation (APACHE) II score, duration of ventilator care, length of ICU stay, and length of hospital stay, was investigated. Finally, the additional risk factors for MAE after cardiac surgery were investigated.

## Materials and Methods

### Patients

This study was approved by the Institutional Review Board (Pusan National University Hospital, Busan, Republic of Korea, No. 1702-003-051, date of approval 10/02/2017), and written informed consent was obtained from all participants on the day before surgery. This study was conducted in accordance with the ethical principles of the Helsinki Declaration-2013 and followed good clinical practice guidelines. This prospective, observational, single-center study was conducted between February 2017 and May 2019 at a tertiary university hospital. The study adhered to the applicable STROBE statement. Adult patients aged > 18 years who were scheduled for elective on-pump cardiac surgeries were included. The exclusion criteria were pregnancy, the inability to tolerate VOT (e.g., patients with arm deformities, arteriovenous shunts, and burns), or refusal to participate in the study.

### Anesthesia

The standard monitoring for cardiac surgery was performed in the operating room, which consisted of the following: electrocardiography, arterial blood pressure, pulse oximetry, rectal temperature, bispectral index (BIS), cerebral oximetry, pulmonary artery catheterization (PAC), and transesophageal echocardiography. General anesthesia was induced using 1.0–1.5 mg/kg propofol and a continuous infusion of 0.1 µg/kg/min remifentanyl. After the injection of 0.8 mg/kg rocuronium, tracheal intubation was performed, and mechanical ventilation was commenced with an inspired oxygen fraction (FiO<sub>2</sub>) of 0.5, tidal volume of 6–8 ml/kg, and respiratory rate adjusted to maintain an end-tidal CO<sub>2</sub> of 30–35 mmHg. The general anesthesia was maintained using sevoflurane and remifentanyl to sustain a BIS ranging between 40 and 60 during the surgical procedure, including CPB. The hemodynamic parameters were maintained within 20% of the baseline values. A packed red blood cell (pRBC) transfusion was administered to

maintain a hemoglobin level of 8–10 g/dl. Treatments using fresh frozen plasma, cryoprecipitate, and platelets were considered in case of insufficient surgical coagulation following the normalization of activated clotting time (ACT). The decision to administer vasopressors and inotropes was made by the attending physicians based on the hemodynamic status evaluation.

A Sorin Stockert C5 or S5 heart-lung machine with a centrifugal blood pump and heater-cooler device (Sorin Stockert Instrumente GMBH, Germany) was used for bypass with a phosphorylcholine-coated extracorporeal circuit (Phisio, LivaNova, Italy). The non-pulsatile CPB technique was used with a membrane oxygenator primed with 1,000 ml plasma solution, 250 ml 15% mannitol, 40 ml 8.4% sodium bicarbonate, 100 ml 20% albumin, 20 ml 10% magnesium sulfate, 2 g tranexamic acid, 120,000 units Ulinastatin, 1 g methylprednisolone, 5,000 IU bovine heparin, and 1 g cefazolin. CPB was initiated after heparin administration (300 IU/kg), when the target ACT exceeded 480 s. Myocardial protection was achieved using a 4°C Del Nido solution. The pump flow rate was calculated based on the patient's body surface area and subsequently maintained to ensure a mean arterial pressure (MAP) of 60–80 mmHg with mild-to-moderate hypothermia (28–35°C). After weaning from CPB, protamine was administered in a 1 : 1 ratio, in addition to 2 g of tranexamic acid to achieve normal ACT.

In the ICU, patients were sedated with dexmedetomidine and remifentanyl until the following extubation criteria were met: the patient could obey commands, was stable, and had adequate hemodynamics, insignificant arrhythmia, chest tube drainage < 100 ml/h for two consecutive hours, an arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>) < 50 mmHg, arterial partial pressure of oxygen (PaO<sub>2</sub>) ≥ 70 mmHg with FiO<sub>2</sub> ≤ 50%, and urine output ≥ 1 ml/kg/h.

## VOT

The VOT was performed five times in each patient: before the induction of general anesthesia (baseline, T0), 30 min after the induction of general anesthesia (T1), 30 min after application of CPB (T2), 10 min after protamine injection (T3), and after sternal closure (T4). Before the induction of anesthesia, an NIRS sensor (INVOS™ 5100C Cerebral/Somatic Oximeter; Medtronic, USA) was placed on the thenar eminence and an automated tourniquet (A.T.S® 3000 Automatic Tourniquet System; Zimmer Inc., USA) was placed around the upper arm. The arterial catheter was placed in the contralateral radial artery, and the baseline blood pressure was measured. When the baseline tissue oxygen saturation (StO<sub>2</sub>) stabilized, the automatic tourniquet was inflated to 50

mmHg over the patient's baseline systolic blood pressure and maintained for 5 min. After a 5 min ischemic period, the tourniquet deflated rapidly. The StO<sub>2</sub> data was recorded continuously during the VOT procedure. The baseline StO<sub>2</sub>, minimum StO<sub>2</sub> during the 5 min tourniquet inflation, and maximum StO<sub>2</sub> during tourniquet deflation were obtained. The occlusion and recovery slopes were calculated based on the measured StO<sub>2</sub> data. The occlusion slope, related to the oxygen extraction, was defined as the slope of the StO<sub>2</sub> descent to the lowest value. The recovery slope, related to the microvascular reactivity, was calculated from the deflation of the tourniquet until the StO<sub>2</sub> recovery reached the highest value. As the range of StO<sub>2</sub> measurable by the INVOS™ is 15–95%, the occlusion and recovery slope calculations were made using 15% as the lowest value and 95% as the highest value, even when the actual values exceeded this range.

## Intraoperative data collection

All the data was recorded at five distinct time points, as described previously. The hemodynamic data was obtained using standard monitoring. The systemic vascular resistance (SVR) was calculated using the measured MAP, central venous pressure (CVP), and cardiac output (CO) using the following equation:  $SVR = (MAP - CVP) / CO \times 80$ . Arterial blood gas analysis was performed to obtain the PaO<sub>2</sub>, PaCO<sub>2</sub>, hemoglobin, and lactate levels. After weaning from CPB at T3 and T4, the vasoactive-inotropic score (VIS) was calculated as follows: dopamine dose (mg/kg/min) + dobutamine dose (mg/kg/min) + 100 × epinephrine dose (mg/kg/min) + 10 × milrinone dose (mg/kg/min) + 10,000 × vasopressin dose (unit/kg/min) + 100 × norepinephrine dose (mg/kg/min) [22]. Post-CPB vasoplegia was defined as MAP < 65 mmHg with a cardiac index > 2.2 L/kg/m<sup>2</sup> and SVR < 800 dyne/s/cm<sup>5</sup> [23].

## Postoperative outcomes

The SOFA and APACHE II scores were assessed in the ICU. Both were calculated within 24 h after ICU admission, and the SOFA score was calculated daily until ICU discharge. Additionally, the duration of ventilator care, ICU stay, and hospital stay were recorded. All postoperative MAE within 30 days post-surgery were recorded. The patients were routinely scheduled to visit the clinic two weeks post-discharge and instructed to visit the emergency center at the occurrence of any MAE. The MAE included death, aggravated heart failure, MI, AKI, stroke or seizure, ARDS, and GI bleeding. Aggravated heart failure was defined as an increase in the functional class or left ventricular ejection fraction of

< 35%. MI was defined by elevated cardiac troponin (cTn) values > 10 × 99th percentile upper reference limit (URL) in patients with normal baseline cTn values (< 99th percentile URL), in addition to either: (a) new pathological Q waves or new left bundle branch block, (b) angiography-documented new graft or new native coronary artery occlusion, or (c) imaging evidence of recent loss of viable myocardium or new regional wall motion abnormalities [24]. AKI was defined in accordance with the Kidney Disease Improving Global Outcomes definition, i.e., 0.3 mg/dl increase in serum creatinine over 48 h or 1.5 times higher than the baseline value within 7 days post-surgery [25]. ARDS was defined as the  $\text{PaO}_2/\text{FiO}_2 \leq 300$  mmHg with a positive end-expiratory pressure or continuous positive airway pressure  $\geq 5$  cmH<sub>2</sub>O. These pressures were associated with bilateral opacities on chest imaging, not fully explained by effusions and lobar/lung collapse or nodules and not fully explained by cardiac failure or fluid overload [26].

## Statistical analysis

The primary outcome of this study was the predictive value of the recovery slope of VOT during CPB. Based on our pilot study consisting of 20 patients before enrollment, three patients had MAE (15%), and the area under the receiver operating characteristic (AUROC) curve was 0.723. A power calculation determined a sample size of 104 patients with two-sided  $\alpha$  risk of 5%,  $\beta$  risk of 20%, and positive/negative ratio of 5.5. Considering the dropout rate of 10%, 115 patients were required for the study.

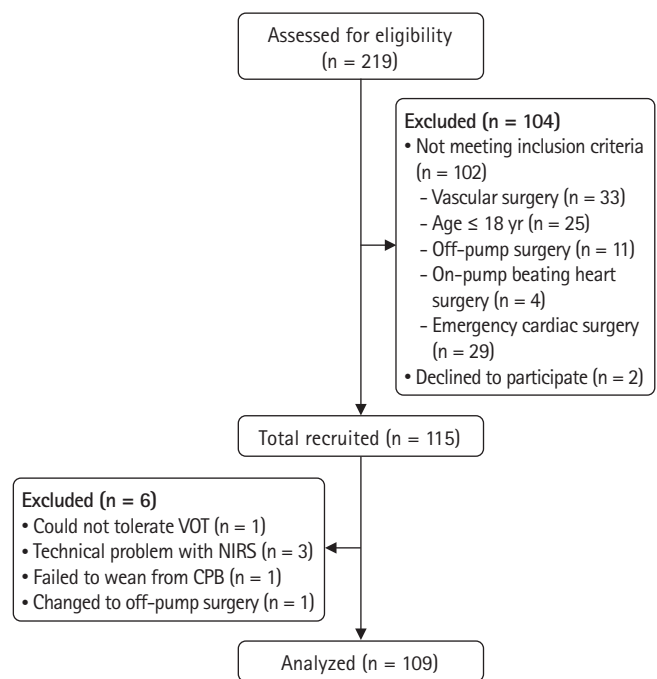
The data is expressed as frequencies (%), median (Q1, Q3), or mean  $\pm$  SD. All the continuous variables were tested for normality using a Q-Q plot and Kolmogorov-Smirnov test. Continuous variables were compared using independent t-tests or Mann-Whitney *U* tests. Categorical variables were compared using the chi-squared or Fisher's exact tests. The intraoperative VOT, hemodynamic, and laboratory data were compared using two-way repeated-measures analysis of variance (ANOVA). For the intra-subject factor analysis, either ANOVA or Friedman analysis was performed. For *post hoc* tests of inter-subject factors, the Bonferroni correction was used. Appropriate adjustments for Bonferroni correction are stated in the tables with multiple P value comparisons.

The patients were divided according to post-surgery MAE. The VOT variables that were significantly different between the two groups were tested for accuracy of predicting MAE using the ROC curve with a 95% CI. The AUROC was compared using a method previously used by DeLong et al. [27]. The optimal cutoff value was selected to maximize the Youden index. Patients were

divided according to the optimal cutoff. The incidence of post-CPB vasoplegia and postoperative outcomes were compared. The association between the occurrences of MAE was analyzed using univariate and multivariate logistic regression analyses. The factors significantly associated with MAE were selected for the univariate analysis ( $P < 0.05$ ). The Spearman's correlation coefficients were computed to evaluate collinearity ( $r > 0.7$ ). If correlation was found between the variables, the ones most relevant from a clinical perspective were chosen. The candidate variables were entered into a forward stepwise multivariate logistic regression model. The model was evaluated using a  $-2$  log-likelihood ratio, Nagelkerke R<sup>2</sup>, Hosmer-Lemeshow test, and predicted probabilities. Statistical significance was set at  $P < 0.05$ . The data analyses were performed using MedCalc® Statistical Software version 19.5.3 (MedCalc Software Ltd., Ostend, Belgium) and SPSS statistics software (IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY, USA).

## Results

Of the 219 eligible patients, 115 were included in the study. Six patients were excluded for the following reasons: could not tolerate the VOT ( $n = 1$ ), technical problems with NIRS ( $n = 3$ ), failed weaning from CPB ( $n = 1$ ), and changed to off-pump surgery ( $n = 1$ ) (Fig. 1). The patient demographics and intraopera-



**Fig. 1.** A CONSORT flow diagram. VOT: vascular occlusion test, NIRS: near-infrared spectroscopy, CPB: cardiopulmonary bypass.

**Table 1.** A Summary of the Patient Demographics and Intraoperative Characteristics

Variable	Total (n = 109)	Patients with MAE (n = 32)	Patients without MAE (n = 77)	P value
Age (yr)	63.7 ± 11.2	66.6 ± 8.9	62.6 ± 11.9	0.086
Sex (Male)	74 (67.9)	19 (59.4)	55 (71.4)	0.220
Height (cm)	162.2 ± 8.6	160.5 ± 9.2	163.0 ± 8.2	0.167
Weight (kg)	63.1 ± 12.0	61.4 ± 12.4	63.8 ± 11.9	0.333
BMI (kg/m <sup>2</sup> )	24.1 ± 3.6	23.9 ± 3.6	24.2 ± 3.6	0.679
BSA (m <sup>2</sup> )	1.7 ± 0.2	1.64 ± 0.19	1.68 ± 0.18	0.238
ASA classification				0.141
II	8 (7.3)	0 (0)	8 (10.4)	
III	99 (90.8)	31 (96.9)	68 (88.3)	
IV	2 (1.8)	1 (3.1)	1 (1.3)	
Smoker	29 (26.6)	7 (21.9)	22 (28.6)	0.471
Type of surgery				0.023
CABG	37 (33.9)	6 (18.8)	31 (40.3)	
Valvular surgery	61 (56.0)	24 (75.0)	37 (48.1)	
CABG + Valvular surgery	1 (0.9)	1 (3.1)	0 (0)	
ASD closure	7 (6.4)	0 (0)	7 (9.1)	
Myxoma removal	3 (2.8)	1 (3.1)	2 (2.6)	
Comorbidities				
Hypertension	72 (66.1)	26 (81.3)	46 (59.7)	0.031
Diabetes mellitus	37 (33.9)	14 (43.8)	23 (29.9)	0.163
Stroke	7 (6.4)	4 (12.5)	3 (3.9)	0.191
Congestive heart failure	4 (3.7)	2 (6.3)	2 (2.6)	0.579
Chronic kidney disease	8 (7.3)	5 (15.6)	3 (3.9)	0.046
Chronic obstructive pulmonary disease	7 (6.4)	2 (6.3)	5 (6.5)	1.000
EuroSCORE II	3.6 (2.4, 4.7)	3.4 (2.3, 7.5)	1.8 (0.9, 2.4)	< 0.001
Surgery time (min)	346.2 (331.1, 361.4)	380 (322.5, 437.5)	330 (280.0, 385.0)	0.005
Anesthesia time (min)	397.7 (382.2, 413.2)	435 (36.0, 480.0)	390 (345.0, 420.0)	0.029
Cardiopulmonary bypass time (min)	135 (105.0, 160.0)	170 (127.0, 229.0)	125 (105.0, 145.0)	< 0.001
Aortic cross clamping time (min)	100 (74.5, 120.0)	120 (79.0, 165.0)	90 (73.0, 113.0)	0.023
Transfusion				
Red blood cell (unit)	4 (2, 6)	5.0 (4.0, 6.0)	3.0 (2.0, 5.0)	< 0.001
Fresh frozen plasma (unit)	3 (2, 3)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	0.575
Platelet (unit)	8 (8, 8)	8.0 (8.0, 8.0)	8.0 (8.0, 8.0)	0.079
Cryoprecipitate (unit)	6 (6, 6)	6.0 (6.0, 6.0)	6.0 (6.0, 6.0)	0.059
Infused crystalloid (ml)	2700 (2100.0, 3500.0)	3000 (2200.0, 3630.0)	2700 (2000.0, 3300.0)	0.307
Urine output (ml)	1300 (947.0, 1720.0)	1000 (820.0, 1345.0)	1370 (1130.0, 1820.0)	0.001
VIS at T3	12.0 (8.0, 20.0)	20.0 (10.0, 24.0)	12.0 (6.0, 16.0)	< 0.001
VIS at T4	12.0 (6.0, 20.5)	20.0 (11.0, 27.0)	10.0 (4.0, 18.0)	0.002
Post-CPB vasoplegia	36 (33.0)	17 (53.1)	19 (24.7)	0.004

Values are presented as mean ± SD, mean (95% CI), and frequency (%). BMI: body mass index, BSA: body surface area, ASA: American Society of Anesthesiologists, CABG: coronary artery bypass graft, ASD: atrial septal defect, MAE: major adverse events, VIS: vasoactive-inotropic score, T3: 10 min after protamine injection, T4: after sternal closure.

tive characteristics are summarized in [Table 1](#). Of the 109 patients, MAE occurred in 32 (29.4%). The patients who experienced MAE underwent valvular surgery more frequently. Hypertension and chronic kidney disease were more common, and the Euro-

SCORE II was significantly higher in the patients with MAE. The surgery durations, anesthesia, CPB, and aortic cross-clamping were significantly longer in the patients with MAE. Additional pRBC transfusions were required, and the urine output was low-



er in patients with MAE. After weaning from CPB, more vaso-pressors and inotropes were administered. Additionally, post-CPB vasoplegia developed more frequently in the patients with MAE.

The hemodynamic and laboratory data are presented in [Supplementary Table 1](#). Baseline hemoglobin and lactate levels were significantly lower in the patients with MAE. The MAP decreased after CPB application, and the HR, CI, and serum lactate levels increased after weaning from CPB. The SVR decreased significantly after weaning from CPB. The rectal temperature was markedly lower and PaO<sub>2</sub> was markedly higher during CPB. [Table 2](#) summarizes the VOT variables at the five specified time points. The MAE were as follows: death (3.7%), aggravated heart failure (4.6%), MI (1.8%), AKI (22.9%), stroke or seizure (4.6%),

ARDS (1.8%), and GI bleeding (1.0%). Most MAE developed within 7 days post-cardiac surgery. Nearly 30 days after surgery, one case of aggravated heart failure and two cases of death occurred.

For the primary outcome, the AUROC of the VOT variables for predicting the post-surgery MAE has been presented in [Table 3](#). The AUROC for the recovery slope during CPB was 0.701 (P < 0.001; 95% CI [0.606, 0.785]). If the recovery slope during CPB was ≤ 1.08%/s, MAE were predicted with a sensitivity of 62.5% and specificity of 72.7%. The AUROC of the recovery slope during CPB was not significantly different from other AUROC associated with the other VOT variables.

The patients were divided according to the cutoff value of the recovery slope during CPB, and the incidences of post-CPB vaso-

**Table 2.** The Vascular Occlusion Test Variables

Parameter	Total (n = 109)	Patients with MAE (n = 32)	Patients without MAE (n = 77)	P value
Baseline StO <sub>2</sub> (%)				
T0	56.0 (48.0, 65.0)	52.0 (44.0, 63.0)	59.0 (52.0, 66.0)	0.014
T1	54.0 (48.5, 62.0)	51.0 (46.5, 57.5)	55.0 (50.0, 64.0)	0.056
T2	64.0 (52.5, 72.0)* <sup>†</sup>	62.0 (49.0, 68.5) <sup>†</sup>	66.0 (54.0, 74.0)* <sup>†</sup>	0.086
T3	71.0 (64.0, 82.0)* <sup>†‡</sup>	70.0 (62.0, 78.5)* <sup>†‡</sup>	74.0 (65.0, 85.0)* <sup>†‡</sup>	0.120
T4	72.0 (64.0, 81.0)* <sup>†‡</sup>	74.0 (65.5, 82.0)* <sup>†‡</sup>	71.0 (62.0, 81.0)* <sup>†‡§</sup>	0.670
Occlusion slope (%/s)				
T0	0.20 (0.15, 0.25)	0.20 (0.15, 0.24)	0.20 (0.15, 0.25)	0.926
T1	0.18 (0.13, 0.23)*	0.16 (0.09, 0.21)	0.18 (0.13, 0.23)*	0.188
T2	0.17 (0.12, 0.22)*	0.15 (0.09, 0.21)	0.19 (0.12, 0.23)	0.034
T3	0.24 (0.16, 0.30) <sup>†‡</sup>	0.20 (0.13, 0.28) <sup>†‡</sup>	0.25 (0.16, 0.30)* <sup>†‡</sup>	0.421
T4	0.23 (0.16, 0.29)	0.19 (0.15, 0.29) <sup>†‡</sup>	0.24 (0.16, 0.30)	0.309
Minimum StO <sub>2</sub> (%)				
T0	15.0 (15.0, 15.0)	15.0 (15.0, 15.0)	15.0 (15.0, 16.0)	0.471
T1	15.0 (15.0, 21.5)	15.0 (15.0, 20.3)	15.0 (15.0, 22.0)	0.919
T2	15.0 (15.0, 25.0)*	17.0 (15.0, 30.0)*	15.0 (15.0, 24.0)	0.067
T3	15.0 (15.0, 23.0)*	15.0 (15.0, 26.8)	15.0 (15.0, 22.5)	0.651
T4	15.0 (15.0, 21.5)	15.0 (15.0, 28.5)*	15.0 (15.0, 19.5)	0.246
Recovery slope (%/s)				
T0	2.96 (2.17, 3.60)	3.02 (2.14, 3.45)	2.96 (2.19, 3.81)	0.272
T1	2.32 (1.82, 2.86)*	2.03 (1.61, 2.51)*	2.50 (1.90, 2.94)*	0.006
T2	1.23 (0.97, 1.91)* <sup>†</sup>	1.01 (0.69, 1.44)* <sup>†</sup>	1.48 (1.03, 2.00)* <sup>†</sup>	0.001 <sup>II</sup>
T3	1.42 (1.02, 1.96)* <sup>†</sup>	1.11 (0.72, 1.46)* <sup>†</sup>	1.54 (1.08, 2.13)* <sup>†</sup>	0.001 <sup>II</sup>
T4	1.57 (1.06, 2.16)* <sup>†‡§</sup>	1.44 (0.91, 1.75)* <sup>†‡§</sup>	1.63 (1.15, 2.46)* <sup>†‡§</sup>	0.024
Maximum StO <sub>2</sub> (%)				
T0	85.0 (78.0, 90.0)	80.5 (70.8, 86.3)	87.0 (80.0, 93.3)	0.001 <sup>II</sup>
T1	88.0 (82.0, 95.0)*	84.0 (76.0, 88.0)*	91.0 (84.5, 95.0)*	< 0.001 <sup>II</sup>
T2	87.0 (79.5, 94.0)	80.0 (73.8, 87.3)	90.0 (83.0, 94.0)	0.001 <sup>II</sup>
T3	89.0 (82.0, 95.0)*	82.0 (79.8, 89.0)	92.0 (87.0, 95.0)*	0.009 <sup>II</sup>
T4	90.0 (83.0, 95.0)* <sup>†</sup>	87.5 (79.8, 92.3)*	92.5 (86.0, 95.0)	< 0.001 <sup>II</sup>

Values are presented as median (Q1, Q3). \*P < 0.05 compared to T0; <sup>†</sup>P < 0.05, compared to T1; <sup>‡</sup>P < 0.05, compared to T2; <sup>§</sup>P < 0.05, compared to T3. <sup>II</sup>P < 0.010 indicates a significant difference between the patients with and without MAE following the Bonferroni correction. T0: prior to anesthesia induction, T1: 30 min post-anesthesia induction, T2: 30 min after CPB initiation, T3: 10 min post-protamine injection, T4: after sternal closure, MAE: major adverse events, StO<sub>2</sub>: tissue oxygen saturation.

**Table 3.** The ROC Curve Analysis for the Prediction of MAE after Surgery

Variable	AUC	95% CI	P value	Threshold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Recovery slope at T1	0.668	0.572, 0.756	0.002	≤ 2.26	68.8	61.0	42.4	82.4
Recovery slope at T2	0.701	0.606, 0.785	< 0.001	≤ 1.08	62.5	72.7	48.8	82.4
Recovery slope at T3	0.705	0.610, 0.788	< 0.001	≤ 1.54	84.4	50.7	41.5	88.6
Recovery slope at T4	0.637	0.540, 0.727	0.013	≤ 1.89	90.6	36.4	37.2	90.3
Maximum StO <sub>2</sub> at T0	0.707	0.612, 0.790	< 0.001	≤ 88	90.6	45.5	40.9	92.1
Maximum StO <sub>2</sub> at T1	0.713	0.619, 0.796	< 0.001	≤ 88	78.1	62.3	46.3	87.3
Maximum StO <sub>2</sub> at T2	0.697	0.601, 0.782	< 0.001	≤ 86	71.9	67.1	47.6	81.1
Maximum StO <sub>2</sub> at T3	0.721	0.627, 0.803	< 0.001	≤ 87	68.8	71.1	49.7	84.5
Maximum StO <sub>2</sub> at T4	0.658	0.561, 0.746	0.003	≤ 93	87.5	42.9	38.9	89.2

ROC: receiver operating characteristic, AUC: area under the curve, PPV: positive predictive value, NPV: negative predictive value, T0: prior to anesthesia induction, T1: 30 min post-anesthesia induction, T2: 30 min after cardiopulmonary bypass initiation, T3: 10 min post-protamine injection, T4: after sternal closure, StO<sub>2</sub>: tissue oxygen saturation.

**Table 4.** Post-CPB Vasoplegia and Postoperative Outcomes

Variable	Total (n = 109)	Recovery slope at T2		P value
		≤ 1.08 (n = 40)	> 1.08 (n = 69)	
Post-CPB vasoplegia	36 (33.0)	14 (35.0)	22 (31.9)	0.739
Initial SOFA	5.0 (4.0, 7.0)	6.0 (4.3, 7.0)	5.0 (4.0, 6.0)	0.105
Maximum SOFA	6.0 (4.0, 7.0)	6.0 (4.3, 8.0)	5.0 (4.0, 6.5)	0.047
APACHE II	14.0 (11.0, 17.0)	14.5 (11.0, 17.8)	12.0 (11.0, 16.5)	0.654
Duration of ventilator care (days)	2.0 (2.0, 2.0)	2.0 (2.0, 2.0)	2.0 (2.0, 2.0)	0.008
Length of ICU stay (days)	3.0 (3.0, 4.0)	3.0 (3.0, 5.8)	3.0 (3.0, 4.0)	0.111
Length of hospital stay (days)	20 (15, 28)	20.5 (15.0, 27.0)	19.0 (15.0, 28.5)	0.669
Major adverse events		19 (47.5)	13 (18.8)	0.002
Death	4 (3.7)	3 (7.5)	0 (0)	0.139
Aggravated heart failure	5 (4.6)	3 (7.5)	2 (2.9)	0.354
Myocardial infarction	2 (1.8)	1 (2.5)	1 (1.4)	1.000
Acute kidney injury	25 (22.9)	15 (37.5)	10 (14.5)	0.006
Stroke or seizure	5 (4.6)	2 (5.0)	3 (4.3)	1.000
ARDS	2 (1.8)	1 (2.5)	1 (1.4)	1.000
Gastrointestinal bleeding	1 (1.0)	1 (1.6)	0(0)	1.000

Values are presented as mean ± SD, mean (95% CI), and frequency (%). T2: 30 min after CPB initiation, CPB: cardiopulmonary bypass, SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiologic and Chronic Health Evaluation, ICU: intensive care unit, ARDS: acute respiratory distress syndrome.

plegia and postoperative outcomes were compared (Table 4). The patients with a recovery slope < 1.08%/s during CPB had a higher maximum SOFA score and longer duration of ventilator care. MAE, particularly postoperative AKI, developed more frequently in the patients with lower recovery slopes during CPB.

As shown in Table 5, we identified the risk factors for post-cardiac surgery MAE using logistic regression analysis. The P value of the Hosmer–Lemeshow test of the model was 0.676. The model had –2 log-likelihood of 77.1, Nagelkerke R<sup>2</sup> of 0.564, and predicted probabilities of 85.3%. According to the multivariate analysis, the independent risk factors for MAE were hemoglobin at T1 (odds ratio [OR]: 0.604, 95% CI [0.433, 0.842], P = 0.003), CPB duration (OR: 1.022, 95% CI [1.007, 1.038], P = 0.005), in-

traoperative urine output × 0.1 (OR: 0.988, 95% CI [0.978, 0.998], P = 0.015), VIS at T3 (OR: 1.097, 95% CI [0.978, 0.998], P = 0.012), and recovery slope at T2 (OR: 0.220, 95% CI [0.076, 0.635], P = 0.005).

## Discussion

This study found that the microvascular reactivity during CPB could be a predictive factor for the occurrence of postoperative MAE. Patients with recovery slopes ≤ 1.08%/s during CPB had higher maximum SOFA scores in the ICU and longer durations of ventilator care. Additionally, MAE developed more frequently in these patients.

**Table 5.** The Univariate and Multivariate Logistic Regression Analysis of Variables Associated with MAE after Cardiac Surgery

Variable	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Hemoglobin at T1 (g/dl)	0.659 (0.506, 0.859)	0.002	0.604 (0.433, 0.842)	0.003
Surgery (CABG)				
Valvular surgery	3.243 (1.297, 8.111)	0.012		
CABG + valvular surgery				
ASD closure				
Myxoma removal				
Comorbidities				
Hypertension	2.920 (1.077, 7.920)	0.035		
CKD	4.568 (1.022, 20.425)	0.047		
Surgery time	1.009 (1.003, 1.015)	0.003		
CPB time (min)	1.018 (1.001, 1.028)	< 0.001	1.022 (1.007, 1.038)	0.005
Intraoperative RBC transfusion	1.409 (1.139, 1.742)	0.002		
Intraoperative urine output/10 (ml)	0.991 (0.984, 0.999)	0.022	0.988 (0.978, 0.998)	0.015
VIS at T3	1.083 (1.033, 1.135)	< 0.001	1.097 (0.978, 0.998)	0.012
Recovery slope at T2 (%/s)	0.322 (0.152, 0.683)	0.003	0.220 (0.076, 0.635)	0.005

Values are presented as mean (95% CI). MAE: major adverse event, T1: 30 min post-anesthesia induction, CABG: coronary artery bypass graft, ASD: atrial septal defect, CKD: chronic kidney disease, CPB: cardiopulmonary bypass, RBC: red blood cell, VIS: vasoactive-inotropic score, T2: 30 min after CPB initiation, T3: 10 min post-protamine injection.

Only one previous study investigated the predictive value of VOT variables during CPB for postoperative outcomes, such as the length of ICU stay and SOFA scores, and reported negative results [18]. However, since they only analyzed 40 patients, the study may have lacked sufficient statistical power. Moreover, VOT was performed using the StO<sub>2</sub>-targeted method, wherein the cuff was deflated upon reaching 40% of the baseline. We used the 5 min time-targeted VOT method, wherein most patients reached StO<sub>2</sub> values of 15%, the lowest possible value measurably by INVOS™. The difference in the recovery slopes between patients with and without MAE was significant in our study because smaller minimum StO<sub>2</sub> values after ischemia result in more defined recovery slopes [28,29].

Other studies have performed VOT at the end of surgery or after ICU admissions [19–21]. The reason for the inconsistent results might be the timing at which the VOT was performed. Microcirculatory alterations occur most severely during CPB via complex mechanisms, including hemodilution, production of free radicals, hypothermia, low flow, low pressure, non-pulsatile perfusion, and ischemia/reperfusion injuries [30,31]. However, the microcirculatory system has microvascular reactivity to recruit capillary reserves, wherein 70% of the capillaries can be opened under stress conditions [32,33]. If the patient has sufficient microvascular reactivity to compensate for the microcirculatory alterations induced by CPB, tissue hypoxemia would be minimized. If not, the tissue hypoxemia progresses, leading to poor clinical outcomes. Another reason the recovery slope during the CPB period

was chosen as the primary outcome was the difference in perfusion pressure or oxygen delivery, which might influence the VOT parameters, making it easier to observe true microvascular reactivity.

In our study, the microcirculatory alterations progressively deteriorated from the induction of anesthesia until the CPB period, following a slow recovery after weaning from CPB. The differences in the VOT recovery slopes between patients with and without MAE might be progressively smaller, as the microcirculatory alterations are restored after weaning from CPB. Similarly, the AUROC for MAE predictions of the recovery slope at T4 was 0.637, which was less accurate than that of T2 or T3. No significant differences were seen in the AUROCs between them, and the specific point wherein the microvascular reactivity was the best MAE predictor could not be pinpointed.

Another notable point in this study was that the maximum StO<sub>2</sub> values differed significantly between the patients with and without MAE throughout the study period. The maximum StO<sub>2</sub> reveals hyperemic areas, which are also representative of microvascular reactivity. However, the maximum StO<sub>2</sub> value was 95% in most cases, which is the upper limit of the INVOS™ measurement range [34]. Because of this ‘ceiling effect,’ the level of hyperoxygenation remained uncertain, potentially limiting the reliability of microvascular reactivity assessment. On the other hand, the recovery slope more accurately reflects the microvascular reactivity as compared to the maximum StO<sub>2</sub> value, because the maximum StO<sub>2</sub> is divided by the time taken regardless of a ceil-

ing effect.

The knowledge and prediction of the postoperative outcomes is best obtained as early as possible to ensure the application of appropriate pre- or intraoperative preventive strategies. Moreover, the preventive strategies should be applied to select patients. Unfortunately, till date, the strategies to protect microcirculation are still under debate, with insufficient clinical evidence. Therefore, even if the prediction of postoperative outcomes is possible at early stages, there is currently a limit to improving the postoperative outcomes. Rather, accurate hemodynamic therapy for microcirculation protection, including precise fluid resuscitation and adjustment of organ perfusion pressure should be applied [35]. Importantly, they must be guided by microcirculatory monitoring, such as NIRS, side-stream or incident dark-field imaging, or peripheral perfusion index [35,36]. Additionally, the implementation of preventive strategies is desirable only in the high-risk groups. Implementing the preventive strategies in all patients is not feasible because the necessary tests or treatments can be delayed and are cost intensive.

Post-CPB vasoplegia is a common complication of on-pump cardiac surgery, with an estimated incidence of 5–25% [37]. Inflammatory mediators released during cardiac surgery result in the derangement of vascular reactivity [38]. A recent study showed that endothelial glycocalyx alterations after CPB were associated with postoperative vasoplegia in the CBP-treated patients [39]. In our study, the patients with MAE experienced post-CPB vasoplegia more frequently. The incidence of post-CPB vasoplegia did not differ between the patients with recovery slopes slope  $\leq 1.08\%/s$  at T2, which may be partially explained by the limited statistical power of the study.

In addition to the recovery slope at T2, additional factors like the hemoglobin at T1, duration of CPB, VIS at T3, and intraoperative urine output were also selected as risk factors for MAE in the multivariate regression model. Preoperative anemia is a well-known risk factor for postoperative complications in cardiac surgery [40]. Anemia may compromise the oxygen delivery, leading to tissue hypoxemia and increased pRBC transfusion, also an independent risk factor [41]. A longer CPB duration leads to longer exposure to inflammatory mediators, longer tissue hypoperfusion, higher risk of coagulopathy, and requirement for transfusion support [42]. A previous study showed that intraoperative inotropic therapy is associated with increased mortality and major postoperative morbidity after cardiac surgery [43]. The higher VIS after weaning from CPB may be related to the higher incidence of post-CPB vasoplegia in our study. A few studies have demonstrated that the urine output during CPB is associated with CSA-AKI [44]. In our study, only three patients had oliguria. Therefore, the

clinical influence of intraoperative urine output on postoperative MAE remains unclear.

There are some limitations of the interpretation of our study results. First, INVOS™ was used to perform the VOT in our study. Our results are not comparable to those of previous studies that used InSpectra™ because of inter-device differences [34]. The baseline StO<sub>2</sub> value was lower, and the recovery and occlusion slopes during VOT were faster on INVOS™ than on InSpectra™. Second, the VOT was performed only once at the beginning of the CPB period. According to previous studies, the recovery slope progressively decreases during CPB and starts to increase after weaning from CPB [18,45]. In our study, the recovery slope at 10 min post-protamine injection was also a reliable predictor for MAE development. However, we assume that the VOT variables at this time point should be interpreted cautiously because the protamine may affect microcirculatory reactivity. Considering that microcirculatory disturbances may occur most severely during the CPB period, we cannot exclude the possibility that the recovery slope measured at the end of the CPB period may have been a better predictor.

In conclusion, our study demonstrated that the recovery slope of VOT during CPB could predict the occurrence of MAE post-cardiac surgery. Additionally, the patients with a lower recovery slope during CPB had higher SOFA scores and longer durations of ventilator care. These results support those of previous studies that showed that the disturbances in microcirculation induced by CPB can predict poor clinical outcomes. Furthermore, the results highlight the potential role of microvascular reactivity as an early predictor of MAE after cardiac surgery.

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## Conflicts of Interest

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## Supplementary Material

Supplementary Table 1. Hemodynamic and laboratory variables

## References

1. Kanoore Edul VS, Ince C, Dubin A. What is microcirculatory shock? *Curr Opin Crit Care* 2015; 2: 245-52.
2. Kara A, Akin S, Ince C. Monitoring microcirculation in critical illness. *Curr Opin Crit Care* 2016; 22: 444-52.
3. van Genderen ME, Lima A, Akkerhuis M, Bakker J, van Bommel J. Persistent peripheral and microcirculatory perfusion alterations after out-of-hospital cardiac arrest are associated with poor survival. *Crit Care Med* 2012; 40: 2287-94.
4. De Backer D, Donadello K, Sakr Y, Ospina-Tascon G, Salgado D, Scolletta S, et al. Microcirculatory alterations in patients with severe sepsis: impact of time of assessment and relationship with outcome. *Crit Care Med* 2013; 41: 791-9.
5. Vellinga NA, Boerma EC, Koopmans M, Donati A, Dubin A, Shapiro NI, et al. International study on microcirculatory shock occurrence in acutely ill patients. *Crit Care Med* 2015; 43: 48-56.
6. Pérez-Bárcena J, Goedhart P, Ibáñez J, Brell M, García R, Llinás P, et al. Direct observation of human microcirculation during decompressive craniectomy after stroke. *Crit Care Med* 2011; 39: 1126-9.
7. Wijntjens GW, Fengler K, Fuernau G, Jung C, den Uil C, Akin S, et al. Prognostic implications of microcirculatory perfusion versus macrocirculatory perfusion in cardiogenic shock: a CUL-PRIT-SHOCK substudy. *Eur Heart J Acute Cardiovasc Care* 2020; 9: 108-19.
8. De Backer D, Creteur J, Dubois MJ, Sakr Y, Vincent JL. Microvascular alterations in patients with acute severe heart failure and cardiogenic shock. *Am Heart J* 2004; 147: 91-9.
9. Le Dorze M, Legrand M, Payen D, Ince C. The role of the microcirculation in acute kidney injury. *Curr Opin Crit Care* 2009; 15: 503-8.
10. Tarnawski AS, Ahluwalia A, Jones MK. The mechanisms of gastric mucosal injury: focus on microvascular endothelium as a key target. *Curr Med Chem* 2012; 19: 4-15.
11. Orbegozo Cortés D, Rahmania L, Irazabal M, Santacruz C, Fontana V, De Backer D, et al. Microvascular reactivity is altered early in patients with acute respiratory distress syndrome. *Respir Res* 2016; 17: 59.
12. Koning NJ, Atasever B, Vonk AB, Boer C. Changes in microcirculatory perfusion and oxygenation during cardiac surgery with or without cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 2014; 28: 1331-40.
13. De Backer D, Dubois MJ, Schmartz D, Koch M, Ducart A, Barvais L, et al. Microcirculatory alterations in cardiac surgery: effects of cardiopulmonary bypass and anesthesia. *Ann Thorac Surg* 2009; 88: 1396-403.
14. Dekker NA, Veerhoek D, Koning NJ, van Leeuwen AL, Elbers PW, van den Brom CE, et al. Postoperative microcirculatory perfusion and endothelial glycocalyx shedding following cardiac surgery with cardiopulmonary bypass. *Anaesthesia* 2019; 74: 609-18.
15. Dubin A, Pozo MO, Casabella CA, Pálizas F Jr, Murias G, Moiseinco MC, et al. Increasing arterial blood pressure with norepinephrine does not improve microcirculatory blood flow: a prospective study. *Crit Care* 2009; 13: R92.
16. Tanaka S, Escudier E, Hamada S, Harrois A, Leblanc PE, Vicaut E, et al. Effect of RBC transfusion on sublingual microcirculation in hemorrhagic shock patients: a pilot study. *Crit Care Med* 2017; 45: e154-60.
17. Koning NJ, Vonk AB, Meesters MI, Oomens T, Verkaik M, Jansen EK, et al. Microcirculatory perfusion is preserved during off-pump but not on-pump cardiac surgery. *J Cardiothorac Vasc*

- Anesth 2014; 28: 336-41.
18. Morel J, Bouchet JB, Vola M, Béraud AM, Clerc M, Awad S, et al. Tissue near infra red spectroscopy change is not correlated with patients' outcome in elective cardiac surgery. *Acta Anaesthesiol Scand* 2014; 58: 835-42.
  19. Butler E, Mahendran S, Nguyen J, Aneman A. Microvascular reactivity, assessed by near-infrared spectroscopy and a vascular occlusion test, is associated with patient outcomes following cardiac surgery: a prospective observational study. *Eur J Anaesthesiol* 2018; 35: 356-64.
  20. Kim TK, Cho YJ, Min JJ, Murkin JM, Bahk JH, Hong DM, et al. Microvascular reactivity and clinical outcomes in cardiac surgery. *Crit Care* 2015; 19: 316.
  21. Scolletta S, Franchi F, Damiani E, Cennamo A, Domizi R, Meola A, et al. Tissue oxygen saturation changes and postoperative complications in cardiac surgery: a prospective observational study. *BMC Anesthesiol* 2019; 19: 229.
  22. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med* 2010; 11: 234-8.
  23. Dayan V, Cal R, Giangrossi F. Risk factors for vasoplegia after cardiac surgery: a meta-analysis. *Interact Cardiovasc Thorac Surg* 2019; 28: 838-44.
  24. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. *Eur Heart J* 2012; 33: 2551-67.
  25. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012; 120: c179-84.
  26. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012; 307: 2526-33.
  27. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988; 44: 837-45.
  28. Lipcsey M, Eastwood GM, Woinarski NC, Bellomo R. Near-infrared spectroscopy of the thenar eminence: comparison of dynamic testing protocols. *Crit Care Resusc* 2012; 14: 142-7.
  29. Iannetta D, Inglis EC, Soares RN, McLay KM, Pogliaghi S, Murias JM; CAPES scholarship holder. Reliability of microvascular responsiveness measures derived from near-infrared spectroscopy across a variety of ischemic periods in young and older individuals. *Microvasc Res* 2019; 122: 117-24.
  30. Wan S, LeClerc JL, Vincent JL. Inflammatory response to cardiopulmonary bypass: mechanisms involved and possible therapeutic strategies. *Chest* 1997; 112: 676-92.
  31. Laffey JG, Boylan JF, Cheng DC. The systemic inflammatory response to cardiac surgery: implications for the anesthesiologist. *Anesthesiology* 2002; 97: 215-52.
  32. Chade AR. Renal vascular structure and rarefaction. *Compr Physiol* 2013; 3: 817-31.
  33. Levy BI, Schiffrin EL, Mourad JJ, Agostini D, Vicaut E, Safar ME, et al. Impaired tissue perfusion: a pathology common to hypertension, obesity, and diabetes mellitus. *Circulation* 2008; 118: 968-76.
  34. Lee JH, Park YH, Kim HS, Kim JT. Comparison of two devices using near-infrared spectroscopy for the measurement of tissue oxygenation during a vascular occlusion test in healthy volunteers (INVOS® vs. InSpectra™). *J Clin Monit Comput* 2015; 29: 271-8.
  35. Pan P, Su L, Liu D, Wang X. Microcirculation-guided protection strategy in hemodynamic therapy. *Clin Hemorheol Microcirc* 2020; 75: 243-53.
  36. Ince C. Hemodynamic coherence and the rationale for monitoring the microcirculation. *Crit Care* 2015; 19 Suppl 3(Suppl 3): S8.
  37. Fischer GW, Levin MA. Vasoplegia during cardiac surgery: current concepts and management. *Semin Thorac Cardiovasc Surg* 2010; 22: 140-4.
  38. Shaefi S, Mittel A, Klick J, Evans A, Ivascu NS, Gutsche J, et al. Vasoplegia after cardiovascular procedures—pathophysiology and targeted therapy. *J Cardiothorac Vasc Anesth* 2018; 32: 1013-22.
  39. Abou-Arab O, Kamel S, Beyls C, Huette P, Bar S, Lorne E, et al. Vasoplegia after cardiac surgery is associated with endothelial glycocalyx alterations. *J Cardiothorac Vasc Anesth* 2020; 34: 900-5.
  40. Karkouti K, Wijeyesundera DN, Beattie WS; Reducing Bleeding in Cardiac Surgery (RBC) Investigators. Risk associated with preoperative anemia in cardiac surgery: a multicenter cohort study. *Circulation* 2008; 117: 478-84.
  41. Loor G, Koch CG, Sabik JF 3rd, Li L, Blackstone EH. Implications and management of anemia in cardiac surgery: current state of knowledge. *J Thorac Cardiovasc Surg* 2012; 144: 538-46.
  42. Salis S, Mazzanti VV, Merli G, Salvi L, Tedesco CC, Veglia F, et al. Cardiopulmonary bypass duration is an independent predictor of morbidity and mortality after cardiac surgery. *J Cardiothorac Vasc Anesth* 2008; 22: 814-22.
  43. Nielsen DV, Hansen MK, Johnsen SP, Hansen M, Hindsholm K, Jakobsen CJ. Health outcomes with and without use of inotropic therapy in cardiac surgery: results of a propensity score-matched analysis. *Anesthesiology* 2014; 120: 1098-108.

44. Song Y, Kim DW, Kwak YL, Kim BS, Joo HM, Ju JW, et al. Urine output during cardiopulmonary bypass predicts acute kidney injury after cardiac surgery: a single-center retrospective analysis. *Medicine (Baltimore)* 2016; 95: e3757.
45. Smith RS, Murkin JM. A novel assessment of peripheral tissue microcirculatory vasoreactivity using vascular occlusion testing during cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 2014; 28: 1217-20.

## Case Report

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# Obstructive fibrinous pseudomembrane tracheitis after double-lumen tube intubation -a case report-

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**Background:** Obstructive fibrinous pseudomembrane tracheitis (OFPT) is a rare complication of endotracheal intubation.

**Case:** We describe the case of a 73-year-old woman who underwent short-term intubation for video-assisted thoracoscopic surgery and developed an acute life-threatening stridor two days after extubation. The patient required an emergency tracheostomy to maintain airway patency and a microscopic direct laryngoscopy procedure was performed thereafter with removal of the obstructive pseudomembrane. Subsequently, the patient also suffered a non-ST-elevation myocardial infarction. The patient successfully recovered, and the tracheostomy was subsequently decannulated two months later. Histological examination revealed mucosal ulcerations and inflammatory changes.

**Conclusions:** OFPT is an uncommon cause of life-threatening airway obstruction after extubation that is not often recognized immediately but can usually be treated with early bronchoscopic intervention or microscopic direct laryngoscopy.

**Keywords:** Airway management; Airway obstruction; Respiratory insufficiency; Respiratory tract diseases; Tracheal stenosis; Tracheitis.

Endotracheal intubation is widely performed for airway control during anesthesia. Obstructive fibrinous pseudomembrane tracheitis (OFPT) is a rare but life-threatening complication of endotracheal intubation that can mimic other pathologies, such as vocal cord palsy, laryngeal edema, and tracheomalacia. Patients usually present with stridor and voice hoarseness hours to days after intubation. Here, we report the case of a patient who experienced respiratory distress two days after thoracic surgery. Written informed consent was obtained from the patient for publication.

## Case Report

A 73-year-old woman (height: 154 cm, weight: 55 kg) was diagnosed with a malignant lung nodule in the left lower lobe that was incidentally discovered on computed tomography. The patient was a non-smoker with a history of hypertension, non-insulin-dependent diabetes mellitus on oral hypoglycemic agents, and epilepsy on sodium valproate. She had a surgical history of a laparoscopic cholecystectomy 11 years ago, which was un-



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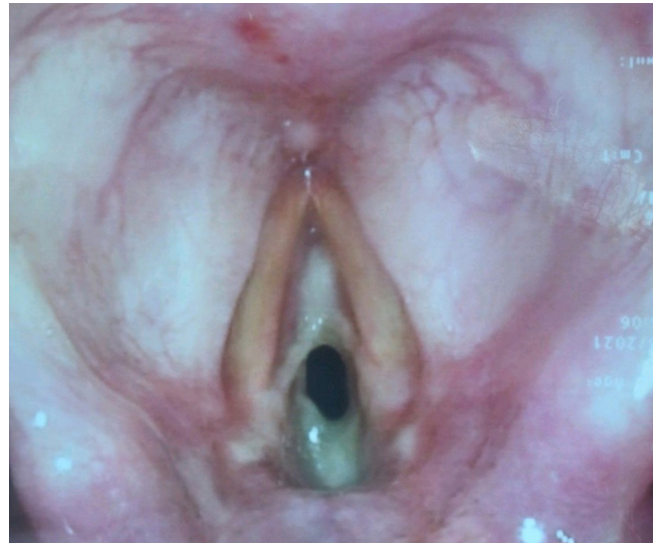


complicated according to the patient; however, no records were available for review. Additionally, the patient had a history of hyperthyroidism, had received radioactive iodine treatment more than 10 years prior, and was on oral levothyroxine replacement. The preoperative thyroid function test results were normal, and the patient was clinically euthyroid. No pre-existing voice hoarseness or dyspnea was noted. Her functional capacity was 4–10 metabolic equivalents, as she was able to walk 200 m at normal speed.

On preoperative assessment, the patient had a normal airway (Mallampati grade 2, interincisor distance of at least 5 cm, full neck range of movement, no neck masses), and the patient was edentulous. Routine tests for thoracic surgery showed normal spirometry (FEV1: 1.44 L [85% of the predicted value], FVC: 1.72 L [92% of the predicted value], and DLCO 94% of the predicted value). Transthoracic echocardiography revealed an ejection fraction of 66% and an absence of regional wall motion abnormalities. The patient had aortic valve sclerosis but no stenosis, and all other valves were normal.

The patient underwent video-assisted thoracoscopic surgery for left lower lobectomy. Induction of anesthesia was uneventful, and a direct laryngoscopy was performed, which showed a grade 1 Cormack-Lehane view with no abnormality of the vocal cords. A size 37 left double-lumen endotracheal tube (DLT) was easily inserted on the first attempt, and no excessive pressure or force was used. A DLT of this size was chosen instead of a smaller bore to facilitate fiberoptic bronchoscopy and tracheal suctioning. The bronchial tip was directed into the left mainstem bronchus on the first attempt atraumatically with fiberoptic bronchoscopic guidance. The tracheal cuff was maintained at 20 cmH<sub>2</sub>O. The DLT was in place for 2 h 10 min, and the surgery was uneventful. Anesthesia was fully reversed, and the patient was then extubated with a face mask. The patient reported mild sore throat, but no hoarseness was noted. She was subsequently discharged from the post-anesthesia care unit.

A total of 48 h later, however, she was noted to have a hoarse voice with mild stridor in the ward. No swallowing issues were observed. A bedside nasoendoscopy was performed, which showed anterior and posterior webbing in the subglottic area, just inferior to the level of the true cords, corresponding to Cotton-Myer grade II stenosis (Fig. 1). Since the nasoendoscope was narrow-bored and thus did not have the features to allow for a therapeutic excision to be performed, and because monitoring was limited at the bedside, the membrane was not removed. At this time, the patient only had mild hoarseness and no dyspnea or respiratory distress, and was able to maintain adequate oxygenation on room air. Bronchoscopy was not performed to avoid ag-

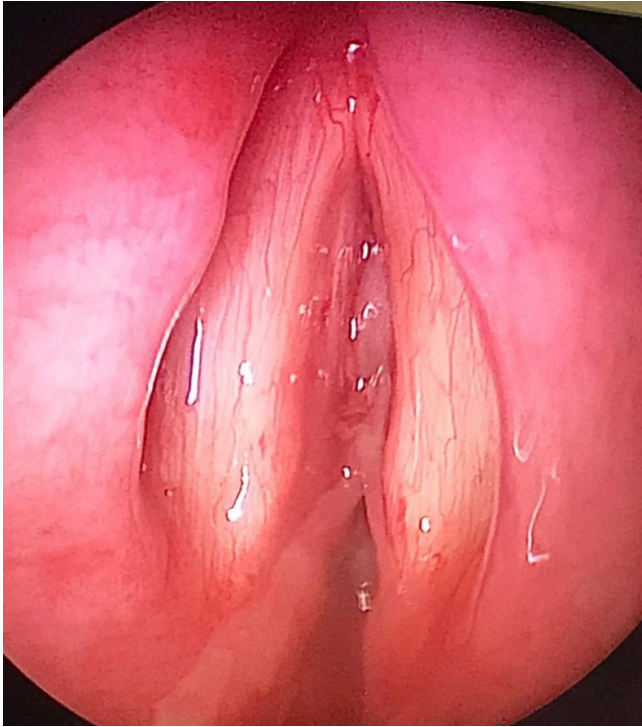


**Fig. 1.** Thick rubbery whitish pseudomembrane at the anterior and posterior region, in the subglottic area, just inferior to the level of the true vocal cords.

gravating the laryngeal edema. She was subsequently started on inhaled budesonide.

The next day, the patient quickly deteriorated, requiring emergency surgical intervention for critical upper airway obstruction (Fig. 2). The oral pharynx was topicalized with lidocaine, and an awake videolaryngoscopy was performed; however, visualization of the glottic opening was poor, and thus an awake tracheostomy was performed under local anesthesia with oxygenation via a Hudson mask. Upon securing the airway through tracheostomy, a microscopic direct laryngoscopy was performed, which showed white adherent fibrinous material at the glottis and subglottic area, with a residual 1-mm pinpoint glottic gap posteriorly, corresponding to Cotton-Myer grade III subglottic stenosis. The adherent fibrinous material appeared fixed initially, but on palpation, it was found to be removable. After the material was removed using a microlaryngeal forceps, the subglottic area appeared less than 50% stenotic (Cotton-Myer grade I stenosis). The underlying mucosa appeared healthy anteriorly, but the posterior commissure mucosa was edematous. Over the following few days, serial nasoendoscopic evaluation showed that the pseudomembrane had cleared.

The next day, however, the patient suffered a non-ST-elevation myocardial infarction, presenting with T-wave inversion without any angina or evidence of hypoxemia. She underwent percutaneous coronary intervention and stenting of the culprit left anterior descending artery occlusion, which was caused by an underlying structural lesion that had not been detected preoperatively. The patient was subsequently discharged two weeks after hospital ad-



**Fig. 2.** Near-complete upper airway obstruction requiring emergency tracheostomy.

mission. Serial outpatient nasoendoscopy showed no reaccumulation of the subglottic pseudomembrane, and the tracheostomy was successfully decannulated two months later.

Histological analysis of the subglottic material revealed inflammatory changes, namely, squamous-lined mucosa with extensive ulceration and formation of organizing fibrinopurulent acute inflammation in the lamina propria. No bacteria or fungi were detected on staining.

## Discussion

OFPT is a rare but potentially fatal complication of endotracheal intubation. However, the exact pathophysiology of pseudomembrane formation remains unclear. One hypothesis is that the subglottic mucosa is prone to injury during intubation because it is the narrowest part of the adult larynx and completely surrounded by the complete ring of the cricoid cartilage. After injury, the accumulation of desquamated epithelial cells may result in the formation of a membranous-like material [1]. Indeed, the most common location of the tracheal pseudomembrane is in the subglottic area, but it can also be found distally, such as in the mid-trachea or carina [2–5].

Risk factors may include female sex, tracheal tube cuff pressure > 25 cmH<sub>2</sub>O, traumatic intubation, use of a DLT, prolonged en-

dotracheal intubation, airway stenting, a compromised immune system, and bacterial or fungal infection [1,2,6–15]. Additionally, aspiration of gastric contents leading to caustic injury has also been proposed as a contributory factor to the formation of OFPT after an initial disruption of the tracheal mucosa followed by an abnormal healing process [1,13]. Patients should be observed closely, since OFPT can occur in the absence of prolonged intubation, and the time to onset of symptoms after extubation can vary widely [3,5]. Before confirming the diagnosis, patients usually receive empirical treatment consisting of salbutamol bronchodilator, epinephrine, and corticosteroids.

To confirm the diagnosis, an endoscopic evaluation is performed [1,5]. Histology typically reveals the presence of inflammatory infiltrates, fibrin, and ulcerations. Bacteria, viruses, or fungi may also be observed as they may also cause OFPT. Treatment typically involves using rigid or flexible bronchoscopy to remove the pseudomembrane and relieve the obstruction. Rigid bronchoscopy, however, is safer as it can be used to maintain ventilation during the intervention. Although it is uncommon, recurrence of the tracheal membrane can occur and result in repeated obstructions [1].

In conclusion, OFPT is a rare cause of airway obstruction after extubation that is often not immediately recognized, but can usually be treated with mechanical removal of the lesion with bronchoscopic intervention or microscopic direct laryngoscopy as in our patient's case.

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## References

1. Sehgal IS, Dhoria S, Bal A, Aggarwal AN, Behera D, Agarwal R. Obstructive fibrinous tracheal pseudomembrane after endotracheal intubation. *Respir Care* 2016; 61: 1260-6.
2. Talwar A, Patel N, Omonuwa K, Lisker G. Postintubation obstructive pseudomembrane. *J Bronchology Interv Pulmonol* 2008; 15: 110-2.
3. Lins M, Dobbeleir I, Germonpré P, Waelput W, Pauwels P, Jorens PG. Postextubation obstructive pseudomembranes: a case series and review of a rare complication after endotracheal intubation. *Lung* 2011; 189: 81-6.
4. Vanderheyde K, Pieters T, Rodenstein D. A 19-year-old man with dyspnea and stridor after surgery. *Respiration* 2011; 81: 63-6.
5. Ammar Y, Vella-Boucaud J, Launois C, Vallerand H, Dury S, Lebargy F, et al. Obstructive fibrinous tracheal pseudomembrane. *Anesth Analg* 2017; 125: 172-5.
6. Manassero A, Ugues S, Bertolaccini L, Bossolasco M, Terzi A, Coletta G. A very early stage of obstructive fibrinous tracheal pseudo-membrane formation. *J Thorac Dis* 2012; 4: 320-2.
7. Deslée G, Brichet A, Lebuffé G, Copin MC, Ramon P, Marquette CH. Obstructive fibrinous tracheal pseudomembrane. A potentially fatal complication of tracheal intubation. *Am J Respir Crit Care Med* 2000; 162: 1169-71.
8. Kawakami N, Ito M, Takahashi K, Moriya T, Saito H, Wakai Y, et al. Pseudomembranous tracheobronchitis with severe tracheal stenosis and masked bronchial obstruction. *J Emerg Med* 2021; 60: e39-44.
9. Lee YH, Seo H, Cha SI, Kim CH, Lee J. A case of pseudomembranous tracheitis caused by *Mycoplasma pneumoniae* in an immunocompetent patient. *Ann Transl Med* 2019; 7: 205.
10. Grosu HB, Bashoura L, Ost D, Ordóñez NG, Faiz SA. Critical airway obstruction due to pseudomembranous *Aspergillus* tracheitis. *Am J Respir Crit Care Med* 2014; 190: e65-6.
11. Sahu SR, Madan K, Mohan A, Mittal S. Obstructive fibrinous tracheal pseudomembrane following tracheal stent placement: an underrecognized entity. *Lung India* 2020; 37: 453-4.
12. Yildirim BB, Karalezli A, Hasanoglu HC, Kandemir O. Obstructive fibrinous tracheal pseudomembrane. *J Bronchology Interv Pulmonol* 2012; 19: 129-31.
13. Kang HH, Kim JW, Kang JY, Kim JS, Kim MS, Kim SS, et al. Obstructive fibrinous tracheal pseudomembrane after tracheal intubation: a case report. *J Korean Med Sci* 2010; 25: 1384-6.
14. Nakwan N. Obstructive fibrinous tracheal pseudomembrane: a rare condition in postextubation stridor. *Respir Care* 2014; 59: e91-3.
15. Jee DL, Kim YD, Park J, Choi KH, Koo BU. Fiberoptic bronchoscopic evaluation of laryngotracheal injury following short-term endotracheal intubation. *Korean J Anesthesiol* 1994; 27: 1108-17.

## Letter to the Editor

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# Postoperative opioid consumption data repository incorporated in electric medical record based on PCA device data extraction program

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Pain is often referred to as the ‘fifth vital sign’ and is a crucial element of contemporary patient care. It is increasingly recognized that assessment and adequate control of pain are just as important as the other vital signs. In particular, the importance of postoperative analgesia cannot be overstated since it is known to be related to various postoperative complications and the quality of recovery. Therefore, the issue of postoperative analgesia is an indispensable and constant mission for perioperative care physicians. Patient-controlled analgesia (PCA) is one of the valuable tools providing optimal postoperative analgesia. PCA devices allow the patient to self-administer small boluses of analgesic to relieve pain [1]. Use of PCA has been recommended over intermittent bolus dosing of opioids initiated by health care providers [2].

Several electrical or elastomeric PCA devices are being widely used. Among these, some electrical devices incorporate settings to calibrate various parameters, such as bolus dose, lockout interval, background infusion rate, dose limits, and loading dose. In addition, the detailed device usage data can easily be stored and extracted via designated software. Here we briefly introduce the integrated data management system (Dr. PCA, Data repository for postoperative clinical audit), which is incorporated into the electronic medical record (EMR) system at our institution (Supplemental File 1).

At our institution, the PCA device is returned to a designated place for data extraction upon completion of its use. Using the dedicated software of our PCA device installed in computers connected to the hospital network, PCA data are extracted and the detailed log records are automatically saved to a repository server. For security, the raw data is stored in a separate server, and only the processed relevant information is retrieved from the EMR. The software of the PCA device generates data based on the event logs, which makes it possible to calculate the operating time of the device and to process the accumulated data over time.

The data management system consists of mainly four types of information (Table 1):

1. Patient-specific clinical information
2. PCA device settings
3. Processed data regarding the device used
4. Clinical assessments done by the PCA management team

As noted above, the system integrates not only the information extracted from the device but also the data from the PCA management team. In Korea, the operation of the ‘PCA management team’ is one of the items of interest for quality assessment of anesthetic



**Table 1.** Variable Category Types and Descriptions of Variables

Category	Variables
Patient-specific clinical information - Expansion of patient information considered necessary in the management window by adding additional columns	Patient ID, name, age, sex, height, weight, department, surgery name, order date, order drug, etc.
PCA device settings	Total drug amount (unit), total volume, infusion rate (unit), bolus dose, lockout time (min), loading dose, bolus attempt, bolus given, demand, and delivery ratio.
Processed data regarding the device use	Cumulative consumption amount per pre-determined hour (in our institution, we have set 3, 6, 9, 12, 24, 48 h after completion of surgery) To check the time setting error of PCA device, compare the last log recording time of the device (device time) and the time the data was transmitted to the server (real-time).
Clinical assessments done by the PCA management team	Ward round information of PCA management team recorded at the ward site using mobile EMR (PONV, pain score min/max at postoperative day 0, 1, 2)

PCA: Patient-controlled analgesia, EMR: electronic medical record, PONV: postoperative nausea and vomiting.

sia practice. The clinical assessment at our institution routinely includes pain score (numerical rating scale – maximum and minimum) and adverse effects relevant to PCA (e.g., postoperative nausea and vomiting, somnolence, and dizziness). This is an efficient means to enable clinicians to evaluate their practice and gain feedback. Moreover, as this system regularly operates and consistently stacks comprehensive ‘pain-related’ outcomes, it can enable systematic evaluation and modification of a certain protocol or regimen for postoperative analgesia.

Alongside the ‘opioid crisis,’ there are increasing concerns about chronic opioid use beyond the acute phase of the postoperative period [3]. Therefore, minimizing or optimizing perioperative opioid use is also a noteworthy issue. The establishment of a model to deal with this issue may require a large dataset of detailed information regarding postoperative analgesia. Therefore, the establishment of a system for accumulating relevant data is a key imperative. Analysis of the temporal patterns of analgesic demand in individual patients may provide valuable insights into perioperative analgesia. Resolution of the concerns about device hacking by wireless network connection will facilitate remote monitoring of real-time usage patterns and pain assessments. This would ultimately enable the provision of more advanced acute pain services. In addition, the use of big data technology to analyze PCA data may help predict opioid use for individual surgery patients [4].

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## Conflicts of Interest

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## Supplementary Material

Supplementary File 1. Workflow of data repository of patient controlled analgesia device and clinical information

## References

1. Macintyre PE. Safety and efficacy of patient-controlled analgesia. *Br J Anaesth* 2001; 87: 36-46.
2. Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016; 17: 131-57.
3. Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic opioid use after surgery: implications for perioperative management in the face of the opioid epidemic. *Anesth Analg* 2017; 125: 1733-40.
4. Chae D. Data science and machine learning in anesthesiology. *Korean J Anesthesiol* 2020; 73: 285-95.

## Letter to the Editor

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# Cadaveric investigation of the spread of the thoracoabdominal nerve block using the perichondral and modified perichondral approaches

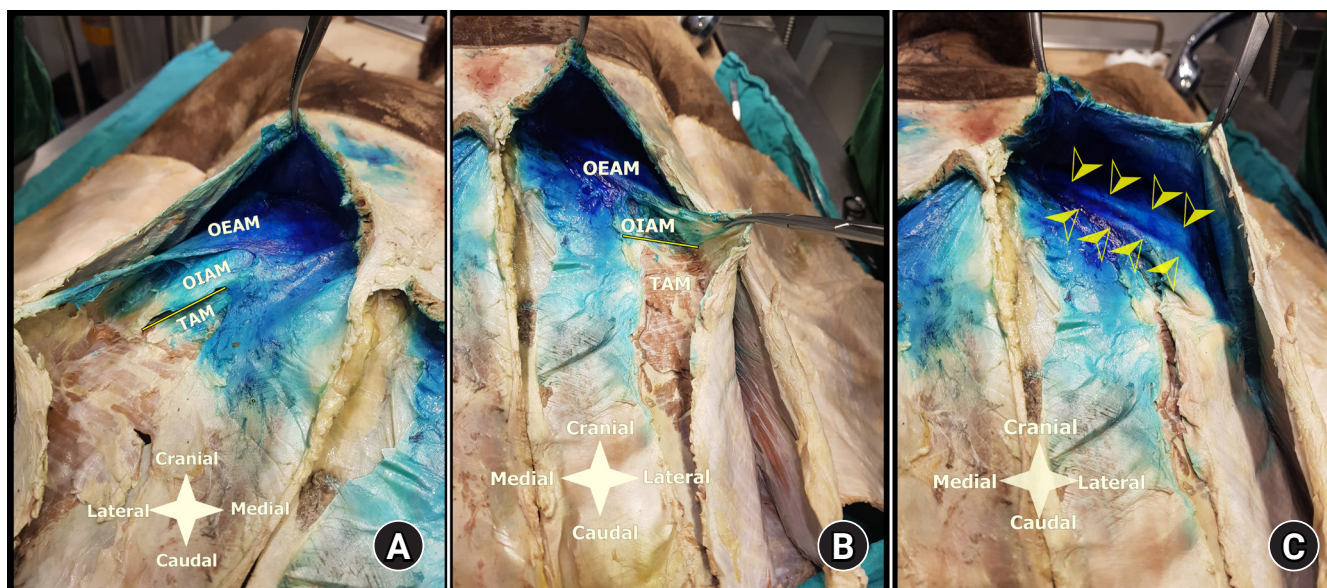
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Interfascial plane blocks and associated nomenclature are currently popular topics in the field of anesthesia. While several novel plane blocks have been described, cadaveric studies on the spread of novel blocks are important for determining appropriate applications [1]. Recently, Tulgar et al. [2] defined the thoracoabdominal nerve block using a perichondral approach (TAPA). They reported that local anesthetic (LA) administered on the upper and lower aspect of the 9th through the 10th costal cartilages would block both the anterior and lateral cutaneous branches, thus providing abdominal analgesia. After describing the TAPA, the authors also redefined the approach, naming it the modified TAPA (M-TAPA). They reported that administering LA only to the lower surface of the costal cartilage would provide successful analgesia similar to that provided by the TAPA [3]. In the literature, there are some case reports and observational studies on the TAPA and M-TAPA [2,3]; however, to the best of our knowledge, no reliable cadaveric investigation has demonstrated the spread of these blocks. Therefore, in this cadaveric investigation, we aimed to evaluate the areas of spread associated with the TAPA and M-TAPA. This study was approved by the Istanbul Medipol University Ethics and Research Committee (Decision No. 36, 06.01.2022).

One fresh human male cadaver was obtained from Istanbul Medipol University. Injections were performed by two investigators with 10 and 20 years of experienced in administering regional anesthesia. With the cadaver in the supine position, the M-TAPA was performed on the right side, and the TAPA was performed on the left side. The blocks were performed under ultrasound guidance using a linear transducer. The transducer was placed at the costochondral angle in the sagittal view and then advanced to view the lower side of the chondrium. For the TAPA, 20 ml of 0.25% methylene blue dye was injected into both the upper and lower sides of the chondrium (40 ml total). For the M-TAPA, 40 ml of 0.25% methylene blue dye was injected into the lower side of the chondrium.

An anatomical dissection was performed 30 min after the procedure. For both the TAPA and M-TAPA, the dye had spread over the lower surface of the upper part of the rectus abdominis and over the thoracoabdominal nerve on both sides. The lower surface of the external abdominal oblique muscle (EAOM) was completely stained with the dye (over the 8th, 9th, and 10th ribs), and so were the upper and lower surfaces of the internal abdominal oblique muscle (IAOM). Additionally, the dye had spread over the upper surface of the costal margin and from T4 to T11-T12 on both sides. However, the dye spread over the transverse abdominis muscle (TAM) to a greater degree with the M-TAPA compared with the TAPA (limited to the upper part of the muscle) (Figs. 1A and 1B).



**Fig. 1.** (A) Dissection of the M-TAPA. (B) Dissection of the TAPA. (C) Dye spread of thoracoabdominal nerves. The yellow lines show the thoracoabdominal nerve region between the IAOM and TAM. The yellow arrows show the thoracoabdominal nerves that spread the dye. M-TAPA: modified thoracoabdominal nerves perichondrial approach, TAPA: thoracoabdominal nerves perichondrial approach, EAOM: external abdominal oblique muscle, IAOM: internal abdominal oblique muscle, TAM: transverse abdominis muscle.

Thoracoabdominal nerves are thoracic spinal nerves with ventral and dorsal branches. Sensorial and muscular innervation of the abdomen is provided by the anterior primary rami of T7–T12, which exit through the intercostal areas and enter the plane between the IAOM and TAM (i.e., the transverse abdominis plane [TAP]). The intercostal nerves pass just below the costal cartilage and terminate at the TAP in the abdominal region [2–4]. The anterior primary rami of T10–12 enter the TAP at the mid-axillary line, which is why additional posterior block applications may fail. The sixth and ninth nerves enter the TAP at the level of the anterior axillary line, which can help explain the failure of the lateral and posterior TAP blocks in the upper abdomen [4]. The TAM arises from the inner aspect of the costal margin, while the IAOM arises from the lower aspects of the costal cartilages of the 4 ribs, and the EAOM arises from the outer aspects of the 5th through the 12th ribs. Therefore, injecting LA at the point where these three muscles intersect would provide abdominal analgesia through thoracoabdominal nerve blockage [2–4]. Aikawa et al. [5], in their study, evaluated sensory loss after performing the M-TAPA in patients undergoing gynecological surgery. In that study, the authors reported that the M-TAPA provided limited dermatomal coverage, with greater anterior sensorial loss compared with lateral sensorial loss. In contrast to the clinical results of the study conducted by Aikawa et al., the dye was found to have spread between T4 and T11–12 in our cadaveric study. Notably, these authors used 25 ml of the LA, while we

used 40 ml of dye.

In conclusion, multiple factors may affect the success of plane blocks. A high-volume M-TAPA may be preferable since fascial plane blocks are volume-related. Based on our results, both the TAPA and M-TAPA may provide analgesia following various abdominal procedures. However, the M-TAPA may provide greater spread over the TAM compared with the TAPA. Since the thoracoabdominal nerves enter the subcutaneous area in the anterior abdominal wall as the anterior and lateral cutaneous branches of the skin, TAPA blocks may be a good alternative for abdominal analgesia due to its region of spread. The literature shows successful analgesia associated with the TAPA for several surgical procedures such as abdominal and gynecological laparoscopic surgery [2,3,5]. However, there may be limitations related to volume. Therefore, further cadaveric and clinical studies are needed to determine the exact effects of the M-TAPA and TAPA blocks.

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## References

1. Altıparmak B, Ciftci B, Tekin B, Sakul BU, Alici HA. Is the deep supraspinatus muscle plane block and suprascapular nerve block the same approach? A cadaveric nomenclature study. *Korean J Anesthesiol* 2022; 75: 193-5.
2. Tulgar S, Senturk O, Selvi O, Balaban O, Ahiskalioglu A, Thomas DT, et al. Perichondral approach for blockage of thoracoabdominal nerves: anatomical basis and clinical experience in three cases. *J Clin Anesth* 2019; 54: 8-10.
3. Tulgar S, Selvi O, Thomas DT, Devci U, Özer Z. Modified thoracoabdominal nerves block through perichondrial approach (M-TAPA) provides effective analgesia in abdominal surgery and is a choice for opioid sparing anesthesia. *J Clin Anesth* 2019; 55: 109.
4. Chin KJ, McDonnell JG, Carvalho B, Sharkey A, Pawa A, Gadsden J. Essentials of our current understanding: abdominal wall blocks. *Reg Anesth Pain Med* 2017; 42: 133-83.
5. Aikawa K, Yokota I, Maeda Y, Morimoto Y. Evaluation of sensory loss obtained by modified-thoracoabdominal nerves block through perichondrial approach in patients undergoing gynecological laparoscopic surgery: a prospective observational study. *Reg Anesth Pain Med* 2022; 47: 134-5.

# Notice

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See also the National Library of Medicine’s policy on retractions and the recommendations of the International Committee of Medical Journal Editors (ICMJE) concerning corrections and retractions, or <https://publicationethics.org/resources/guidelines>.

## 9-3. Appeals and complaints

KJA adheres to COPE guidelines regarding appeals to editorial decisions and complaints. For additional information, please visit <https://publicationethics.org/core-practices>.

## Data sharing statement

KJA accepts the ICMJE Recommendations for data sharing statement policy (<http://icmje.org/icmje-recommendations.pdf>). All manuscripts reporting clinical trial results should submit a data sharing statement following the ICMJE guidelines from 1 July 2018. Authors may refer to the editorial, “Data Sharing statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors,” in *Annals* on 6 June 2017 ([http://www.icmje.org/news-and-editorials/data\\_sharing\\_june\\_2017.pdf](http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf)).

## Manuscript preparation

### 1. Word processors and format of manuscript

A manuscript must be written in proper and clear English. The manuscript, including tables and their footnotes, and figure legends, must be typed in one double space. Materials should be prepared with a standard 12-point typeface or greater (Times

New Roman typeface is preferred). The manuscript should be in the following sequence: cover letter (optional), title page file, manuscript (title and running title, abstract and keywords, introduction, materials and methods, results, discussion, references, tables, and figure legends), figures, other submission elements. All pages should be numbered consecutively starting from the title page. All numbers should be written in Arabic numerals throughout the manuscripts. Our preferred file format is DOCX or DOC. A single PDF file containing all materials in a file including figures and figure legends. In that case, authors should add line numbers throughout the document. Manuscript containing anything in headers and footers, except of page numbers, will be returned to authors. If your PDF submission is accepted, you will be asked to upload your final document file in DOCX or DOC format as well. Make sure to update your PDF file with the most recent version of your manuscript.

### 2. Abbreviation of terminology

Abbreviations should be avoided as much as possible. When they are used, full expression of the abbreviations following the abbreviated word in parentheses should be given at the first use. Common abbreviations, however, may be used, such as DNA. Abbreviation can be used if it is listed as a MeSH subject heading (<http://www.ncbi.nlm.nih.gov/mesh>).

### 3. Word-spacing

- 1) Leave 1 space for each side, using arithmetic marks as +, −, ×, etc.  
Leave no space for hyphen between words.
- 2) Leave 1 space after “,” and “;”. Leave 2 spaces after “.” and “:”.
- 3) Using parentheses, leave 1 space each side.
- 4) Brackets in parentheses, apply square brackets.

### 4. Citations

- 1) If a citation has 2 authors, write as “Hirota and Lambert.” If there are more than 3 authors, apply ‘et al.’ at the end of the first author’s surname. Ex) Kim et al. [1].
- 2) Citation should be applied after the last word or author’s surname.
- 3) Apply citation before a comma or period.
- 4) Identify reference by several or coupled Arabic numbers, enclosed in square brackets on the line as [1,3,5].

### 5. Arrangement of manuscript

ALL articles should be arranged in the following order.  
Cover letter (optional)

Title Page file, uploaded separately

Manuscript, as a single file in word processing format (eg, .doc), consisting of Title and running title, Abstract (if required for the article type; see relevant section), Body Text, References, Tables, Figure Legends, if any (in numerical order, on the same page); be sure to number all pages of the manuscript file  
Figures (each Figure should be a separate file in figure file format)  
Other submission elements (Supplemental Digital Content, etc.)

Each new section's title should begin on a new page. The conclusion should be included in the discussion section. Number pages consecutively, beginning with the first page. Page numbers should be placed at the middle of the bottom of page. For survey-based clinical studies, the original survey document does not need to be included in the body of the manuscript but may be supplemented in an appendix.

## 6. Statistical Analysis

- 1) Describe the statistical tests employed in the study with enough detail so that readers can reproduce the same results if the original data are available. The name and version of the statistical package should be provided.
- 2) Authors should describe the objective of the study and hypothesis appropriately. The primary/secondary endpoints are predetermined sensibly according to the objective of the study.<sup>1</sup>
- 3) The characteristics of measured variables should determine the use of a parametric or nonparametric statistical method. When a parametric method is used, the authors should describe whether the basic statistical assumptions are met.<sup>2,3</sup>
- 4) For an analysis of a continuous variable, the normality of data should be examined. Describe the name and result of the particular method to test normality.
- 5) When analyzing a categorical variable, if the number of events and sample is small, exact test or asymptotic method with appropriate adjustments should be used. The standard chi-squared test or difference-in-proportions test may be performed only when the sample size and number of events are sufficiently large.
- 6) The Korean Journal of Anesthesiology (KJA) strongly encourages authors to show confidence intervals. It is not recommended to present the P value without showing the confidence interval. In addition, the uncertainty of estimated values, such as the confidence interval, should be described consistently in figures and tables.<sup>4</sup>
- 7) Except for study designs that require a one-tailed test, for example, non-inferiority trials, the P values should be two-

tailed. A P value should be expressed up to three decimal places (not as "P < 0.05"). If the value is less than 0.001, it should be described as "P < 0.001" but never as "P = 0.000." For large P value greater than 0.1, the values can be rounded off to one decimal place, for example, P = 0.1, P = 0.9.

- 8) A priori sample size calculation should be described in detail.<sup>5</sup> Sample size calculation must aim at preventing false negative results pertaining to the primary, instead of secondary, endpoint. Usually, the mean difference and standard deviation (SD) are typical parameters in estimating the effect size. The power must be equal to or greater than 80 percent. In the case of multiple comparisons, an adjusted level of significance is acceptable.<sup>6</sup>
- 9) It is recommended using mean  $\pm$  SD or median (Q1, Q3) format to present representative values of continuous variables. Results must be written in significant figures. The measured and derived numbers should be rounded off to reflect the original degree of precision. Calculated or estimated numbers (such as mean and SD) should be expressed in no more than one significant digit beyond the measured accuracy. Therefore, the mean  $\pm$  SD of body weight in patients measured on a scale that is accurate to 0.1 kg should be expressed as 65.45  $\pm$  2.52 kg.
- 10) Except when otherwise stated herein, authors should conform to the most recent edition of the American Medical Association Manual of Style.<sup>7</sup>

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<sup>1</sup>Lee S, Kang H. Statistical and methodological considerations for reporting RCTs in medical literature. *Korean J Anesthesiol* 2015; 68: 106-15.

<sup>2</sup>Kim TK. T test as a parametric statistic. *Korean J Anesthesiol* 2015; 68: 540-6.

<sup>3</sup>Nahm FS. Nonparametric statistical tests for the continuous data: the basic concept and the practical use. *Korean J Anesthesiol* 2016; 69: 8-14.

<sup>4</sup>Park S. Significant results: statistical or clinical? *Korean J Anesthesiol* 2016; 69: 121-5.

<sup>5</sup>In J. Considerations when calculating the sample size for an inequality test. *Korean J Anesthesiol* 2016; 69: 327-31.

<sup>6</sup>Lee S and Lee DK. What is the proper way to apply the multiple comparison test? *Korean J Anesthesiol* 2018; 71: 353-60.

<sup>7</sup><http://www.amamanualofstyle.com/>

## 7. Organization of manuscript

### 1) Clinical or Experimental research

#### (1) Title page

##### ① Title

Title should be concise and precise.

For the title, only the first letter of the first word should be capitalized.

##### ② Author information

First name, middle initial, and last name of each author, with their highest academic degree(s) (M.D., Ph.D., etc.), and institutional affiliations; make sure the names of and the order of authors as they appear on the Title Page and entered in the system match exactly.

##### ③ Running title

A running title of no more than 40 characters, including letters and spaces, should be described. If inappropriate, the editorial board may revise it.

##### ④ Corresponding Author

Name, mailing address, phone number, and e-mail address of the corresponding author

##### ⑤ Previous presentation in conferences

Title of the conference, date of presentation, and the location of the conference may be described.

##### ⑥ Conflict of interest

It should be disclosed here according to the statement in the Research and publication ethics regardless of existence of conflict of interest. If the authors have nothing to disclose, please state: "No potential conflict of interest relevant to this article was reported."

##### ⑦ Funding

Funding to the research should be provided here. Providing a FundRef ID is recommended including the name of the funding agency, country and if available, the number of the grant provided by the funding agency. If the funding agency does not have a FundRef ID, please ask that agency to contact the FundRef registry (e-mail: [fundref.registry@crossref.org](mailto:fundref.registry@crossref.org)). Additional detailed policy of FundRef description is available from <http://www.crossref.org/fundref/>.

##### ⑧ Acknowledgments

Any persons that contributed to the study or the manuscript, but not meeting the requirements of an authorship could be placed here. For mentioning any persons or any organizations in this section, there should be a written permission from them.

##### ⑨ IRB number

##### ⑩ Clinical trial registration number

If any of these elements are not applicable to your submission, write "not applicable" after the number and topic; for example, "Prior Presentations: Not applicable."

#### (2) Manuscript

##### ① Title and Running title

##### ② Abstract

All manuscripts should contain a structured abstract that is written only in English. Provide an abstract of no more than 250 words. It should contain 4 subsections: Background, Methods, Results, and Conclusions. Quotation of references is not available in the abstract. A list of keywords, with a minimum of 6 and maximum of 10 items, should be included at the end of the abstract. The selection of keywords should be from MeSH (<http://www.ncbi.nlm.nih.gov/mesh>) and should be written in small alphabetic letters with the first letter in capital letter. Separate each word by a semicolon (;), and mark a period (.) at the end of the last word.

##### ③ Introduction

The introduction should address the purpose of the article concisely and include background reports that are relevant to the purpose of the paper.

##### ④ Materials and Methods

- The materials and methods section should include sufficient details of the design, subjects, and methods of the article in order, as well as the data analysis methods and control of bias in the study. Sufficient details need to be addressed in the methodology section of an experimental study so that it can be further replicated by others.
- When reporting experiments with human or animal subjects, the authors should indicate whether they received approval from the IRB for the study and the IRB approval number needs to be provided. When reporting experiments with animal subjects, the authors should indicate whether the handling of the animals was supervised by Institutional Board for the Care and Use of Laboratory Animals. "American Society of Anesthesiologists physical status classification" should not be abbreviated. As a rule, subsection titles are not recommended.
- Clearly describe the selection of observational or experimental participants. Ensure correct use of the terms sex (when reporting biological factors) and gender (identity, psychosocial or cultural factors), and, unless inappropriate, report the sex and/or gender of study participants, the sex of animals or cells, and describe the methods used to determine sex and gender. If the study was done involving an exclusive population, for example in only one sex, authors



should justify why, except in obvious cases (e.g., prostate cancer). For additional information, please visit <http://www.icmje.org/about-icmje/faqs/icmje-recommendations/>.

- Reports of randomized trials must conform to the revised CONSORT guidelines and should be submitted with the CONSORT flow diagram. The CONSORT checklist should be submitted as a separate file along with the manuscript. The CONSORT statement, checklist, and flow diagram can be found at <http://www.consort-statement.org> or EQUATOR Network (<https://www.equator-network.org/home/>)

- Units

Laboratory information should be reported in International System of Units [SI]. Please refer to A Guide for Biological and Medical Editors and Authors, 6th Edn. Baron DN and Clarke HM, ed. (2008), CRC Press. or visit <http://www.icmje.org/about-icmje/faqs/icmje-recommendations/>

- Exceptions

- A. The unit for volume is “L”, others in “dl, ml, µl”.
- B. The units for pressure are mmHg or cmH<sub>2</sub>O.
- C. Use Celsius for temperature
- D. Units for concentration are M, mM, µM.
- E. When more than 2 items are presented, diagonal slashes are acceptable for simple units. Negative exponents should not be used.
- F. Leave 1 space between number and units.  
Exception) 5%, 36°C

- Drug Names and Equipment

Use generic names. If a brand name must be used, insert it in parentheses after the generic name. Provide ® or ™ as a superscript and manufacturer’s name, and country.

- Ions

Ex) Na<sup>+</sup> [O], Mg<sup>2+</sup> [O], Mg<sup>++</sup> [X], Mg<sup>+2</sup> [X]

- Statistics

Statistical methods must be described with enough detail so that readers can reproduce the same results if the original data available. The KJA strongly encourages authors to show confidence intervals. It is not recommended to present the P value without showing the confidence interval. A sample size calculation should be described in detail. Sample size calculation must aim at preventing false negative results pertaining to the primary, instead of secondary, endpoint.

#### ⑤ Results

Results should be presented in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat all of the data in the tables or il-

lustrations in the text; emphasize or summarize only the most important observations. Results can be sectioned by subsection titles but should not be numbered. Citation of tables and figures should be provided as Table 1 and Fig. 1.

#### ⑥ Discussion

The discussion should be described to emphasize the new and important aspects of the study, including the conclusions. Do not repeat the results in detail or other information that is given in the Introduction or the Results section. Describe the conclusions according to the purpose of the study but avoid unqualified statements that are not adequately supported by the data. Conclusions may be stated briefly in the last paragraph of the Discussion section.

#### ⑦ References

The description of the journal reference follows the descriptions below. Otherwise, it follows the NLM Style Guide for Authors, Editors, and Publishers (Patrias, K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling, DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007 [updated 2009 Jan 14; cited 2009 May 1]. Available at: [www.nlm.nih.gov/citingmedicine](http://www.nlm.nih.gov/citingmedicine)).

- References should be obviously related to documents and should not be exceed 50. For exceeding the number of references, it should be negotiated with the Editorial Board. References should be numbered consecutively in the order in which they are first mentioned in the text. Provide footnotes in the body text section. All of the references should be stated in English, including author, title, name of journal, etc.
- If necessary, the editorial board may request original documents of the references.
- The journal title should be listed according to the List of Journals Indexed for MEDLINE, available at: [www.nlm.nih.gov/archive/20130415/tsd/serials/lji.html](http://www.nlm.nih.gov/archive/20130415/tsd/serials/lji.html) or the List of KoreaMed Journals, available at: [koreamed.org](http://koreamed.org).
- Six authors can be listed. If more than 6 authors are listed, only list 6 names with ‘et al.’
- Provide the start and final page numbers of the cited reference.
- Abstracts of conferences are not allowed to be included in the references. The American Society of Anesthesiologists (ASA) refresher course lecture is not acceptable as a reference.
- Description format
  - A. Regular journal  
Author name. Title of journal Name of journal published

year; volume: start page-final page.

Ex) Rosenfeld BA, Faraday N, Campbell D, Dorman T, Clarkson K, Siedler A, et al. Perioperative platelet activity of the effects of clonidine. *Anesthesiology* 1992; 79: 256-61.

Ex) Hirota K, Lambert DG. Ketamine: its mechanism(s) of action and unusual clinical uses. *Br J Anaesth* 1996; 77: 441-4.

Ex) Kang JG, Lee SM, Lim SW, Chung IS, Hahm TS, Kim JK, et al. Correlation of AEP, BIS, and OAA/S scores under stepwise sedation using propofol TCI in orthopedic patients undergoing total knee replacement arthroplasty under spinal anesthesia. *Korean J Anesthesiol* 2004; 46: 284-92.

Ex) '2006; 7(Suppl 1): 64-96' '2007; 76: H232-8'

B. Monographs

· Author. Book name. Edition. Place, press. Published year, pp (start page)-(End page).

· If reference page is only 1 page, mark 'p'.

· Mark if it is beyond the 2nd edition.

Ex) Nuwer MR. Evoked Potential monitoring in the operating room. 2nd ed. New York, Raven Press. 1986, pp 136-71.

C. Chapter

Ex) Blitt C. Monitoring the anesthetized patient. In: *Clinical Anesthesia*. 3rd ed. Edited by Barash PG, Cullen BF, Stoelting RK: Philadelphia, Lippincott-Raven Publishers. 1997, pp 563-85.

D. Electronic documents

Ex) Grainge MJ, Seth R, Guo L, Neal KR, Coupland C, Vryenhoef P, et al. Cervical human papillomavirus screening among older women. *Emerg Infect Dis* [serial on the Internet]. 2005 Nov [2005 Nov 25]. Available from [wwwnc.cdc.gov/eid/article/11/11/05-0575\\_article](http://wwwnc.cdc.gov/eid/article/11/11/05-0575_article)

E. Online journal article

Ex) Sampson AL, Singer RF, Walters GD. Uric acid lowering therapies for preventing or delaying the progression of chronic kidney disease. *Cochrane Database Syst Rev* 2017; 10: CD009460.

F. Papers that have been submitted and accepted for publication should be included in the list, with the phrase 'in press' replacing volume and page number. Authors should be prepared to give the volume and page number at the time of proof correction.

Ex) Baumbach P, Gotz T, Gunther A, Weiss T, Meissner W. Chronic intensive care-related pain: Exploratory analysis on predictors and influence on health-related quality of

life. *Eur J Pain* 2017. Advance Access published on Nov 5, 2017. doi:10.1002/ejp. 1129.

### ⑧ Table

· Type or print each table on a separate sheet of paper.

· Number tables consecutively in the order of their first citation in the text.

· Supply a brief title

Tables should be more than 4 rows and should not be over 1 page.

· Except for titles and first letters, all of the text in the tables should be written in small alphabetic letters.

· In demographic data, sex would be provided as M/F, and age in yr. Data of year, weight, height, and any other units would be provided with 1 decimal place.

· "±" sign in the upper column of table should be lined up with the lower column.

· Footnotes should be provided consecutively in order of the cited tables or statistics.

· Marks for footnote should be given in order of \*, †, ‡, §, ||, ¶, \*\*, ††, ‡‡... When marks are used to explain items of the table, indicate them with superscripts.

· Define all abbreviations except those approved by the International System of Units. Define all abbreviations every time they are repeated.

### ⑨ Legends for figures and photographs

· All of the figures and photographs should be described in the text separately.

· The description order is the same as in the footnotes in tables and should be in recognizable sentences.

· Define all abbreviations every time they are repeated.

### (3) Figures and illustrations

① The KJA publishes in full color, and encourages authors to use color to increase the clarity of figures. Please note that color figures are used without charge for online reading. However, since it will be charged upon the publication, authors may choose to use colors only for online reading.

② Standard colors should be used (black, red, green, blue, cyan, magenta, orange, and gray). Avoid colors that are difficult to see on the printed page (e.g., yellow) or are visually distracting (e.g., pink). Figure backgrounds and plot areas should be white, not gray. Axis lines and ticks should be black and thick enough to clearly frame the image. Axis labels should be large enough to be easily readable, and printed in black.

③ Figures should be uploaded as separate tif, jpg, pdf, gif, ppt files. Width of figure should be 84 mm (one column). Contrast of photos or graphs should be at least 600 dpi. Contrast

of line drawings should be at least 1,200 dpi. Number figures as “Fig. (Arabic numeral)” in the order of their citation. (ex. Fig. 1).

④ Photographs should be submitted individually. If Figure 1 is divided into A, B, C and D, do not combine it into 1, but submit each of them separately. Authors should submit line drawings in black and white.

⑤ In horizontal and vertical legends, the letter of the first English word should be capitalized.

⑥ Connections between numbers should be denoted by “-”, not “~”. Do not space the numbers (ex. 2–4).

⑦ Figures (line drawings) should be clearly printed in black and white.

⑧ Figures should be explained briefly in the footnotes. The format is the same as the table format.

⑨ An individual should not be recognizable in the photographs or X-ray films unless written consent of the subject has been obtained and is provided at the time of submission.

⑩ Pathological samples should be pictured with a measuring stick.

#### (4) Other submission elements (Video submission)

The KJA publishes supplemental video (movie) clip(s) that will be available online. Not only recording of the abstract, text, audio or video files, but also data files should be added here.

Each video clip should clearly illustrate the primary findings within an adequate amount of viewing time and be discussed in the text. Authors should provide appropriate labeling (e.g., arrows, abbreviations of anatomic structures, etc.) in the video clips. However, all identifying information, including patient name and/or ID number, hospital name, and date of the procedure, should be removed.

Video clips should contain succinct teaching points that must be supported by the current literature or standard reference texts, preferably those most accessible to the general reader. The adequacy of the teaching points will be evaluated during the review process and finally confirmed by the editorial board at the end of the review process.

Video clips are uploaded as the last file(s) at the time of manuscript submission and should be marked as supplementary video files.

① The video clip(s) should have simple file names (e.g., Video 1\*\*\*, Video 2\*\*\*) and include the appropriate extension (e.g., .mov, .mpg).

② The maximum number of video clips is 20.

③ The video clip(s) should be playable on both Windows and MAC computers. The video clip(s) should be tested for play-

back before submission, preferably on computers not used for their creation, to check for any compatibility issues.

④ Individual video files should be a minimum of 480 x 320 pixels (smaller clips will not be accepted) and a maximum of 2 GB. Files of < 15 MB will be rejected outright unless special arrangements have been made with the editorial board prior to submission. Approval of files of > 2 GB will be made at the end of the review process.

⑤ Supplemental still images that correspond to the respective video clip(s) should be, but are not always required to be, accompanied by legends. The video clip file name(s) should refer to the corresponding figure number(s).

#### 2) Systematic review and meta-analysis

Systematic reviews are systematic, critical assessments of literature and data sources in order to answer a specific question, and/or includes a statistical technique leading to a quantitative summary of results and examining sources of differences in results among studies, if any. The subtitle should include the phrase “A systematic review” and/or “A Meta-analysis.”

Organization of systematic review and meta-analysis: Same as clinical and experimental studies, except,

- All systematic reviews and meta-analyses should be registered at an appropriate online public registry (eg, PROSPERO; <http://www.crd.york.ac.uk/PROSPERO/>), and registration information should be included with the submission.
- Authors of reports of meta-analyses of clinical trials should submit the PRISMA flow diagram. The PRISMA checklist should be submitted as a separate file along with the manuscript. For information regarding PRISMA guidelines, please visit <http://www.prisma-statement.org> or EQUATOR Network (<https://www.equator-network.org/home/>). Systematic reviews and meta-analyses of observational studies in epidemiology should be reported according to MOOSE guidelines. For more information regarding MOOSE guidelines, please visit <http://www.equator-network.org/reporting-guidelines/meta-analysis-of-observational-studies-in-epidemiology-a-proposal-for-reporting-meta-analysis-of-observational-studies-in-epidemiology-moose-group/>.
- No limitation the number of the references.

#### 3) Case Reports

A case report is almost never a suitable means to describe the efficacy of a treatment or a drug; instead, an adequately powered and well-controlled clinical trial should be performed to demonstrate such efficacy. The only context in which a case report can be used to describe efficacy is in a clinical scenario, or

population, that is so unusual that a clinical trial is not feasible.

Case reports of humans must state in the text that informed consent to publication was obtained from the patient or guardian. Authors should submit copies of written informed consents by using the online manuscript submission system. If it is unavailable, the IRB approval should be needed. Copy of IRB approval should be kept. If necessary, the editor or reviewers may request copies of these documents. Rarity of a disease condition is itself not an acceptable justification for a case report.

(1) Title page: Same as clinical and experimental studies.

(2) Manuscript

① Title and Running title.

② Abstract: All case reports should contain a structured abstract that is written only in English. Provide an abstract of no more than 150 words. It should contain 3 subsections: Background, Case, and Conclusions. A list of keywords, with a minimum of 6 and maximum of 10 items, should be included at the end of the abstract. The selection of keywords should be from MeSH (<http://www.ncbi.nlm.nih.gov/mesh>) and should be written in small alphabetic letters with the first letter in capital letter. Separate each word by a semicomma (;), and mark a period (.) at the end of the last word.

③ Introduction: Should not be separately divided. Briefly describe the case and background without a title.

④ Case report: Describe only the clinical statement that is directly related to diagnosis and anesthetic management.

⑤ Discussion: Briefly discuss the case, and state conclusions at the end of the case. Do not structure the conclusion section separately.

⑥ References: Do not exceed 15 references. For exceeding the number of references, it should be negotiated with the Editorial Board.

⑦ Tables and figures: Proportional to clinical and experimental studies.

4) Reviews

Review articles synthesize previously published material into an integrated presentation of our current understanding of a topic. Review articles should describe aspects of a topic in which scientific consensus exists, as well as aspects that remain controversial and are the subject of ongoing scientific disagreement and research. Review articles should include unstructured abstracts equal to or less than 250 words in English. Figures and tables should be provided in English. References should be obviously related to documents and should not be exceed 100. For exceeding the number of references, it should be negotiated with the Editorial Board. Body text should not exceed 30 A4

pages, and the number of figures and tables should be equal to or less than 6.

5) Letters to the Editor

Letters to the Editor also should include brief constructive comments on the articles published in KJA and interesting cases. Book reviews as well as news of scientific societies and scientific meeting dates in Korea or abroad can be included. Letters to the editor of humans must state in the text that informed consent to publication was obtained from the patient or guardian. Authors should submit copies of written informed consents by using the online manuscript submission system. If it is unavailable, the IRB approval should be needed. Copy of IRB approval should be kept. If necessary, the editor or reviewers may request copies of these documents. Letters to the Editor cover individual articles not described by any of the above categories. The short manuscripts with a constructive note on the Journal or the anesthesiology at large are welcome.

Cover pages should be formatted as those of clinical research papers. The body text should not exceed 1,000 words and should have no more than 5 references. For exceeding the number of references, it should be negotiated with the Editorial Board. A figure or a table may be used. A maximum of five authors is allowable. Letter may be edited by the Editorial Board and if necessary, responses of the author of the subject paper may be provided.

6) Statistical Round

A Statistical Round is a narrative review of the application of contemporary quantitative sciences to issues of concern to anesthesia researchers. A Statistical Round involves a focused discussion on one or more unique or interesting statistical analysis methods that has previously been published in this journal or expresses the general policies or opinions of the Statistical Round Board. They are solicited by the Statistical Round Board and reviewed by the Statistical Editor. There are no word limits to or rules regarding the structure of a Statistical Round. They should have an unstructured abstract of no more than 250 words in English. All articles in a Statistical Round will be published in English and translated into Korean for the convenience of Korean readers. The Korean version of the Statistical Round will be published only on the Web page of the Journal (<https://ekja.org>). The inclusion of sample datasets as Web (Supplemental) content is encouraged.

**8. Recently revised instructions for authors are applied from February 2021 submissions.**