Considerations regarding anesthesia for renal transplantation

Multimodal management strategies for chronic pain after spinal surgery: a comprehensive review

Challenging issues of implementing enhanced recovery after surgery programs in South Korea

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Aims and Scope

Anesthesia and Pain Medicine (APM) is the official journal of the following ten subsocieties of the Korean Society of Anesthesiologists: Korean Society of Neuroscience in Anesthesiology and Critical Care, the Korean Society for Anesthetic Pharmacology, the Korean Society of Obstetric Anesthesiologists, the Korean Society of Pediatric Anesthesiologists, the Korean Neuromuscular Research Society, the Korean Society of Cardiothoracic and Vascular Anesthesiologists, the Korean Society of Transplantation Anesthesiologists, the Korean Spinal Pain Society, the Korean Society of Regional Anesthesia, and the Korean Society for Airway Management. Its abbreviated title is “Anesth Pain Med”. It is published four times a year, in English, on the last days of January, April, July, and October.

APM aims to improve the safety and care of patients receiving anesthesia and the quality of anesthesiologists’ clinical practice by publishing articles on anesthesiology, including perioperative management, critical care, and pain medicine.

The scope of APM includes the following:
• Anesthesia-related issues from the affiliated field of neuroanesthesiology
• Experimental and laboratory work or studies of clinical relevance in anesthetic pharmacology
• Anesthesia care and perioperative management for obstetric patient, pain relief in labor, and perinatal physiology and pharmacology
• Anesthetic care, perioperative management, and alleviation of pain in children
• Physiology of neuromuscular transmission and blockage, the pharmacology of neuromuscular blocking agents and their reversal agents, the principles and applications of neuromuscular monitoring, and drug interactions between neuromuscular blocking agents and other substances
• Anesthesia for cardiothoracic and vascular surgery and the management of patients undergoing surgery for cardiac, pulmonary, and vascular diseases
• Perioperative anesthesia care of transplantation surgery, physiology or pharmacology related to transplantation anesthesia
• Pathophysiology, pharmacology, and all respects of spine-related pain
• Clinical techniques of regional blocks, anatomy, patient safety issues, and basic sciences such as pharmacology of local anesthetics or sedative drugs
• All fields of airway management, including difficult airways and complications
• Educational fundamentals and practical implications for clinical and experimental research related to anesthesia, perioperative care and pain management.

The journal’s regional focus is mainly Korea, but it welcomes submissions from researchers all over the world.

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In 2023, your journal *Anesthesia and Pain Medicine* (APM) was newly indexed in SCOPUS and the Directory of Open Access Journals (DOAJ). In the realm of anesthesiology, which encompasses perioperative management, critical care, and pain, APM has achieved significant progress, achieved acclaim, and strengthened its standing as a global journal.

We are privileged to hold the positions of Editor-in-Chief and Editorial Board members for APM. The editorial team has been, and remains, dedicated to ensuring the success of this exceptional publication.

Our main goals for APM in the coming years are to a) raise its profile in the clinical and research communities and advance its position as the top journal in this area; b) keep searching for and publishing excellent reviews and original articles that offer the most up-to-date clinical and research information; c) maintain the quality, standard, and transparency of our editorial and review process while fast-tracking our response time to submissions; and d) strengthen regional and global networks to better meet the needs of our society and scientific community.

To achieve these objectives, the APM editorial team will proactively pursue the latest and most captivating research papers and establish communication channels with subsocieties of the Korean Society of Anesthesiologists, members of the Korean Society of Anesthesiologists, and other academics worldwide specializing in this domain.

**JOURNAL METRICS AND STATISTICS**

The APM was first indexed in the Korean Citation Index in 2015 and PubMed Central in December 2020. In 2023, the APM was newly indexed in SCOPUS and DOAJ and applied to Embase coverage. The annual volume of articles submitted is approximately 100-150, and since 2020, the proportion of overseas submissions has escalated significantly. Currently, more than 60% of articles were from foreign countries. Detailed descriptions of the authors’ countries in 2021, 2022, and 2003 are presented in Fig. 1. The number of countries submitting articles to the APM increased to 11 to 19, since 2021.

The APM articles published in 2021 and 2022 were cited 118 times by Web of Science articles published in 2023 (available from https://www.webofscience.com/wos/woscc/...
The total number of original articles and reviews published in 2021 and 2022 were 32 and 40, respectively. The manually calculated impact factor for 2023 in the Web of Science was 1.639 (118/[32+40]). The three most cited articles since 2021 are “Trial sequential analysis: novel approach for meta-analysis” by Kang [1] (cited by 54), “Remimazolam: pharmacological characteristics and clinical applications in anesthesiology” by Kim [2] (cited by 45), and “Comparison of postoperative pulmonary complications between sugammadex and neostigmine in lung cancer patients undergoing video-assisted thoracoscopic lobectomy: a prospective double-blinded randomized trial” by Lee et al. [3] (cited by 17).

The CiteScore Tracker 2023 (last updated on January 5th, 2024, available from: https://www.scopus.com/sourceid/21101166816 Last accessed: 2024 January 11th) calculated by Scopus was 2.2 (509 citations to date/234 documents 2018 to date). The APM has been developed to publish 14 highly qualified reviews, 27 original articles, and 19 other items, including case reports, letters to the editor, and corrigenda in 2023.

**APPRECIATION TO REVIEWERS**

The APM editorial team expresses its sincere appreciation to the reviewers who generously dedicated their time to assessing manuscripts. Their contributions were vital for maintaining the integrity of the journal.

The names of the 172 reviewers in 2023 are listed below. The list is in alphabetical order of family names in Korean.

- Woon Seok Kang
- Hyoseok Kang
- Hoon Kang
- Jae Chul Koh
- Yu gyeong Kong
- Mi-Young Kwon
- Woojin Kwon
- Won-Kyoung Kwon
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- Sang Tae Kim
- Sang Hun Kim
- Seong-Hyop Kim
- So Yeon Kim
- Seung Hyun Kim
- Shin Hyung Kim
- Yeon-Dong Kim

*Fig. 1. Number of articles submitted to Anesthesiology and Pain Medicine in 2021, 2022, and 2023 according to the author's country.*
Young Sung Kim  Yonghee Park  Seung Zhoo Yoon  Hae Wone Chang
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Young Uk Kim  Jun-young Park  Ka Young Rhee  Kyoung-Woon Joung
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Won-joong Kim  Hue Jung Park  Myeong-jong Lee  Sung-moon Jeong
Eunsoo Kim  Seunguk Bang  Sangseok Lee  Seongtae Jeong
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Jung Eun Kim  Sung Hye Byun  Seung Young Lee  Jun-Young Chung
Jong-Yeop Kim  Kwang Suk Seo  Seung Cheol Lee  Ji Seon Jeong
Jonghae Kim  Young-Joo Seo  Ae Ryung Lee  Chan Jong Chung
Jun Hyun Kim  Jeong Hwa Seo  Oh haeng Lee  Suk Ju Cho
Ji Young Kim  Tae-Yun Sung  Wonjin Lee  Sung-Ae Cho
Jin-kyoung Kim  Ju-Tae Sohn  Yoon Kyung Lee  Sooyoung Cho
Jin-Tae Kim  Hee-Jeong Son  Jae Hoon Lee  Ah-Reum Cho
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Ha-yeon Kim  Young Song  Je Jin Lee  Han Bum Joe
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Hye Jin Kim  Sang-Wook Shin  Cheol Lee  Geun Joo Choi
Hyo-jin Kim  Seokyoung Shin  Chung-hun Lee  Dae-kee Choi
Hee Young Kim  Woo Jong Shin  Hae JIn Lee  Byung Moon Choi
Heezoo Kim  Won-jung Shin  Hyeon Jeong Lee  Seong-Soo Choi
Sungwon Na  Hwa Yong Shin  Ho Jin Lee  Yoon Ji Choi
Hyoe-seok Na  Woo-Seok Sim  Heeseung Lee  Eun-Su Choi
Sun Woo Nam  Eun-Jin Ahn  Junyong In  Eun Joo Choi
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**CONFLICTS OF INTEREST**

Jun Hyun Kim has been the associate editor of the *Anesthesiology and Pain Medicine* since 2023, and Hyun Kang has been an editor-in-chief of the *Anesthesia and Pain Medicine* since 2023. However, They were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.
AUTHOR CONTRIBUTIONS


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REFERENCES

Renal transplantation is the most common surgery for end-stage renal disease (ESRD) caused by a variety of different conditions. The first successful renal transplantation was reported in 1954 [1]. In more recent years, the one-year survival rates of deceased-donor grafts in the United States, Europe, Canada, Australia, and New Zealand have consistently exceeded 90% [2]. Living donor renal transplantation is widely performed in many African and Asian countries, whereas deceased donor renal transplantation is predominantly performed in some European countries [3].

The history of renal transplantation in South Korea began with the first living donor transplantation in 1969 and the first deceased donor transplantation in 1979 [4]. In 2021, 2,227 renal transplantations were performed in South Korea, with a one-year survival rate of 95.9% for deceased donors and 98.8% for living donor transplants [5].

Renal transplantation is recommended for patients with ESRD due to various underlying conditions. In the United States, the most prevalent indication for renal transplantation is nephropathy associated with hypertension and diabetes [6]. Renal transplantation is a highly complex surgical procedure that requires intricate anesthetic planning to en-
sure patient safety and optimal functioning of the transplanted kidneys. Herein, we aimed to comprehensively review considerations related to anesthesia in renal transplantation surgery.

**PREOPERATIVE MANAGEMENT**

**Preoperative optimization**

Preoperative assessment and optimization of identified risks can be applied to mitigate perioperative risks, such as cardiovascular, pulmonary, or other medical complications. Jaszcuk et al. [7] proposed the following recommendations: (1) Patients presenting with unstable coronary syndromes, decompensated heart failure, significant valvular disease, or arrhythmias should undergo reevaluation of their cardiac status. (2) Echocardiography should be performed in individuals with impaired ventricular function, valvular abnormalities, or a risk of developing pulmonary hypertension. (3) Cardiologist assessment is necessary for recipients with pulmonary systolic pressure exceeding 45 mmHg, and symptomatic patients should undergo pulmonary function testing. (4) Patients should cease smoking for a minimum of four weeks prior to surgery, and nicotine replacement therapy should therefore be offered to smokers. (5) Preoperative screening for frailty should be conducted to assess the patient risk.

**Preoperative anemia correction**

Anemia is prevalent among patients with chronic kidney disease (CKD), with higher rates in patients with stage 5 CKD [8]. Adverse outcomes, including increased mortality, infection, and iron overload, are all associated with blood transfusion [9]. Avoiding transfusions is recommended for potential kidney transplant recipients [10]. The consideration of erythropoiesis-stimulating agent treatment is recommended for renal transplantation recipients with hemoglobin levels < 9–10 g/dl [7].

**INTRAOPERATIVE MANAGEMENT**

**Intraoperative hemodynamic monitoring**

The primary objectives of intraoperative monitoring are to ensure adequate renal blood flow to the renal graft and maintain optimal intravascular volume status. The basic noninvasive monitoring methods include noninvasive blood pressure monitoring, electrocardiography, pulse oximetry [11]. Capnography, urine output monitoring, and temperature monitoring have also been implemented [11].

Owing to the high prevalence of significant cardiac comorbidities among patients, as well as the potential for recipients to become unstable during the intraoperative period, the use of a central venous catheter is recommended [12]. In the presence of a central venous catheter, it is possible to administer vasoactive drugs and monitor central venous pressure. However, central venous pressure is not considered a reliable indicator of fluid status or responsiveness [13].

An intra-arterial catheter can be used to continuously monitor arterial blood pressure and hemodynamic parameters, such as stroke volume, stroke volume variation, and cardiac output. Additionally, it can facilitate intermittent blood sampling for point-of-care laboratory testing, including the measurement of electrolytes (potassium and sodium), arterial oxygen partial pressure, arterial oxygen saturation, arterial carbon dioxide partial pressure, and glucose and hemoglobin concentrations. In patients with advanced coronary artery disease, ventricular dysfunction, and pulmonary hypertension, the use of a pulmonary artery catheter or transesophageal echocardiographic monitoring may be considered [14]. During renal transplantation, delayed graft function can occur if the mean arterial pressure (MAP) falls below 70 mmHg. Several studies have recommended maintaining an MAP range of 80–110 mmHg [7,15].

Adequate expansion of the intravascular volume through the administration of crystalloids or colloids has been shown to increase renal blood flow, leading to improved immediate graft function [11]. To avoid hypotension, the maintenance of an appropriate intravascular volume and control of anesthetic agents are necessary. If hypotension persists despite an adequate intravascular volume, administration of small doses of vasopressors may be considered [16]. Dopamine is not recommended owing to its potentially harmful effects [17], while norepinephrine is the preferred choice [18,19].

**Anesthetic technique**

Patients with ESRD are known to be at an increased risk of aspiration. To reduce this risk, the administration of an oral non-particulate antacid may be considered to increase gastric pH and an intravenous H-2 blocker can be administered to decrease gastric acid secretion prior to anesthesia induction [14].
General anesthesia is the most frequently used routine technique for renal transplantation [20]. Rapid sequence induction is preferred to prevent aspiration pneumonia [14].

1. **Induction of anesthesia**

Propofol and thiopental are both considered safe drugs to induce general anesthesia. Ketamine should be avoided in patients with ischemic heart disease (IHD) due to its potential for sympathetic stimulation. In contrast, etomidate may be a suitable choice for patients with IHD or impaired ventricular function owing to its high cardiovascular stability [7]. Fentanyl, alfentanil, sufentanil, and remifentanil can be safely used, whereas morphine should be avoided because of the potential for its metabolite morphine-6-glucuronide to cause end-stage renal failure [7].

2. **Maintenance of anesthesia**

In animal studies, sevoflurane has shown potential nephrotoxic effects linked to its metabolites, compound A, and fluoride ions. However, research conducted in humans has not provided evidence of any harmful effects on renal function [21,22]. Desflurane, isoflurane, and propofol can be used for anesthesia [7].

3. **Neuromuscular blocking agents and reversal agents**

Neuromuscular monitoring is recommended for patients with ESRD, especially those undergoing renal transplantation [12,23]. Succinylcholine can be administered when the serum potassium level is < 5 mEq/L [24]. The use of rocuronium and vecuronium is possible, although it may result in an increased duration of action [7]. Atracurium and cisatracurium are also used to promote organ-independent drug clearance. However, its metabolite laudanosine has the potential to induce seizures [7,14].

The clearance of the sugammadex-rocuronium complex is reduced in patients with ESRD as it is primarily eliminated through the kidneys. However, sugammadex appears to be safe and effective in renal transplant recipients [25,26].

**Perioperative glycemic control and temperature management**

Perioperative hyperglycemia can lead to unfavorable outcomes in both diabetic and nondiabetic patients [27]. The recommended blood glucose ranges vary slightly depending on the study, with ranges of 110-160 mg/dl [27] and 140-189 mg/dl [28,29] both being reported.

Perioperative hypothermia is associated with a variety of complications, including surgical site infection, coagulopathy, pain, prolonged response to neuromuscular blocking agents, adverse cardiac events, and longer hospital stay [30]. While research specifically on target body temperature in renal transplantation is not extensive, Jaszczuk et al. [7] recommend maintaining a minimum temperature of at least 36.5°C during surgery and checking the patient’s temperature every 30 min during surgery and every 15 min during the recovery phase.

**Diuretics and albumin**

Mannitol, an osmotic diuretic, is commonly administered in renal transplantation patients to induce rapid intravascular volume expansion, improve renal flow, protect against posttransplantation tubular necrosis, eliminate free radicals, and increase prostaglandin production [18,31,32]. The administration of 250 ml of 20% mannitol prior to reperfusion has been shown to enhance renal function and reduce the incidence of delayed graft function (DGF) during renal transplantation [23]. Excessive administration of mannitol can lead to adverse effects, including heart failure, pulmonary edema, and hypertonic kidney failure [31]. However, evidence supporting the efficacy of mannitol and other agents in reducing the incidence of acute tubular necrosis remains limited.

Furosemide (3–5 mg/kg) is routinely administered 10–15 min prior to clamp release during renal transplantation [7]. It exhibits nephroprotective effects by counteracting the antidiuretic hormone response and reducing renal oxygen consumption by blocking active tubular transport, which provides resistance against ischemia [24]. However, the evidence supporting the beneficial effects of furosemide in patients with acute kidney injury (AKI) is not robust [12,23]. Furthermore, there is research to indicate that low urine output following furosemide administration predicts the need for postoperative renal replacement therapy [33,34]. Finally, there is no significant advantage associated with the use of albumin compared with crystalloids in renal transplant recipients [35].

**POSTOPERATIVE MANAGEMENT**

The recommendations for enhanced recovery after surgery (ERAS) that can be applied to renal transplantation are listed in Table 1 [10].
Recommendation
Blood transfusion should be avoided in renal transplantation recipients. Response to iron treatment should be avoided. Cardiac output monitoring should be applied to assess fluid respon

Renal transplantation recipients should be offered exercise therapy two to three times a week, lasting more than 30 min.

Fluid overload should be avoided. Cardiac output monitoring should be applied to assess fluid respon

It is advisable for patients to discontinue smoking for a minimum of four weeks prior to surgery, and nicotine replacement therapy should therefore be offered to individuals who smoke. Cessation of high-risk alcohol consumption for a period of four to eight weeks before the surgical procedure is further recommended. Preoperative screening for frailty is advised as part of the risk assessment process.

Renal transplantation recipients should be offered exercise therapy two to three times a week, lasting more than 30 min.

Renal transplantation recipients should be evaluated, and malnourished patients should be referred to a dietician. Diet and exercise advice should be provided to all obese renal transplantation recipients.

A drink containing at least 45 g of carbohydrates should be offered to all patients, except those with diabetes mellitus or anticipated delayed gastric emptying.

Blood transfusion should be avoided in renal transplantation recipients. Response to iron treatment should be assessed in patients with anemia. ESA treatment should be considered for anemic renal transplantation recipients with hemoglobin levels of 90-100 g/L, and a balance should be maintained between the benefits of reducing blood transfusion and risk of side effects. Do not start ESA in patients with iron deficiency.

Anxiolytic should be administered to anxious patients before anesthesia. Avoid routine use of sedative agents.

For patients diagnosed with gastroparesis, it is recommended to administer proton pump inhibitors or H2 inhibitors. It is important to avoid using anesthetic agents that have a tendency to accumulate in individuals with end-stage renal disease. During surgery, it is crucial to prevent hypotension, and to maintain mean arterial pressure levels above 80 mmHg. Noradrenaline can be considered as a vasoconstrictor if required. Prior to reperfusion, the administration of 250 ml of 20% mannitol is recommended. Patients with oliguria experiencing post-transplant metabolic acidosis should be offered dialysis as a treatment option.

A drink containing at least 45 g of carbohydrates should be offered to all patients, except those with diabetes mellitus or anticipated delayed gastric emptying.

Blood transfusion should be avoided in renal transplantation recipients. Response to iron treatment should be assessed in patients with anemia. ESA treatment should be considered for anemic renal transplantation recipients with hemoglobin levels of 90-100 g/L, and a balance should be maintained between the benefits of reducing blood transfusion and risk of side effects. Do not start ESA in patients with iron deficiency.

Anxiolysis
Anxiolytic should be administered to anxious patients before anesthesia. Avoid routine use of sedative agents.

Anesthetic protocol
For patients diagnosed with gastroparesis, it is recommended to administer proton pump inhibitors or H2 inhibitors. It is important to avoid using anesthetic agents that have a tendency to accumulate in individuals with end-stage renal disease. During surgery, it is crucial to prevent hypotension, and to maintain mean arterial pressure levels above 80 mmHg. Noradrenaline can be considered as a vasoconstrictor if required. Prior to reperfusion, the administration of 250 ml of 20% mannitol is recommended. Patients with oliguria experiencing post-transplant metabolic acidosis should be offered dialysis as a treatment option.

Perioperative fluid management
Fluid overload should be avoided. Cardiac output monitoring should be applied to assess fluid responsiveness. Balanced crystalloids should be administered.

Glycemia should be maintained within the recommended range of 140-180 mg/dl in the perioperative period.

During the surgical procedure, it is essential to ensure that the patient's core temperature remains at a minimum of 36.5 °C. Temperature monitoring should be conducted every 30 min intraoperatively and every 15 min during the recovery period.

Implementing strategies for reducing opioid usage in pain management; employing multimodal analgesia, including non-opioid analgesics, opioids, and regional anesthesia techniques; utilizing self-reporting scales to assess and promptly address moderate to severe pain; initiating oral analgesics as soon as the patient can tolerate oral intake.

Risk stratification and postoperative nausea and vomiting prophylaxis should be administered for all patients.

The risk of delirium should be minimized. Cerebral monitoring should be performed in elderly patients during anesthesia. We recommend postoperative screening for postoperative delirium and early management.

Early mobilization after surgery should be performed.

An early return to oral diet should be ensured. Enteral and parenteral nutrition should be administered when recommended.

Table 1. Recommendations for ERAS That Can Be Applied to Renal Transplantation [7]

<table>
<thead>
<tr>
<th>ERAS intervention</th>
<th>Recommendation</th>
</tr>
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<tbody>
<tr>
<td>Preoperative optimization</td>
<td>Patients presenting with unstable coronary syndromes, decompensated heart failure, significant valvular disease, or arrhythmias should undergo reevaluation of their cardiac status, particularly when under consideration of renal transplantation. Echocardiography should be considered for individuals with impaired ventricular function or valvular abnormalities, as well as those at risk of developing pulmonary hypertension. Recipients with pulmonary systolic pressure exceeding 45 mmHg should undergo assessment by a cardiologist. Symptomatic patients should undergo pulmonary function testing.</td>
</tr>
<tr>
<td>Patient education</td>
<td>It is advisable for patients to discontinue smoking for a minimum of four weeks prior to surgery, and nicotine replacement therapy should therefore be offered to individuals who smoke. Cessation of high-risk alcohol consumption for a period of four to eight weeks before the surgical procedure is further recommended. Preoperative screening for frailty is advised as part of the risk assessment process.</td>
</tr>
<tr>
<td>Pre-habilitation</td>
<td>Renal transplantation recipients should be offered exercise therapy two to three times a week, lasting more than 30 min.</td>
</tr>
<tr>
<td>Improving nutritional status</td>
<td>Renal transplantation recipients should be evaluated, and malnourished patients should be referred to a dietician. Diet and exercise advice should be provided to all obese renal transplantation recipients.</td>
</tr>
<tr>
<td>Carbohydrate drink before surgery</td>
<td>A drink containing at least 45 g of carbohydrates should be offered to all patients, except those with diabetes mellitus or anticipated delayed gastric emptying.</td>
</tr>
<tr>
<td>Anemia correction</td>
<td>Blood transfusion should be avoided in renal transplantation recipients. Response to iron treatment should be assessed in patients with anemia. ESA treatment should be considered for anemic renal transplantation recipients with hemoglobin levels of 90-100 g/L, and a balance should be maintained between the benefits of reducing blood transfusion and risk of side effects. Do not start ESA in patients with iron deficiency.</td>
</tr>
<tr>
<td>Anxiolysis</td>
<td>Anxiolytic should be administered to anxious patients before anesthesia. Avoid routine use of sedative agents.</td>
</tr>
<tr>
<td>Anesthetic protocol</td>
<td>For patients diagnosed with gastroparesis, it is recommended to administer proton pump inhibitors or H2 inhibitors. It is important to avoid using anesthetic agents that have a tendency to accumulate in individuals with end-stage renal disease. During surgery, it is crucial to prevent hypotension, and to maintain mean arterial pressure levels above 80 mmHg. Noradrenaline can be considered as a vasoconstrictor if required. Prior to reperfusion, the administration of 250 ml of 20% mannitol is recommended. Patients with oliguria experiencing post-transplant metabolic acidosis should be offered dialysis as a treatment option.</td>
</tr>
<tr>
<td>Perioperative fluid management</td>
<td>Fluid overload should be avoided. Cardiac output monitoring should be applied to assess fluid responsiveness. Balanced crystalloids should be administered.</td>
</tr>
<tr>
<td>Perioperative glycemic control</td>
<td>Glycemia should be maintained within the recommended range of 140-180 mg/dl in the perioperative period.</td>
</tr>
<tr>
<td>Temperature management</td>
<td>During the surgical procedure, it is essential to ensure that the patient's core temperature remains at a minimum of 36.5 °C. Temperature monitoring should be conducted every 30 min intraoperatively and every 15 min during the recovery period.</td>
</tr>
<tr>
<td>Perioperative pain control</td>
<td>Implementing strategies for reducing opioid usage in pain management; employing multimodal analgesia, including non-opioid analgesics, opioids, and regional anesthesia techniques; utilizing self-reporting scales to assess and promptly address moderate to severe pain; initiating oral analgesics as soon as the patient can tolerate oral intake.</td>
</tr>
<tr>
<td>Prevention of PONV</td>
<td>Risk stratification and postoperative nausea and vomiting prophylaxis should be administered for all patients.</td>
</tr>
<tr>
<td>Prevention of delirium</td>
<td>The risk of delirium should be minimized. Cerebral monitoring should be performed in elderly patients during anesthesia. We recommend postoperative screening for postoperative delirium and early management.</td>
</tr>
<tr>
<td>Bed rest and early mobilization</td>
<td>Early mobilization after surgery should be performed.</td>
</tr>
<tr>
<td>Nutrition after surgery</td>
<td>An early return to oral diet should be ensured. Enteral and parenteral nutrition should be administered when recommended.</td>
</tr>
</tbody>
</table>


**Perioperative pain control**

Significant variations in pain after renal transplantation have been reported, with some patients experiencing severe and challenging pain management [7,14]. The pharmacokinetics of most opioid medications are altered in patients with renal failure, necessitating dose reduction. Furthermore, postoperative pain in renal transplant recipients can...
be influenced by pre-existing chronic pain conditions and opioid dependence, which are prevalent in 40-60% of dialysis patients [36].

According to the ERAS guidelines, multimodal analgesia, including opioids, non-opioid analgesics, and regional anesthesia, is recommended to optimize postoperative pain control, facilitate early recovery, and expedite oral intake and mobilization. The guidelines also highlight the importance of using self-reporting scales to assess and promptly manage moderate-to-severe pain and initiating oral analgesia as soon as the patient is able to tolerate oral intake [7].

Prevention of postoperative delirium

Postoperative delirium (POD) can occur in renal transplant recipients, particularly those who are vulnerable or frail. This condition is characterized by an acute decline in cognitive function and presents with inattention, impaired consciousness, disorientation, memory impairment, hallucinations, delusions, and psychomotor disorders. POD, which can occur in up to 50% of older surgical patients, is further associated with adverse outcomes, including prolonged length of hospital stay, graft loss, and mortality. Appropriate interventions can reduce the incidence of POD by 40% [37]. To prevent POD, routine premedication with benzodiazepines and anticholinergic drugs should be avoided [7]. Non-pharmacological preventive measures, such as cognitive orientation, sensory enhancement with visual/hearing aids, noise reduction, optimizing sleep hygiene, avoiding unnecessary internal catheters, medication reviews, early mobilization, and ensuring good nutrition are all recommended [38].

Cerebral monitoring is recommended in elderly patients undergoing anesthesia. In addition, screening for POD is crucial. Early detection via screening enables prompt management and intervention [7].

CONCLUSION

Renal transplantation is not only an important surgery that saves the lives of patients, but is also important to their family members. Similar to the surgery itself, anesthesia plays a significant role in renal transplantation. As such, it is crucial for anesthesiologists to be involved in the entire process, from preoperative preparation to postoperative care. Preoperative optimization involves the identification and management of risks to reduce perioperative complications. Intraoperative management focuses on monitoring hemodynamics, maintaining intravascular volume, and carefully selecting anesthetic techniques. Neuromuscular monitoring and appropriate utilization of neuromuscular blocking and reversal agents are crucial. Hemodynamic targets include maintenance the mean arterial pressure between 80-110 mmHg. Perioperative attention is required to monitor anemia, glycemic control, temperature regulation, and diuretic use. In postoperative management, multimodal analgesia and prevention of postoperative delirium contribute to optimal recovery. Overall, optimal outcomes are achieved when surgeons, anesthesiologists, and other healthcare professionals all work together with patients.

FUNDING

None.

CONFLICTS OF INTEREST

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

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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INTRODUCTION

Recently, as the frequency of spinal surgery has increased, the incidence of failed back surgery syndrome (FBSS), in which patients experience postoperative pain, has also increased.

The International Association for the Study of Pain (IASP) defines FBSS as "lumbar spinal pain of unknown origin either persisting despite surgical intervention or appearing after surgical intervention for spinal pain originally in the same topographical location" [1]. It is a non-specific term that generally refers to an event wherein the final outcome of surgery does not meet the preoperative expectations of patients and surgeons [2].

This refers to cases in which pain does not decrease but rather increases, or other complications occur after spinal surgery. Although it is a term that does not assume negligence on the part of the medical staff, the meaning of the word 'failed' it is associated with medical staff’s negligence. To avoid this, FBSS was referred to with other terms that did not imply surgical failure, such as post-laminectomy syndrome, post-spine surgery syndrome, and post-lumbar surgery syndrome. The International Classification of Diseases (ICD)-11 published by the World Health Organization in June 2018 called FBSS “chronic pain after spinal surgery” (CPSS) [3]. In this review, we will refer to FBSS as CPSS in accordance with the ICD-11 classification.

CPSS is difficult to treat for spinal surgeons who perform surgery and pain physicians responsible for pain management. Since pain persists even after spinal surgery, patients with post-spinal surgery syndrome often distrust medical staff and treatments during their outpatient visits, hindering further treatment.

Therefore, physicians involved in pain management...
should identify the cause of pain and become familiar with the most suitable treatment for each situation in advance. Herein, we reviewed the overall aspects of CPSS and introduced treatments (including interventional procedures) that may be effective for pain management.

**ETIOLOGY**

A single cause for CPSS is difficult to determine. Pain typically results from a combination of factors. The etiological factors for CPSS have been divided into patient, operative, and postoperative factors (Table 1).

**Patient factors**

Appropriate surgery that meets the clinical conditions must be performed to achieve optimal outcomes in spinal surgery. If the chosen surgery is not suitable for a patient’s structural problems, there is a high probability that pain will persist postoperatively.

Undiagnosed or inadequately treated spinal stenosis at nonoperative levels can exacerbate pain and limit surgical success [4]. If the patient mainly shows axial back pain and undergoes decompression or intervertebral disc resection without fusion, the conducted surgery cannot be considered the most suitable for the patients’ clinical problem; thus, the pain will likely to continue postoperatively.

Preoperative magnetic resonance imaging (MRI) studies have shown that patients’ psychosocial factors are more powerful than the structural abnormalities, and that patients’ depression, anxiety disorders, somatization disorders, and health concerns have a negative impact on the prognosis of spinal surgery [5-7]. Therefore, it is more desirable to identify the psychosocial factors of the patient, prepare for proper preoperative treatment, actively implement postoperative pain education, and request cooperation from the Department of Psychiatry if necessary. It is important to accurately identify the psychosocial predisposition of patients before surgery and establish a treatment plan accordingly.

The economic impact of issues such as litigation or workers’ compensation is also known to affect CPSS. These factors can create complex issues such as secondary gains, which may hinder patients’ motivation for pain improvement after surgery. Several studies have shown that financial compensation concerns inappropriately affect all outcomes, including postoperative pain severity, postoperative opioid use, postoperative functional improvement, and emotional stability [8-10]. Smoking is also associated with increased preoperative or postoperative complications such as impaired wound healing, increased infection rates, and increased spinal nonunion [11,12]. These results indicate that behavioral modification should also be recommended for successful surgery.

**Operative factors**

Spinal surgery includes surgery to improve lower extremity pain (e.g., decompression of a nerve root or intervertebral disc resection to treat spinal nerve symptoms) and surgery to improve axial back pain (e.g., fusion to treat intervertebral disc pain or instability) [13,14].

Common operative factors for CPSS include incomplete

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**Table 1. Summary of Factors Leading to Chronic Pain after Spinal Surgery**

<table>
<thead>
<tr>
<th>Patient factors</th>
<th>Operative factors</th>
<th>Postoperative factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back pain from multiple pathologies</td>
<td>Incomplete decompression</td>
<td>Degenerative changes</td>
</tr>
<tr>
<td>Undiagnosed</td>
<td>Residual disc herniation</td>
<td>New onset foraminal stenosis</td>
</tr>
<tr>
<td>Adjacent segment disease</td>
<td>Hardware complications</td>
<td>New &amp; recurrent disc herniation</td>
</tr>
<tr>
<td>Preoperative psychiatric disorders (depressive and anxiety)</td>
<td>Implant migration</td>
<td>Scar tissue formation</td>
</tr>
<tr>
<td>Litigation</td>
<td>Screw loosening</td>
<td>Epidural fibrosis</td>
</tr>
<tr>
<td>Worker’s compensation</td>
<td>Fusion failure</td>
<td>Infection</td>
</tr>
<tr>
<td>Smoking</td>
<td>Non-union</td>
<td>Altered biomechanics</td>
</tr>
<tr>
<td></td>
<td>Pseudoarthrosis</td>
<td>Joint, muscular hypertrophy, atrophy, and spasm</td>
</tr>
</tbody>
</table>

www.anesth-pain-med.org
decompression, nerve damage, adjacent segment disease, and residual disc herniation. If the surgical procedure does not adequately relieve pressure on the nerves or remove the source of pain, patients may continue to experience symptoms [1].

CPSS also occurs when the effects of surgery on the motion segment are not fully considered. For example, suppose a patient with lower extremity pain has spinal stenosis and very weak spondylolisthesis, and if decompensation is performed without fusion, spondylolisthesis progresses and progressive back pain develops in many cases. Suboptimal removal of compressive structures, such as herniated discs or bone spurs, can leave residual pressure on the neural structures, contributing to CPSS [15].

Hardware-related issues such as implant migration, screw loosening, irritation, and adjacent segment degeneration may necessitate revision surgery and contribute to CPSS [16]. Pain may also occur around the screw, causing chronic irritation of the surrounding soft tissue and bursa formation. Non-union or pseudarthrosis occurs when fusion surgery fails. Some non-union patients experience pain, but there are also patients who experience no pain [17]. Surgical alterations can increase stress on adjacent segments, leading to accelerated degeneration and CPSS [18]. If the nerve root is excessively pulled or damaged during surgery, pain may occur owing to abnormal nerve function after surgery. The larger the surgery with excessive incisions, the more severe the damage to muscles and ligaments, and the higher the possibility of adhesions around the nerves after surgery, which increases the likelihood of developing CPSS [19].

**Postoperative factors**

Even if the surgery is successful, the possibility of recurrence remains. The recurrence of foraminal stenosis or intervertebral disc herniation may be due to the worsening of an existing disease, incomplete surgery, or changes in the structures around the surgery [20]. Spinal fusion surgery can place additional stress on the adjacent vertebrae, leading to accelerated degeneration and pain in those segments [21]. In some cases, spondylolisthesis or spinal stenosis progresses rapidly due to increased dynamics in the adjacent segments above and below the surgical site. This can lead to spinal instability.

After spinal surgery, fibrous scar tissue can form around the surgical site, leading to compression or irritation of the nerves and this can result in pain and other neurological symptoms [22]. Epidural fibrosis results in the epidural space due to spinal surgery-related fibrosis is about 20–36% of all patients after spinal surgery experience pain due to epidural adhesion [23]. Some of the direct and indirect causes of pain are pulling of spinal nerves due to epidural adhesion, ischemia, and obstruction of the flow of cerebrospinal fluid, which supplies nutrients around the nerves, [23]. However, fibrosis inevitably occurs in almost all patients during spinal surgery, and there has been an ongoing controversy as to whether this phenomenon is necessarily connected to pain and why each patient has a different prognosis [24].

Infections usually occur early but sometimes do not become apparent until weeks or months have passed. If accidental durotomy is not detected, it may lead to a pseudo-meningocele [25].

Altered biomechanics due to back surgery can result in increased tension in the prevertebral and postvertebral muscles that directly control the movement of the spine. Increased tension in these muscles can lead to stiffness, inflammation, spasms, and fatigue, all of which can cause pain in the paraspinal areas of the back [26].

**ASSESSMENT**

**History taking**

History taking is the most important part of evaluating CPSS patients. This is because it not only provides the information necessary to interpret other diagnostic factors but also serves as the basis for evaluation. Through history taking, pain physicians can gather essential information about a patient’s symptoms, medical history, and psychosocial factors [27]. The most important aspect of history-taking is to thoroughly describe the current pain, compare the pain before and after surgery, progress of pain recurrence over time, and pain responses to specific activities. It is also important to analyze whether the type of surgery performed on the patient is appropriate for the preoperative symptoms.

If the pain before and after surgery was almost the same in terms of severity, pain area, characteristics, and response to physical examination, then the problematic condition has not been corrected. This may be a diagnostic error, error of appropriate surgical selection, or incomplete surgery. However, if the symptoms change significantly, it is very likely that a new pathological condition has occurred, which could be a complication of surgery, technical failure, or progression of an underlying disease.
If back pain does not improve at all or recurs within days to months of surgery, it is highly likely that the pathology of the symptomatic structure was not properly resolved during the surgery, or the surgery could have been performed at the wrong level leading to complications, or an incorrect surgery was performed on a specific patient. If pain is partially relieved, it means that only some of the structural problems were corrected.

Similar to other common spinal diseases, the use of red and yellow flag concepts when evaluating CPSS patients can be an effective approach. Red flags are potential indicators of severe underlying conditions requiring immediate attention and further investigation. Identifying red flags can prevent potentially life-threatening or destructive situations from being overlooked through appropriate diagnostic testing and management. In contrast, yellow flags are psychosocial factors that can increase the risk of chronicity or disability in CPSS patients. Identifying and resolving yellow flags can guide appropriate referrals for psychological support and help manage overall pain. The typical red and yellow flags reported for CPSS are listed in Table 2 [28].

### Table 2. Identification of Red and Yellow Flags in Chronic Back Pain after Spinal Surgery

<table>
<thead>
<tr>
<th>Red flags</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recent trauma</strong></td>
<td>Onset &lt; 20 or &gt; 50 years</td>
</tr>
<tr>
<td><strong>Indicates possible nerve involvement and requires urgent attention</strong></td>
<td></td>
</tr>
<tr>
<td><strong>History of cancer</strong></td>
<td>Any trauma, minor or major, especially in people &gt; 50 years old</td>
</tr>
<tr>
<td><strong>Indicates possible nerve involvement and requires urgent attention</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Unexplained weight loss</strong></td>
<td>Especially if new back pain in patients with known cancer history</td>
</tr>
<tr>
<td><strong>Can indicate cancer or systemic disease</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Failure to improve</strong></td>
<td>Pain not improving after 4-6 weeks of appropriate conservative treatment</td>
</tr>
<tr>
<td><strong>Night pain</strong></td>
<td>Pain that wakes you up at night</td>
</tr>
<tr>
<td><strong>Fever, chills, sweats</strong></td>
<td>May indicate infection or systemic disease</td>
</tr>
<tr>
<td><strong>History of intravenous drug use</strong></td>
<td>Often indicates a serious condition</td>
</tr>
<tr>
<td><strong>History of long-term steroid use</strong></td>
<td>Increased risk of infection</td>
</tr>
<tr>
<td><strong>Neurologic symptoms</strong></td>
<td>Increased risk of osteoporosis and vertebral fractures</td>
</tr>
<tr>
<td><strong>Bowel or bladder dysfunction</strong></td>
<td>Such as weakness, numbness, or altered sensation in lower extremities</td>
</tr>
<tr>
<td><strong>Severe or progressive neurological deficit</strong></td>
<td>Could indicate cauda equina syndrome, a surgical emergency</td>
</tr>
<tr>
<td><strong>Yellow flags</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Fear-avoidance behavior</strong></td>
<td>Avoiding movement due to fear of causing more pain</td>
</tr>
<tr>
<td><strong>Belief that pain means harm</strong></td>
<td>Incorrectly associating all pain with harm can inhibit recovery</td>
</tr>
<tr>
<td><strong>Catastrophizing</strong></td>
<td>An exaggerated negative view of the pain’s impact</td>
</tr>
<tr>
<td><strong>Expectation of passive treatments only participation</strong></td>
<td>Belief that only treatments performed on the person (like surgery, injections) will help, rather than active</td>
</tr>
<tr>
<td><strong>Depression, anxiety, or Stress</strong></td>
<td>Psychological factors can influence the perception of pain and recovery</td>
</tr>
<tr>
<td><strong>Over-reliance on medication</strong></td>
<td>May indicate lack of active coping strategies</td>
</tr>
<tr>
<td><strong>Poor job satisfaction or difficulties at work</strong></td>
<td>Could influence chronicity and disability</td>
</tr>
</tbody>
</table>

Data from the article of Miękisiak (Medicina (Kaunas) 2023; 59: 1255) [28].

### Imaging

Simple radiographs with an upright flexion/extension lateral view can determine the surgical location, arrangement of the spine, imbalance of the spine, instability, and degenerative changes. It can also be used to determine the degree of intervertebral space stenosis, anterior spondylolisthesis, and pseudoarthrosis when fusion is performed [29].

Computed tomography (CT) can scan the surrounding area where spinal instruments are inserted more accurately than MRI can. Degenerative changes in the area adjacent to the surgical site, worsening of spondylolisthesis, and degenerative changes in the facet joint are easy to identify. CT myelogram can better reveal areas where spinal nerves are compressed by bony structures [30]. In addition, CT myelogram is a useful alternative because the presence of metallic implants can reduce the quality of images and the usefulness of diagnosis if the use of MRI is limited [31].

MRI is useful for detecting structural abnormalities such as herniated discs, fibrosis, infection, or hardware-related issues (e.g., screws or rods misplacement). It can also indicate...
a compression of the spinal nerves or nerve roots owing to disc protrusion or stenosis. Identifying nerve compression is crucial because it can explain the patients’ pain, and guide treatment decisions [32,33]. Information provided by MRI can help determine the appropriate course of treatment for CPSS patients, including further surgery, conservative management, or pain management techniques.

Technetium-99 single-photon emission computed tomography (SPECT) shows the anatomical sites of the radiotracer uptake, revealing enhancement of inflammatory areas, osteoblastic bone remodeling activity, and subtle segmental instability responsible for pain generation [34]. Various studies have investigated SPECT, identifying it as a promising technique for locating the foci of aseptic inflammation that serve as potential pain generators to help determine appropriate invasive or non-invasive treatment strategies [35]. It has therefore been proposed as a valuable tool for the localization of axial neck or back pain in patients who continue to experience unexplained CPSS [36].

Positron emission tomography (PET) can identify areas of inflammation, infection, or metabolic abnormalities in the spine [37]. PET is not routinely used for CPSS but can provide additional information when other imaging modalities yield inconclusive findings [38].

Diagnostic procedures

CPSS patients require examination because the facet joints and sacroiliac joints can cause pain [39]. Diagnostic articular injection is the standard method for diagnosing facet joint and sacroiliac joint syndrome [40]. CPSS may also result from disc herniation; in this case, a method of causing pain through lumbar discography is proposed [41]. It is important to determine the cause of lower extremity radiating pain in CPSS patients through physical examination and MRI to determine the area of spinal nerve compression. A transforaminal epidural block may be used to investigate whether nerves that appear compressed on MRI or CT are the pain-causing factors [42].

Epiduroscopy is the best minimally invasive method for visualizing the epidural space without damaging anatomical structures. It can be used to detect fibrosis, dissolve adhesions, and administer drugs to conventional fibrotic bands [43]. In CPSS patients, epiduroscopy can confirm epidural fibrosis and immediately confirm adhesion dissolution even if MRI reveals normal findings [44].

MANAGEMENT STRATEGIES

Persistent or recurrent pain associated with CPSS can severely impact a patient’s quality of life, making it imperative to explore innovative pain management strategies beyond traditional approaches. Multimodal pain management, which combines various interventions, can be promising management strategy in the complex nature of CPSS.

Causative treatments

In CPSS patients, corrective treatments such as spinal stabilization, fusion, or decompression procedures, or interactive treatment are the rational first-line approach when the underlying cause for the associated pain is evident. For example, in surgical cases of inadequate decompression or fusion failure, intraoperative factors, inappropriate treatment, or also in non-surgical cases of pain.

Conservative management

1. Physical therapy

Physical therapy plays a crucial role in the management of CPSS by improving mobility, strength, and overall function. It can also address musculoskeletal imbalances that contribute to pain [45]. Advanced physical therapy, including targeted exercises and stretching therapy can benefit CPSS patients because these methods address musculoskeletal imbalances, promote flexibility, and improving the overall function. These therapies should be individualized to patients’ specific condition and needs [46]. Chiropractic and osteopathic manipulations are alternative therapies that involve manual manipulation of the spine and musculoskeletal system. Although some CPSS patients may consider these therapies for pain relief or symptom management, they should be approached with caution. These treatments help relieve certain types of pain and improve functional abilities [47,48].

2. Pharmacological management

Before pharmacologically managing pain, it is important to understand the characteristics of pain (such as nociceptive or neuropathic pain) and its effects on daily life. Nociceptive pain is caused by tissue damage or inflammation and can be treated with nonsteroidal anti-inflammatory drugs (NSAIDs) [49]. If these are ineffective, non-opioid medications, such as high-dose NSAIDs, cyclo-oxygenase-2 (COX-2) inhibitors, or short-term corticosteroids can be in-
1. Epidural blocks

Epidural blocks are the most common pain treatment worldwide. This procedure is primarily considered for patients experiencing pain after spinal surgery when conservative treatment is ineffective (Fig. 1). Epidural steroid injections can be used to diagnose and establish a treatment plan for CPSS by selecting an appropriate approach based on the patients’ symptoms [3].

2. Facet joint procedures

In cases where facet joint pathology contributes to CPSS, corticosteroid or anesthetic injections into the affected joints can provide diagnostic and therapeutic benefits [60]. Radiofrequency ablation can be performed in anticipation of a 6-24 month reduction in pain if a diagnostic medial branch or facet joint block provides positive results in patients with CPSS caused by a facet joint (Fig. 2) [61].

3. Epidural adhesiolysis

In any surgery, postoperative scar formation is a natural phenomenon during the tissue healing process. The same is true for the formation of epidural fibrotic adhesions after spinal surgery, but these adhesions may compress the nerve roots in 20-36% of patients, causing back or lower extremity pain [23]. Theoretically, adhesions can be lysed, thereby minimizing pain scores. Epidural adhesiolysis can be performed with hyaluronidase or hypertonic saline, and the combination of steroids and hyaluronidase may be more effective and last longer than either steroid alone [62]. Patients with epidural adhesions who are treated with hyaluronidase via a fluoroscopy-guided catheter can experience a significant decrease in pain score, disability index, and functional improvement (Fig. 3) [63]. Epidural adhesiolysis is more effective than epidural steroid injections [64].

The use of balloon expansion in the epidural space has also been recently introduced [65]. The method of including the balloon expansion function in the endoscopic catheter has the advantage of safely and effectively removing adhesions in a slightly wider area than that affected by the existing method because the balloon expansion function is included in the function of the existing catheter. However, more research is required for this.

Epiduroscopy makes it easy to remove adhesions while directly checking the area [66,67]. It achieves good long-term results in approximately 40% of CPSS patients who do not respond to other conventional treatments such as adhesiolysis with a Racz catheter [43,68]. A systematic review showed that pain and disability scores were clinically relevant 6-12 months after mechanical adhesiolysis in CPSS patients. The common complications associated with epiduroscopy in-
Fig. 1. (A) Anterior posterior view of caudal epidural block. (B) Lateral view of caudal epidural block. (C) Anterior posterior view of transforaminal epidural block at the left L5/S1 level. (D) Lateral view of transforaminal epidural block at the left L5/S1 level.

Fig. 2. (A) Anterior posterior view of lumbar medial branch block at the right L4 level. (B) Oblique view of facet joint block at the right L4/5 level.
include nerve injury, bleeding, infection, macular hemorrhage, and intracranial pressure [69,70].

4. Neuromodulation

Spinal cord stimulation (SCS) and intrathecal drug delivery systems (IDDS) have been shown to have promising effects in managing CPSS. These techniques can modulate pain signals and improve function [71,72]. SCS or IDDS can be used for refractory pain patients who do not respond to conventional treatment for CPSS. But, given the complications and management problems associated with after insertion, care should be taken when selecting this procedure.

Considerations for surgical revision

Revision surgery may be considered when the CPSS results from technical errors, inadequate decompression, or hardware-related issues. Careful patient selection and multidisciplinary teams are essential for successful outcomes [9]. However, revision surgery for CPSS has a low success rate and high morbidity risk. In patients who underwent instrumental fusion for CPSS treatment, only 35% reported a reduction in pain for approximately 15 months [73]. The absolute indications for revision surgery are the progression of neurological damage due to decreased functioning of organs or bladders, muscle weakness, and spinal nerve damage; and the relative indications are severe sciatica that persists or worsens despite 4 weeks of complete bed rest, recurrent
episodes of incapacitating sciatica, pseudoarthrosis, abnormalities, or instability of surgical instruments [52].

CONCLUSION

CPSS is expected to occur continuously as long as spinal surgeries are performed. The greatest difficulty in its treatment is that patients are less responsive to conservative treatment, and nonsurgical treatment often does not result in satisfactory improvement. Multimodal pain management approaches represent a promising avenue for addressing the complex and debilitating nature of CPSS. Combining various methods, including pharmacological, interventional, physical, psychological, and complementary therapies allows for a holistic approach to pain relief. Although individual responses to these treatments vary, tailored multimodal approaches can significantly improve the quality of life for CPSS patients. Further research and personalized treatment plans are essential to optimize the outcomes in this challenging patient population.

FUNDING

None.

CONFLICTS OF INTEREST

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

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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INTRODUCTION

Enhanced recovery after surgery (ERAS) is a comprehensive perioperative care concept that focuses on an evidence-based, multidisciplinary, standardized, and patient-centered approach [1] with the aim of minimizing perioperative stress and enhancing the quality of postoperative recovery [2]. With its proven efficacy, ERAS has demonstrated remarkable benefits, including a reduction in hospital stay duration and a decrease in postoperative complications [3-5]. Originally introduced for colorectal surgery, the application of this innovative approach has expanded to various surgical specialties, including major abdominal, head and neck, spinal, obstetric, orthopedic, breast, thoracic, and cardiac surgeries [6]. Consequently, ERAS has gradually emerged as the gold standard for perioperative care across different types of surgical interventions.

Despite the well-documented benefits of ERAS in improving postoperative recovery, effective implementation in clinical settings remains challenging. The successful implementation of ERAS in clinical practice necessitates alterations to conventional clinical workflows, fostering interdisciplinary collaboration, and embracing evidence-based practices. Unfortunately, various barriers impede ERAS [7]. Additionally, the cultural and organizational context of healthcare facilities significantly influences the introduction and implementation of ERAS. Consequently, understanding these factors is pivotal for tailoring strategies that can overcome barriers.
riers and foster the successful implementation of ERAS in clinical practice.

Therefore, we review the current status of ERAS implementation in South Korea and discuss the challenges surrounding its adoption. By addressing these hurdles, Korean anesthesiologists can improve patient outcomes and enhance perioperative care. The main purpose of this review was to discuss the barriers to implementing ERAS in the Korean medical environment, taking into consideration Korea's unique healthcare setting. Such considerations will aid in devising effective strategies for the successful implementation of ERAS in South Korea.

CURRENT STATUS OF ERAS IN SOUTH KOREA

Several surveys conducted among general surgeons to examine the current status of ERAS implementation in South Korea [8-10]. In a survey of 89 gastric surgeons, 65.2% said that they were familiar with the concepts and details of ERAS, but only 33.7% applied it with all patients [8]. In another survey of 127 hepatobiliary-pancreatic surgeons, only 18.2% and 35.0% of ERAS protocol items for pancreaticoduodenectomy and hepatectomy, respectively, were followed by more than half of the respondents [9]. In a survey of general surgeons from various specialties, 68.6% of the respondents said they were aware of the concept of ERAS, but only 33.7% said they were implementing an ERAS program in their practice [10]. According to these surveys, the rate of actual ERAS implementation in clinical settings was markedly lower than the level of awareness of ERAS.

However, no study has examined the implementation status of ERAS from the perspective of anesthesiologists. In addition, there was a critical issue with the items of the aforementioned surveys, as they were limited to the clinical practices of surgeons, thereby excluding other important aspects such as perioperative pain management, management of postoperative nausea and vomiting (PONV), and intraoperative anesthetic management. Owing to these limitations, it is likely that the aforementioned surveys did not accurately reflect the actual implementation rate of ERAS in South Korea, which emphasizes a multidisciplinary approach. To address this, we conducted a Web of Science search for studies published in South Korea with the title containing the phrase “enhanced recovery after surgery.” As a result, a total of 34 studies were retrieved. Of these, 16 that did not specifically focus on the effects of ERAS were excluded. Additionally, one study was conducted in a foreign country and another did not include details about the ERAS protocol, leading to their exclusion. Finally, the remaining 16 studies were analyzed [11-26]. Table 1 presents the authorship status of anesthesiologists in these studies, along with the inclusion of ERAS items related to the field of anesthesiology. Among the studies examined, general surgery was the most common department (75%), with colorectal surgery (n = 5) and gastrectomy (n = 4) being predominant. With respect to authorship, only four studies (25.0%) included an anesthesiologist as a coauthor. Multimodal analgesia was the most frequently included item related to anesthesiology (68.8%), and half of the studies included reduced fasting time and intraoperative hypothermia prevention. However, intraoperative fluid restriction was included in five studies (31.3%) and multimodal PONV prophylaxis in only two studies (12.5%). The limited involvement of anesthesiologists may reflect poor communication and collaboration, which will be further discussed as a major barrier to ERAS implementation.

Furthermore, ERAS has primarily been introduced by individual researchers rather than by institutions or academic societies, and there has been a lack of organized effort related to its implementation in South Korea. This can be attributed to the lack of policy support, especially the absence of financial incentives, when considering South Korea's unique healthcare environment. Although the ERAS program can eventually reduce healthcare costs [27], it initially requires the augmentation of additional personnel to provide a bundle of care. In the Korean health insurance and reimbursement system, it can be difficult to receive compensation for this initial cost investment; therefore, ERAS does not appear to be actively implemented at the institutional level.

BARRIERS TO IMPLEMENTING ERAS IN SOUTH KOREA

To ensure the successful implementation of ERAS, it is crucial to identify the barriers to its implementation. There have been several reports related to the barriers encountered in the implementation of ERAS [28]. In one systematic review on this issue, the commonly mentioned barriers to ERAS implementation were resistance from healthcare professionals, resistance from patients, limited resources, rotating staff and residents, misconceptions about the difficulty of implementing ERAS, and a perceived lack of evidence [28].
The process of implementing the ERAS program in colorectal surgery at seven hospitals affiliated with the University of Toronto can serve as an exemplary case regarding the adoption of ERAS [29]. Based on the knowledge-to-action cycle they utilized, their implementation strategy followed a five-step process. First, they identified the problems related to ERAS implementation in the current situation. Second, they established an institution-specific ERAS protocol. Third, barriers to ERAS implementation were addressed. Fourth, they established a tailored implementation strategy for ERAS. Finally, they developed an audit and feedback system for ERAS [29]. During this process, they conducted structured interviews with perioperative team members to investigate the barriers to ERAS implementation. The key barriers identified were lack of manpower, poor communication and collaboration, resistance to change, and patient factors [30]. They established strategies to overcome these barriers [31], and as a result, the implemented ERAS program significantly reduced postoperative complications after colorectal surgery [3]. Another recent study conducted in China reported a shortage of medical resources, outdated concepts, poor communication and collaboration among multidisciplinary team members, and a lack of policy support as major barriers to ERAS implementation, similar to the aforementioned findings [32]. Based on the domains used in the aforementioned systematic review concerning barriers to implementing ERAS, we compiled the findings from relevant studies published after the review in Table 2 [28,32-34]. As we thought that these factors also serve as significant barriers to the introduction of ERAS in South Korea, we discuss the major barriers further in the following sections.

**Lack of manpower and policy support**

Although ERAS has the potential to reduce medical costs by reducing postoperative complications and length of hospital stay [27], a lack of manpower can serve as a significant barrier to its introduction and implementation. First, for successful implementation of ERAS, tailored ERAS protocols for each institution’s context need to be established, which requires active discussion among various perioperative members [29]. To facilitate perioperative members’ participation in these discussions, they require time flexibility. Second, from the anesthesiologist’s perspective, additional staffing is required for aspects such as the preoperative opti-

<table>
<thead>
<tr>
<th>Reference number</th>
<th>Number of anesthesiologists as authors</th>
<th>Operation type</th>
<th>Reduced preoperative fasting time</th>
<th>Multimodal analgesia</th>
<th>Multimodal PONV prophylaxis</th>
<th>Intraoperative hypothermia prevention</th>
<th>Intraoperative fluid restriction</th>
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<tr>
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<tr>
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<tr>
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<tr>
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<tr>
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<td>-</td>
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<tr>
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<td>Gastrectomy</td>
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<tr>
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<tr>
<td>20</td>
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<td>Spine surgery</td>
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<td>22</td>
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<td>23</td>
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<td>25</td>
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<tr>
<td>26</td>
<td>0</td>
<td>Appendectomy</td>
<td>-</td>
<td>0</td>
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</table>

Values are presented as number (%). ERAS: enhanced recovery after surgery, PONV: postoperative nausea and vomiting.
mization process and multimodal analgesia, including regional analgesia. Third, additional staff are required to operate an ERAS audit program. An ERAS audit program is essential for monitoring compliance, identifying areas for improvement, standardizing care, and evaluating patient outcomes [35,36]. Thus, it plays a crucial role in optimizing the implementation of ERAS protocols. To conduct such a program, personnel must be capable of continuously collecting and analyzing data. Finally, rotating staff and residents have also been cited as barriers to ERAS implementation [28], and those unfamiliar with the ERAS program may decrease their compliance rate. Therefore, periodic education is required to resolve this issue. However, delivering such education requires additional time and labor. There is a lack of manpower in South Korea; thus, 44.4% of the respondents in a survey on ERAS implementation in major hospitals cited the lack of physiotherapists, nurses, and doctors as a major factor preventing the application of programs [10].

Ultimately, to address these issues, policy support is required to facilitate the implementation of ERAS in clinical practice. Policy support can encourage healthcare providers and institutions to actively implement ERAS programs [37]. These include financial incentives, recognition programs, and performance-based bonuses. By offering these benefits, policy support motivates healthcare providers to embrace and adhere to ERAS programs. Furthermore, such policy support can enable more effective allocation of resources, such as funding and staffing, to support the implementation of ERAS programs in routine clinical practice. Adequate resources are essential for training healthcare providers, implementing necessary infrastructure changes, and monitoring program compliance. In addition, to formulate policies that can support ERAS implementation, it is necessary to evaluate its cost effectiveness. Although several studies on the cost-effectiveness of ERAS have been reported in other countries [38-42], such research has yet to be published in South Korea. Future studies are needed to assess whether the application of ERAS is economically viable within the Korean healthcare environment, and such studies could contribute to policy support for ERAS.

### Poor communication and collaboration

The ERAS program involves a team-based approach with healthcare providers from different departments working together to optimize postoperative outcomes. The multidisciplinary team included surgeons, anesthesiologists, nurses, dietitians, and other healthcare professionals. By collaborat-

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**Table 2. Major Barriers to ERAS Implementation according to Previous Studies**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Intervention characteristics</td>
<td>Perceived lack of evidence</td>
<td>Not convinced with current evidence</td>
<td>Lack of individualized management</td>
<td>High medical costs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Low compliance</td>
<td></td>
</tr>
<tr>
<td>Inner setting</td>
<td>Limited resources</td>
<td>Lack of support</td>
<td>Absence of management support</td>
<td>Inconsistent communication</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lack of physical resources</td>
<td>Shortage of medical resources</td>
<td></td>
</tr>
<tr>
<td>Outer setting</td>
<td>Resistance from patients</td>
<td>Difficulties with patient education</td>
<td>Lack of support in the transition from hospital to home</td>
<td>Lack of policy support</td>
</tr>
<tr>
<td>Characteristics of individuals</td>
<td>Resistance from healthcare professionals</td>
<td>Unfamiliar with ERAS</td>
<td>Poor communication</td>
<td>Outdated concepts</td>
</tr>
<tr>
<td></td>
<td>Belief that implementation would be too difficult</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Process of implementation</td>
<td>Rotating staff and residents</td>
<td>Uncertain on implementation process</td>
<td>Lack of feedback on performance</td>
<td>Poor doctor-patient collaboration</td>
</tr>
<tr>
<td></td>
<td>No formal ERAS program</td>
<td>Lack of accessible audit data</td>
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</table>

ERAS: enhanced recovery after surgery.
ing and sharing expertise, a team can develop and implement comprehensive care plans that address all aspects of a patient’s perioperative journey (Fig. 1) \[43\]. However, perioperative care was traditionally provided in isolated service "expertise silos," meaning various perioperative members typically operated solely within their own areas of expertise, with little to no collaboration across different specialties \[44\]. In a structured interview study conducted in five low- and middle-income countries, fragmented perioperative care pathways were identified as one of the key barriers contributing to poor perioperative care \[45\]. In contrast, interprofessional communication and collaboration have been reported as key facilitators of ERAS implementation \[30,46\].

Although there has been little mention of the fragmented perioperative care pathway in South Korea, this issue can be inferred from the ERAS-related studies reported thus far. As mentioned earlier, items related to the roles of anesthesiologists were very limited in surveys on ERAS implementation conducted in South Korea \[8-10\]. The authors of a survey on the attitudes of hepatobiliary-pancreatic surgeons toward ERAS protocols cited inadequate cooperation with various departments, particularly anesthesiology, as one of the reasons for poor implementation \[9\]. Moreover, in the aforementioned studies that focused on ERAS in South Korea (Table 1), the participation of anesthesiologists was relatively low. Considering the significant role of anesthesiologists in ERAS, this lack of involvement could be cautiously interpreted as evidence of poor communication in perioperative care.

**Fig. 1.** A schematic diagram describing the relationship between interprofessional collaboration and patient recovery after surgery. When there is considerable distance and limited interconnection among professions, surgical patients face a higher risk of “falling” into perioperative stress until they reach recovery (above). Conversely, with robust interprofessional collaboration and communication, patients can minimize exposure to perioperative stress and achieve faster and enhanced recovery (below).
Resistance to shifting away from outdated concepts

Evidence-based medicine is a fundamental principle of ERAS, with ERAS programs comprising several evidence-based perioperative care elements. Evidence-based perioperative care has the potential to improve postoperative recovery. Nevertheless, adherence in clinical practice remains inconsistent and falls short of the desired level. However, in clinical practice, it is common to make decisions based not only on evidence but also on experiences or traditional practices passed down by senior colleagues. Sometimes, these experiences may conflict with evidence-based recommendations, leading to resistance to evidence-based guidelines [47]. A review of previous studies quantifying the time lag between the emergence of new concepts and real-world applications suggests a 17-year gap [48].

A prominent example of anesthesiologists’ resistance to shifting away from outdated concepts is prolonged preoperative fasting. Several guidelines have already suggested a shortened preoperative fasting time of clear liquids up to 2 h before induction of anesthesia [49-51]. However, most hospitals in South Korea adhere to the traditional practice of preoperative midnight nil per os (NPOs). There is no evidence supporting the necessity of a preoperative fasting time of more than 8 h for clear fluids in elective surgical patients, and implementing a shortened preoperative fasting time does not require additional resources. In a survey of Korean gastric surgeons, all patients fasted beginning no later than midnight before surgery; however, only 10.1% were administered carbohydrate-rich drinks before surgery [8]. Similarly, in hepato-biliary-pancreatic surgery, only 3-5.6% of cases followed the ERAS guidelines, and the authors noted that it is difficult to change traditional experience-based practice [9]. This resistance to evidence-based perioperative care can be attributed to Korean anesthesiologists’ adherence to traditional practices.

Patient factors

In addition to the aforementioned healthcare provider-related factors, patient-specific risk factors can pose obstacles to ERAS implementation. The risk profile for postoperative recovery can influence compliance with ERAS programs, thereby affecting their effectiveness. In a study conducted on colorectal surgery, a higher American Society of Anesthesiologist physical status classification was significantly associated with lower compliance with the ERAS program [52]. Similarly, a study focusing on patients undergoing laparoscopic distal gastrectomy in South Korea found that a higher American Society of Anesthesiologists physical status classification and advanced age were significantly associated with lower compliance with the ERAS program [53]. Another study reported a significant association between ERAS program failure and CR-POSSUM Score, a predictive tool for postoperative outcomes in colorectal surgery [54].

In high-risk older adult patients or those with multiple co-morbidities, the potential benefits of implementing an ERAS program to reduce perioperative stress and decrease the risk of postoperative complications are likely to be more significant than in healthy patients [55]. Furthermore, ERAS has been reported to have a positive impact on postoperative recovery in emergency surgeries, which are generally considered to have a higher risk than elective surgeries [56]. However, in most prospective clinical trials comparing ERAS with conventional care, the proportion of elderly patients was relatively small, and high-risk patients often demonstrated lower compliance with the ERAS program [52]. This made it challenging to assess the full effectiveness of the ERAS programs in these patient populations. It is crucial to overcome these challenges and apply the ERAS program with a broader range of surgical patients to improve postoperative recovery.

Additionally, patient resistance to the ERAS program has been cited as a barrier to its implementation [28]. All of the three aforementioned surveys in South Korea cited a lack of awareness of ERAS among patients as a major obstacle to its implementation [8-10]. This is particularly relevant in Korea, where the benefits of the ERAS program are not yet well known to the general public. The program has primarily been conducted in the form of research studies, suggesting that there could be significant patient resistance. To resolve this issue, it is essential to not only conduct research on the efficacy of ERAS but also promote its positive effects to the general public.

ROLE OF KOREAN ANESTHESIOLOGISTS IN OVERCOMING BARRIERS TO ERAS IMPLEMENTATION

Korean anesthesiologists can play a pivotal role in overcoming barriers to ERAS implementation. To achieve this, the following are required. First, Korean anesthesiologists should be aware of the significant impact their clinical prac-
Practices can have on postoperative recovery and should identify areas for improvement in their current practices based on recent evidence. In particular, there is an urgent need to change the current perioperative practices, such as prolonged preoperative fasting and opioid-based pain management, which are far from supported by scientific evidence, using the latest evidence-based approaches. Second, active communication and collaboration with other departments are required to incorporate the role of anesthesiologists beyond intraoperative anesthetic management into the ERAS program. The preoperative optimization process and multimodal opioid-sparing analgesia, which are essential components of ERAS, require collaboration with other departments. To achieve this, we need to provide accurate information on the extended role of anesthesiologists in perioperative medicine and their impact on postoperative recovery in other departments. Third, Korean anesthesiologists need to develop the capacity to invest resources in improving postoperative recovery through the efficient allocation of limited resources. As administrators of the operating room management, anesthesiologists can optimize operating room efficiency, reduce medical costs, and provide financial benefits [57].

Finally, Korean anesthesiologists should not only focus on the introduction of ERAS but also establish strategies to enhance compliance after its implementation. To achieve this, collaboration with other departments is essential to develop institution-specific ERAS protocols tailored to local contexts. The establishment of local context-specific protocols has been reported to facilitate successful ERAS implementation [28]. In addition, the creation of customized ERAS protocols that consider patient-specific factors is crucial. As previously mentioned, patient factors have been identified as significant barriers to ERAS compliance. Therefore, Korean anesthesiologists should conduct large-scale prospective studies across diverse patient groups to assess the effectiveness of personalized ERAS protocols. Another method of improving ERAS compliance is to adopt an audit and feedback system. The ERAS® Interactive Audit System, developed by the ERAS® Society, is a representative example of such a system [36]. Introducing an audit system can help monitor ERAS effectiveness, identify areas for improvement, standardize care, and evaluate patient outcomes. Compliance with ERAS can be enhanced by incorporating an audit and feedback system, leading to better patient outcomes and improved perioperative care in South Korea [35].

Furthermore, Korean anesthesiologists should make an effort to garner support for ERAS implementation at the academic society or institution level. For example, in the United Kingdom, the Enhanced Recovery Partnership Programme (ERPP) was introduced in 2009 by national agencies to support the implementation of ERAS programs for various surgery types, resulting in approximately 24,000 patients already recorded in the ERPP database in 2012 [5]. In Alberta, Canada, a fully integrated healthcare system named Alberta Health Services introduced a demonstration project implementing the colorectal ERAS guidelines and included more than 75% of all colorectal surgeries in the province up to 2015 [58]. In addition, ERAS adoption is rapidly gaining momentum in academic institutions and societies across Asia. The Medical City in the Philippines and Tan Tock Seng Hospital in Singapore were designated as the first ERAS Centers of Excellence in Asia in 2016 [59]. Both have played key roles in spearheading ERAS initiatives in their respective countries and in the broader Asian region. In 2019, these institutions collaborated with the ERAS® Society to organize the first Asian ERAS Congress. Recently, Japan joined the ERAS® Society as a new chapter, signifying its intent to actively expand the implementation of ERAS. In China, ERAS has been identified as a vital component of perioperative medicine [60]; the first ERAS group was established there in 2015 [61], and several guidelines have subsequently been published [62,63]. Overall, both institutional and academic endorsement of ERAS in Asia are on an upward trajectory. Korean anesthesiologists should not be limited to the role of individual researchers but must also make organizational efforts to introduce and establish ERAS in South Korea.

From this perspective, it is noteworthy and highly welcome that the recent collaboration between the Korean Society of Anesthesiologists (KSA) and the Korean Surgical Society (KSS) has established a cooperative system for institutional improvements and reached an agreement to propose a pilot project for new incentive fees related to ERAS performance to the Korean Ministry of Health and Welfare [64]. The first meeting of practitioners from the KSA and the KSS for this purpose took place on August 30, 2023. Additionally, under the current leadership of the Korean Society of Surgical Metabolism and Nutrition, Korean ERAS guidelines are being developed for gastric, colorectal, and hepatobiliary pancreatic cancer surgeries. Members of the KSA are also responsible for developing anesthesia-related items within these guidelines. These collective efforts at the academic and societal levels are likely to contribute significantly to the establishment and application of ERAS in the Korean medi-
The challenges ahead for anesthesiologists, as described by authors from our neighboring country, China, hold significant implications for us as well [60]. They delineated several forthcoming tasks for anesthesiologists, which encompass the following aspects. First, they should gain precise comprehension of anesthesiology and perioperative medicine in other departments. Second, they should actively engage in the ERAS program and play a pivotal role in its implementation. Third, they should assume a leadership position in postoperative multidisciplinary team pain management. Fourth, they should augment the educational content on perioperative medicine in the resident training program. Finally, medical research on perioperative medicine should be enhanced. These tasks align with the roles of Korean anesthesiologists mentioned earlier, and such effort will not only act as a facilitator in implementing ERAS but also ultimately expand the role of anesthesiologists in perioperative medicine in South Korea.

CONCLUSION

Although the ERAS has demonstrated remarkable benefits, its effective implementation in clinical settings in South Korea is challenging. Such barriers include a lack of manpower and policy support, poor communication and collaboration among multidisciplinary teams, resistance to shifting away from outdated concepts, and patient-specific risk factors. To overcome these barriers and improve postoperative recovery, Korean anesthesiologists can play a pivotal role by adopting evidence-based practices, enhancing interdisciplinary collaboration, and advocating for policy support. By addressing these challenges, ERAS implementation in South Korea could be more successful, leading to improved patient outcomes and enhanced perioperative care. Efforts to implement ERAS will expand the scope of perioperative medicine in South Korea.

FUNDING

None.

CONFLICTS OF INTEREST

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

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS


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INTRODUCTION

Body temperature monitoring during the perioperative period is essential because of the variability during surgery. Body temperature often decreases during surgery because of thermoregulation disruption due to general anesthesia and cold exposure to procedural surroundings [1-4]. Perioperative hypothermia may cause mild consequences such as patient’s discomfort, shivering and severe complications such as increased bleeding [1] due to abnormal coagulopa-
thy [2], higher risk of surgical site infection [3] and life-threatening arrhythmia [4]. Meanwhile, body temperature may increase soon after the induction of general anesthesia if malignant hyperthermia is triggered by exposure to volatile anesthetic agents or succinylcholine [5]. Immediate recognition and treatment should be started without delay in the occurrence of malignant hyperthermia [6]. Therefore, we should be able to monitor perioperative body temperature accurately.

Nevertheless, skin temperature may differ greatly from the actual body temperature; thus core body temperature must be measured to ensure accuracy [7]. Core body temperature can be obtained from the tympanic membrane, nasopharynx, esophagus, pulmonary artery, bladder and rectum. However, temperature measurements at these sites require using invasive placement of sensors.

Esophageal temperature is strongly associated with pulmonary artery temperature and is used as a basic temperature measurement method for intubated patients [8]. Esophageal probe insertion is usually considered to be a safe method; however, there is the possibility of complications such as esophageal bleeding, perforation, and arrhythmias [8]. Moreover, inserting esophageal probe is difficult when supraglottic airway is used.

To measure core body temperature in a non-invasive way, Fox and Solman [9] first invented the non-invasive zero-heat-flux thermometer in 1971. 3M developed a 3M™ Bair Hugger™ temperature monitoring instrument for use in clinical practice. It is a zero-heat-flux thermometer consisting of two thermistors, a thermal insulator and an electrical heater. A sensor is put on the forehead region and insulates the skin locally by heating. An area of isothermic tunnel is then created from the skin to the core body part such as the brain. At that point, the state of zero heat flux reflects the core body temperature [10-12]. Safety and usefulness of this method have already been reported. Previous studies have proved the reliability of this method through comparison with esophageal probe [10], nasopharyngeal probe [11], and pulmonary artery catheter [13]. The Bair Hugger™ temperature monitoring system (BHTMS) has some advantages, such as its accuracy, ease of use with disposable sensors, and non-invasiveness. However, the BHTMS may not be able to be applied to the forehead area owing to several reasons such as the field of surgery involving the head, skin problem at the attachment site, and interference of other monitoring probes on the forehead.

Therefore, instead of the forehead area, the BHTMS sensor is applied to another area of the body. According to Tachibana et al. [14] a relatively accurate temperature could be obtained even if the BHTMS sensor was attached to the neck. However, temperature obtained at the chest regions did not show accurate values. Considering the principle of zero-heat-flux thermometer, we hypothesized that core body temperature can be obtained from the wrist area using BHTMS. The wrist area has a radial artery running about 5 mm below the skin, has little influence by fatty tissues, and is easy to approach [15]. To date, no studies have focused on the use of BHTMS at the wrist region. Hence this study aimed to determine whether an accurate core body temperature can be obtained from the wrist region using BHTMS in patients under general anesthesia by comparing it with esophageal temperature.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of Chung-Ang University Hospital (registration no: 2112F-030-489) and it was registered at the Clinical Research Information Service clinical trials registry (KCT0007211) before patient recruitment. Written informed consent was obtained from each patient before surgery.

The study was conducted between March 2022 and August 2022. Patients of the American Society of Anesthesiologists physical status I or II who were planned to undergo orthopedic surgery under general anesthesia were included. Pediatric patients, pregnant patients, patients with esophageal lesions such as esophageal varix or stricture, abnormalities at the wrist region, and hematologic disease of bleeding tendency were excluded. We included patients with minimal risk of massive bleeding during surgery.

Before the induction of general anesthesia, the BHTMS sensor (3M™ Bair Hugger™ Temperature Monitoring Patient Sensor, 36000 and 3M™ Bair Hugger™ Temperature Monitoring System, 37000) was attached to the patient’s wrist. The center of the sensor was placed at the radial artery pulsation site. Anesthesia was induced by propofol (1.5–2.0 mg/kg) and remifentanil (0.5 μg/kg), and tracheal intubation was performed 90 s after injecting 0.6–0.9 mg/kg rocuronium.

Maintenance of anesthesia was performed using air-oxygen-sevoflurane with FiO₂ 0.5. Sevoflurane dosage was adjusted at 1.5–2.0 minimum alveolar concentration to maintain patient state index of 25–50 at the SEDLine monitor (SEDLine™, Masimo, CA). After the tracheal intubation, an
esophageal probe (ETP1040, Ewha Biomedics) was inserted through the mouth with the insertion depth determined using the equation \( \text{depth (cm)} = 0.228 \times \text{standing height (cm)} - 0.194 \) to target the region of esophagus bounded by the left ventricle and aorta [16]. Temperature recording began after equilibration, which was defined as 0 min \( T_{\text{es}} \). Patients were warmed appropriately at the upper body using a Bair Hugger\textsuperscript{TM} forced-air warming unit (3M\textsuperscript{TM} Bair Hugger\textsuperscript{TM} Warming Unit Model 775, 3M) and Bair Hugger\textsuperscript{TM} upper body warming blankets (3M\textsuperscript{TM} Bair Hugger\textsuperscript{TM} Warming Blanket Model 622, Multi-position, 3M), under high operating temperature (43°C). Warming blanket covered the whole upper body including the wrist area. The warming system was turned off when esophageal temperature \( T_{\text{eso}} \) reached over 37.3°C. \( T_{\text{es}} \) and BHTMS at the wrist region \( T_{\text{wrist}} \) were recorded every 10 min until the end of the surgery. Before extubation, esophageal temperature probe and BHTMS sensor were removed. The operating room temperature was maintained at 20–24°C throughout the study period.

Our primary end point was comparison of consistency between \( T_{\text{eso}} \) and \( T_{\text{wrist}} \). The secondary end points include the accuracy and correlation between \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) by times at 0, 10, 20, 30, and 40 min \( (T_{\text{sp}}, T_{\text{sp}}, T_{\text{sp}}, T_{\text{sp}}, T_{\text{sp}} \text{, and } T_{\text{sp}}, \text{ respectively}) \), and accuracy between \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) after 30 min of anesthesia induction.

**Statistical analysis**

During the research planning, we performed a pilot study, collecting 132 pairs of data from 11 patients. After the pilot study, the sample size was calculated with G Power software (Ver. 3.1.9.7, Heinrich-Heine-Universität Düsseldorf) using a paired \( t \)-test. The mean difference was 0.15 and the standard deviation (SD) was 0.38. When calculated with an alpha value of 0.01 and power of 0.8, the sample size was 79. In the pilot study, the shortest duration of surgery was 40 min. It means 1 patient yielded a minimum of 5 data sets. Therefore, we divided 79 by 5 to calculate minimum number of participants. Then, considering 20% of drop out rate, 20 patients were decided as the total number of participants.

The distribution of parameters was evaluated for normality using the Kolmogorov-Smirnov test. Non-normally distributed data were compared using the Wilcoxon signed rank test and Spearman correlation and are expressed as median and interquartile range. Normally distributed data were compared using the paired \( t \)-test and Pearson correlation and are expressed as mean and SD. For the comparison of \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) data by times, Bonferroni correction was performed. P value < 0.01 was considered significant. Bland-Altman plots were also used to evaluate the limits of agreement and were expressed as mean bias \( (T_{\text{eso}} - T_{\text{wrist}}) \pm 2\text{SD} \). All statistical analyses were performed using dBSTAT for Windows (Ver. 5.0, dBSTAT).

**RESULTS**

A total 258 pairs of data were collected from 20 patients. **Table 1** summarizes the demographic data and duration of anesthesia. In one case, a pair of data at 0 min was deleted because of \( T_{\text{wrist}} \) missing data due to an electronic problem. Therefore, 257 pairs of data were analyzed using the Wilcoxon signed rank test and Spearman correlation. Median (1Q, 3Q) of \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) were 36.5°C (35.95°C, 36.8°C) and 36.4°C (35.8°C, 36.8°C), respectively. \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) had no statistically significant difference \( (P = 0.103) \) (Fig. 1). The Spearman’s correlation coefficient was 0.567 (Fig. 2).

Each patient had a different length of anesthesia time according to the type of surgery. **Table 2** summarizes the types of surgery. The shortest surgery duration was 40 min. Overall, 99 pairs of data were organized and analyzed according to the measurement time intervals (0, 10, 20, 30 and 40 min). The paired \( t \)-test and Pearson correlation were performed, and **Table 3** summarizes the result of paired \( t \)-test. A significant difference was observed at \( T_{\text{sp}}, T_{\text{sp}}, \text{ and } T_{\text{sp}} \), whereas no significant difference was observed at \( T_{\text{sp}}, T_{\text{sp}}, T_{\text{sp}}, \text{ and } T_{\text{sp}}, \text{ respectively} \). Fig. 3 shows the Pearson’s correlation coefficients of \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) by times, which were 0.262, 0.606, 0.679, 0.746, and 0.718 at \( T_{\text{eso}}, T_{\text{eso}}, T_{\text{eso}}, \text{ and } T_{\text{eso}} \), respectively.

A Bland–Altman analysis was also performed. For the primary outcome, mean difference \( (T_{\text{eso}} - T_{\text{wrist}}) \) of 257 pairs of data was 0.14°C with a 2SD of \( \pm 1.44 \) (Fig. 4). For the second-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>11/9</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>47.8 ± 19.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.8 ± 8.8</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.9 ± 12.8</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>25.3 ± 3.2</td>
</tr>
<tr>
<td>Anesthesia time (min)</td>
<td>129 ± 52.7</td>
</tr>
<tr>
<td>ASA-PS (I/II)</td>
<td>10/10</td>
</tr>
</tbody>
</table>

Values are presented as number only or mean ± SD. BMI: body mass index, ASA PS: American Society of Anesthesiologists physical status.
This study aimed to determine whether an accurate core body temperature can be obtained from the wrist region using BHTMS in patients under general anesthesia by comparing it with esophageal temperature. We compared \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) by times. The mean bias (\( T_{\text{eso}} - T_{\text{wrist}} \)) ± 2SD were 1.49°C ± 2.00, 0.82°C ± 1.30, 0.29°C ± 1.32, –0.03°C ± 0.84, –0.12°C ± 0.82 at T\(_0\), T\(_{10}\), T\(_{30}\), T\(_{60}\), and T\(_{90}\) respectively (Fig. 5).

### DISCUSSION

The primary outcome, the Bland–Altman plot was constructed for \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) by times. The mean bias (\( T_{\text{eso}} - T_{\text{wrist}} \)) ± 2SD were 1.49°C ± 2.00, 0.82°C ± 1.30, 0.29°C ± 1.32, –0.03°C ± 0.84, –0.12°C ± 0.82 at T\(_0\), T\(_{10}\), T\(_{30}\), T\(_{60}\), and T\(_{90}\) respectively (Fig. 5).

![Fig. 1. Comparison of \( T_{\text{eso}} \) and \( T_{\text{wrist}} \). Wilcoxon signed rank test was performed, and no statistical difference was observed (\( P = 0.103 \)). \( T_{\text{eso}} \): esophageal temperature, \( T_{\text{wrist}} \): temperature recorded using the Bair Hugger™ core body temperature monitoring system at the wrist.](image1)

![Fig. 2. Spearman correlation between \( T_{\text{eso}} \) and \( T_{\text{wrist}} \). \( T_{\text{eso}} \): esophageal temperature, \( T_{\text{wrist}} \): temperature recorded using the Bair Hugger™ core body temperature monitoring system at the wrist, \( R_s \): Spearman correlation coefficient.](image2)

\( R_s = 0.567 \)

### Table 2. Types of Surgery

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthroscopic surgery of knee or shoulder</td>
<td>3</td>
</tr>
<tr>
<td>Total knee replacement</td>
<td>4</td>
</tr>
<tr>
<td>Metal removal of ankle or knee or clavicle</td>
<td>6</td>
</tr>
<tr>
<td>ORIF of ankle or hand or humerus</td>
<td>3</td>
</tr>
<tr>
<td>Ligament reconstruction of elbow or knee</td>
<td>2</td>
</tr>
<tr>
<td>Ulnar osteotomy</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
</tr>
</tbody>
</table>

Values are presented as number only. ORIF: open reduction and internal fixation.

### Table 3. Comparison of \( T_{\text{eso}} \) and \( T_{\text{wrist}} \) (°C) by Times

<table>
<thead>
<tr>
<th>Time</th>
<th>( T_{\text{eso}} ) (°C)</th>
<th>( T_{\text{wrist}} ) (°C)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min</td>
<td>36.31 ± 0.54</td>
<td>34.82 ± 0.99</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>10 min</td>
<td>36.18 ± 0.53</td>
<td>35.36 ± 0.82</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>20 min</td>
<td>36.18 ± 0.50</td>
<td>35.89 ± 0.88</td>
<td>0.063</td>
</tr>
<tr>
<td>30 min</td>
<td>36.21 ± 0.53</td>
<td>36.24 ± 0.62</td>
<td>0.751</td>
</tr>
<tr>
<td>40 min</td>
<td>36.25 ± 0.52</td>
<td>36.38 ± 0.56</td>
<td>0.203</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD. \( T_{\text{eso}} \): esophageal temperature, \( T_{\text{wrist}} \): temperature recorded using the Bair Hugger™ core body temperature monitoring system at the wrist. The two groups were compared using the paired t-test. Bonferroni correction was performed on the data. \( P \) value < 0.01 was considered significant.
Fig. 3. Pearson correlation between $T_{\text{eso}}$ and $T_{\text{wrist}}$ by times. $T_{\text{eso}}$ and $T_{\text{wrist}}$ were recorded at 0 min (A), 10 min (B), 20 min (C), 30 min (D) and 40 min (E). $T_{\text{eso}}$: esophageal temperature, $T_{\text{wrist}}$: temperature recorded using the Bair Hugger™ core body temperature monitoring system at the wrist, $R$: Pearson correlation coefficient.

For the secondary outcomes, the $T_0$, $T_{10}$, $T_{20}$, $T_{30}$ and $T_{40}$ data were analyzed. $T_0$ and $T_{10}$ showed significant differences in the paired t-test, whereas $T_{30}$, $T_{30}$ and $T_{40}$ showed no significant difference. Additionally, there was a positive correlation between $T_{\text{eso}}$ and $T_{\text{wrist}}$ at $T_0$–$T_{40}$, although the $T_0$ showed a weak correlation. However, $T_{10}$, $T_{20}$, $T_{30}$ and $T_{40}$ showed moderate to strong correlations. From the Bland–Altman analysis result, we noticed that only $T_{30}$ and $T_{40}$ could...
be accepted as reliable, which met the earlier LOA standard [14]. For further analysis, we also performed Bland-Altman analysis with data collected from 30 min to the end of the surgery. It showed a mean bias \( (T_{eso} - T_{wrist}) \pm 2SD \) of 0.08 ± 0.96°C, which met the agreed standard. Considering these results, temperature measurement using the BHTMS at the wrist is relatively accurate and equivalent to the esophageal temperature at least 30 min after the first temperature measurement.

In this study, at \( T_0 \) 10 of 20 patients showed immediate close approximation between \( T_{eso} \) and \( T_{wrist} \leq \pm 1.0°C \). However, the remaining half of patients showed a wide difference between \( T_{eso} \) and \( T_{wrist} \) up to 3.1°C, and the wide difference decreased progressively. The exact mechanism of the close approximation of \( T_{wrist} \) to \( T_{eso} \) after 30 min needs to be explicit. One reason, we assume, is the redistribution of body heat. Before the induction of general anesthesia, the peripheral compartment distant from the heart, such as the wrist region, typically shows a 2–4°C lower temperature than the core body temperature. This is the normal core-to-peripheral temperature gradient. General anesthesia is known to reduce vasoconstriction and cause peripheral vasodilation, which leads to perioperative hypothermia. The following redistribution increases the temperature of the peripheral region [17]. Furthermore, we assumed that the other reason is the direct heating effect of the upper body warming blanket. When we turned off the warming system owing to concern of hyperthermia, we could observe a wider difference between \( T_{eso} \) and \( T_{wrist} \). Therefore, we believed that the upper body warming blanket has a direct heating effect. The time interval for the calibration of the BHTMS sensor and the time interval until the application of a warming blanket is a factor considered in the direct heating effect. Considering the calibration time, we applied the BHTMS sensor before intubation. Calibration was done within 5 min in every patient before placing the esophageal temperature probe. A warming blanket was applied after intubation or after positioning the patients for the operation. The time interval was not correctly measured during the study; however, it might have been up to 15 min.

Our study had several limitations. First, we monitored and analyzed an esophageal temperature range of 35.2–37.2°C in patients undergoing orthopedic surgeries. Therefore, we could not assure that BHTMS would correctly measure hyperthermia or hypothermia out of that range or in other surgery types. Second, for the secondary outcome, we did not compare the temperature by times after 40 min because the surgery time length differed in every patient. Thus, we could not perform comparisons of data by times after 40 min. Third, we did not include patients who did not use the warming system in the study because of the potential ethical issues. Also, we did not use warming system other than the upper body warming blanket. Further study using warming system other than the upper body warming blanket is needed. Fourth, we did not measure the BHTMS temperature at the forehead region and the peripheral skin temperature for comparison. Further studies comparing temperatures recorded using the BHTMS at the forehead, wrist, and peripheral skin temperature is needed. Fifth, the peripheral circulation of each patient was not evaluated although it might be concerned whether the location of radial artery was temperature of the fluid were not evaluated. However, considering the result of the secondary outcome, under the Bair Hugger upper body warming blankets, the influence of fluid after 30 min could be considered minimal.

Limitations stated above may lower the strength of this study. However, this study has meaningful number of participants and well documented methodology to be replicated. Also, Ethical guidelines were followed and potential threat of hypothermia or hyperthermia was prevented. Further studies should be proceeded with larger number of participants for longer duration of time, overall control of the potential
Fig. 5. Bland-Altman plots of $T_{eso}$ and $T_{wrist}$ at 0 min (A), 10 min (B), 20 min (C), 30 min (D), and 40 min (E). $T_{eso}$: esophageal temperature, $T_{wrist}$: temperature recorded using the Bair Hugger™ core body temperature monitoring system at the wrist, SD: standard deviation.
variables that may affect body temperature, and comparison with other temperature sites. In this study, results were inconclusive about the accuracy of BHTMS at wrist area. Even though, this study has significance for the suggestion of another possible alternative method for monitoring body temperature.

In conclusion, the accuracy of BHTMS at wrist area under upper body warming blanket is comparable to that of esophageal temperature after 30 min of anesthesia induction. Therefore, BHTMS may be another possible alternative method for monitoring body temperature after 30 min of anesthesia induction.

**FUNDING**

None.

**CONFLICTS OF INTEREST**

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

**DATA AVAILABILITY STATEMENT**

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**AUTHOR CONTRIBUTIONS**

Writing - original draft: Kyung Seo Oh. Writing - review & editing: Kyung Seo Oh, Young-Cheol Woo. Conceptualization: Young-Cheol Woo. Methodology: Young-Cheol Woo. Project administration: Kyung Seo Oh. Investigation: Kyung Seo Oh. Supervision: Yong-Hee Park, Chongwha Baek, Young-Cheol Woo.

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Effects of remimazolam combined with remifentanil on quality of recovery after ambulatory hysteroscopic surgery: a prospective, observational study

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\(^1\)Department of Anesthesiology and Pain Medicine, Seoul National University Bundang Hospital, Seongnam, \(^2\)Department of Anesthesiology and Pain Medicine, Uijeongbu Eulji Medical Center, Eulji University, Uijeongbu, Korea

Background: Remimazolam, a new benzodiazepine, is known for its quick onset of effects and recovery time. Recently, it has been licensed for general anesthesia and sedation in Korea and its use is increasing in other countries. However, less is known about its effect on postoperative recovery. We used a patient-reported outcome questionnaire to examine the effect of remimazolam on postoperative recovery.

Methods: Patients who underwent hysteroscopy on day surgery basis were administered an induction dose of remimazolam 6 mg/kg/h followed by a maintenance dose of 1–2 mg/kg/h. After surgery, the translated Korean version of 15-item Quality of Recovery scale (QoR-15K) including post-discharge nausea and vomiting (PDNV) and/or pain, was surveyed 24 h after surgery to evaluate patient recovery.

Results: Total of 38 patients were enrolled in this prospective, observational study. All patients successfully completed QoR-15K. Only one patient scored low for moderate pain and PDNV. On average, patients scored 9 and above for all QoR-15K items except for moderate pain (8.66 ± 1.68). When QoR-15K items were grouped into dimensions, all dimensions scored an average of 9 or higher on a 10-point scale. In addition, 19 out of 38 patients gave score range of 148 to 150 out of possible 150.

Conclusions: Psychometric evaluation based on postoperative QoR-15K among patients receiving remimazolam shows satisfactory patient recovery profiles without significant pain or PDNV. Considering its effectiveness and safety, remimazolam could be one of useful agents for general anesthesia of day surgery in terms of postoperative recovery.

Keywords: Ambulatory surgical procedure; Anesthesia, general; Anesthesia recovery period; Patient outcome assessment; Remifentanil; Remimazolam.

INTRODUCTION

Remimazolam is a novel ultra-short acting benzodiazepine with rapid onset of effects, short maintenance and faster recovery time\(^1\). Remimazolam's pharmacological action is similar to midazolam, but there is a difference in its meta-

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Remimazolam effects on quality of recovery

Remimazolam is metabolized via cytochrome P450, remimazolam is metabolized by tissue esterases [2]. Compared to the metabolite of midazolam, CNS7054, which is the metabolite of remimazolam, shows 50 times less potent sedative effect and this difference is thought to contribute to remimazolam’s rapid onset and systemic clearance [3]. In fact, the mean terminal elimination half-life of remimazolam is 0.75 h compared to 4.3 h of midazolam [4]. One major disadvantage of midazolam is its greater cumulative effects due to long-acting metabolite that causes slow recovery of neuropsychiatric function compared to propofol [5,6]. However, the context-sensitive half-time of remimazolam remains constant even after a long-term continuous infusion, and thus the likelihood of delayed recovery after general anesthesia is low [1]. In addition, compared to other intravenous anesthetics, especially propofol, remimazolam-induced sedation can be reversed by flumazenil and this availability of an antagonist is highly advantageous in clinical practice.

Due to its recent development, few studies have investigated the effect of remimazolam on postoperative recovery, primarily focusing on objective parameters such as physiologic endpoints, recovery time, and possible adverse events [2,7-10]. Although these parameters are crucial and require evaluation, they overlook the quality of recovery (QoR) from the patient’s perspective. To date, there has been no study investigating remimazolam’s impact on patients’ QoR.

Various measurement tools have been developed for the psychometric assessment of quality of recovery, including the 24-h functional ability questionnaire, postoperative quality of recovery score, and the Korean version of QoR-15 (QoR-15K) questionnaire [11-14]. Among these assessments, the QoR-15K questionnaire covers a wide range of components, including physical comfort, pain, psychological and emotional state, and cognition, as well as patient’s satisfaction [12]. In a previous randomized controlled study that investigated patient anesthesia satisfaction as a secondary endpoint, patients receiving remimazolam anesthesia reported high satisfaction levels, non-inferior to those of propofol [15]. While we hypothesize that patients will show high satisfaction scores in the recovery assessment, similar to the previous study [15], this is the first study to evaluate additional QoR parameters such as physical independence, pain, and psychological support, for which the associated scores are currently unknown.

Therefore, the aim of this study was to comprehensively evaluate various QoR of patients who received remimazolam general anesthesia, specifically remimazolam-remifentanil total intravenous anesthesia (TIVA) for hysteroscopy performed as day surgery. We used the translated Korean version of the 15-item QoR-15K questionnaire, which has been previously validated in the Korean surgical population, to assess QoR [12,14].

MATERIALS AND METHODS

Study design

This was a prospective, observational study, assessing the QoR and safety of remimazolam-remifentanil TIVA in patients undergoing day surgery. This study was approved by the institutional review board of the Seoul National University Bundang Hospital (Chairperson Hak Chul Jang, IRB no. B-2109-708-309), and registered at ClinicalTrials.gov (Trial no. NCT05320016). All participants provided written informed consent before study entry and the study was conducted in accordance with the Declaration of Helsinki. In addition, all methods were conducted following the Strengthening the Reporting of Observational Studies in Epidemiology guideline [16].

Study participants

Patients over 19 years of age with a physical status I or II of the American Society of Anesthesiology, who were scheduled for elective hysteroscopy as day surgery under the general anesthesia from November 2021 to December 2021, were included in this study. The exclusion criteria were, (1) history of liver dysfunction, renal insufficiency, cranial nervous system disorders, and glaucoma; (2) a body mass index over 35 kg/m²; (3) diagnosed with sleep apnea, severe or acute respiratory failure; (4) history of alcohol or drug dependence; (5) lactose intolerance; (6) dextrin 40 hypersensitivity; (7) shock or coma; (8) allergy or contraindications to both benzodiazepines and opioids. Based on the study flow diagram (Fig. 1), 38 patients were included in the final analysis.

Anesthesia

Premedication with intravenous midazolam (0.02 mg/kg) was administered before entering the operating room. Routine monitoring, including noninvasive blood pressure measurements, electrocardiography, and pulse oximetry were
conducted. In addition, bispectral index (BIS complete 2-channel monitor, Covidien) was applied on the forehead to monitor the depth of anesthesia.

General anesthesia was induced with remimazolam (By-favo Inj., Hana Pharm Co., Ltd., 6 mg/kg/h) and remifentanil (Ultiva Inj., GlaxoSmithKline Manufacturing S.p.A., 3.0 ng/ml of effect site concentration on the target-controlled infusion mode, the Minto model). If all of the following conditions were satisfied, LMA (Supreme™, Teleflex) was inserted: (1) BIS value < 60; (2) Observer’s assessment of alertness/sedation (OAA/S) score = 0; (3) Remifentanil Ce = Cp = 3 ng/ml; (4) loss of spontaneous breathing.

For the appropriate depth of general anesthesia (BIS value between 40 and 60), continuous infusion of remimazolam was carried out by controlling the infusion rate within the range of 1–2 mg/kg/h. Remifentanil was controlled within the range of 2 ng/ml to 6 ng/ml according to the depth of anesthesia. At the end of the surgery, remimazolam and remifentanil were discontinued. If all of the following conditions were satisfied, LMA was removed, (1) BIS value > 80; (2) OAA/S score > 3; (3) Remifentanil Ce < 1 ng/ml; (4) Spontaneous breathing. If the patient’s recovery was delayed 15 min after discontinuation of remimazolam, 0.2 mg of flumazenil was administered.

Recovery

In the post-anesthesia care unit (PACU) and day surgery center after the operation, the degree of consciousness, the level of postoperative pain, and the incidence of nausea and/or vomiting are investigated. Modified OAA/S scores were assessed as soon as patients arrived at the PACU and every 10 min thereafter. If the modified OAA/S score was < 2 in the PACU, 0.1 mg of flumazenil was administered. The total amount of flumazenil administered in the PACU did not exceed 0.5 mg. Twenty-four h after surgery, patients were rated on a scale of 1 to 10 using the translated Korean version of the15-item QoR-15K questionnaire (Supplementary Fig. 1) [14]. QoR-15K dimensions and corresponding QoR-15K items can be found in Supplementary Table 1.

Sample size calculation

The following formula was used for sample size calculation because we aimed to compare the means of two related QoR questionnaire items and dimensions within the same group of patients using a paired $t$-test:

$$n = \frac{2(\sigma^2) (Z_{\alpha} + Z_{1-\beta})^2}{E^2}$$

Where $n$ is the required sample size, $\sigma$ is the estimated standard deviation, $Z_\alpha$ is the $Z$-score corresponding to chosen significance level ($\alpha$), $Z_{1-\beta}$ is the $Z$-score for chosen power level (1-$\beta$), and $E$ is the effect size. The estimated standard deviation was 2 for QoR-15K items and dimension scores, as reported in previous studies [14,17]. The $Z$-score for a two-tailed test at a 5% significance level ($\alpha=0.05$) is approximately 1.96, and the $Z$-score for a power of 0.90 is approximately 1.28. The sample size was calculated to detect a difference of 2 points in the QoR measurements on a 10-point scale. Substituting these values into the equation above yields a minimum sample size of 22 patients. Assuming a sample size with a dropout rate of 20% [14], the adjusted required sample size was 28 patients, which was below the number analyzed in this study.

Statistical analysis

The normal distribution of continuous variable was evaluated using the Shapiro-Wilk test. Normally distributed continuous variable was presented as mean (standard deviations) and if the distribution was not normal, median (IQR, 3Q) was presented. In case of the QoR-15 questionnaire, mean and standard deviation of each item was calculated. The student $t$-test and one-way ANOVA were used to compare mean scores of QoR-15 dimensions. Inter-item and –dimension correlations were measured using the Spearman correlation coefficient ($\rho$). Reliability was measured for the consistency of QoR-15K and it was assessed by internal consistency, split-half reliability and test-retest reliability. Internal consistency was measured using Cronbach’s and test-retest reliability was measured using the intra-class correlation...
coefficient (ICC). All statistical analyses were performed via SPSS software, version 25.0 (IBM Co.). Values were considered statistically significant when P < 0.05.

**RESULTS**

Clinical and demographic characteristics of the total 38 patients are presented in Table 1. The mean age of patients was 48.4 ± 10.2 years with median anesthesia duration of 40.0 (range, 40.0, 56.3) min and median PACU length of stay of 29.5 (range, 22.8, 34.3) min. Two patients (5.3%) received flumazenil in the operating room because it required 15 min to meet our recovery criteria. One (2.6%) patient required flumazenil in the PACU because the modified OAA/S score decreased to 1. All patients successfully answered all items of QoR-15K questionnaires.

Mean scores of QoR-15K questionnaire items are summarized in Table 2 and the number of score ranges per QoR-15 item are shown in Fig. 2. The mean score of QoR-15K items was highest for able to communicate with family or friends (10 ± 0) followed by ability to breathe easy, enjoy food, feel rested and have a good sleep (9.97 ± 0.16) and severe pain (9.95 ± 0.23). In contrast, the mean score of QoR-15K items was lowest for moderate pain (8.66 ± 1.68) followed by feeling rested (9.24 ± 1.17) and having a feeling of general well-being (9.29 ± 1.06) (Table 2). This is because while no patient gave a score of 1–7 for severe pain, seven out of 38 (18.4%) patients claimed to experience moderate pain within a score range of 1–7 (Fig. 2).

For further analysis, the QoR-15K items were grouped into dimensions (i.e. pain, physical comfort, physical independence, psychological support and emotional state), the QoR-15K dimension scores were averaged to a 10-point scale. When comparing the 10-point scale score of pain to that of physical comfort (9.3 vs. 9.6), no statistically significant difference was again noted (P = 0.227, Fig. 3). With regards to physical comfort, one patient and two patients claimed to have experienced nausea or vomiting with a score of 1–3 and 4–7, respectively. No patient experienced difficulty with the ability to breathe easy, enjoy food, feel rested and have a good sleep.

Table 1. Demographic Characteristics and Clinical Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>48.4 ± 10.2</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.6 (20.7, 25.1)</td>
</tr>
<tr>
<td>ASA (I/II)</td>
<td>20 (52.6)/18 (47.4)</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>40.0 (40.0-56.3)</td>
</tr>
<tr>
<td>Flumazenil in the operating room (min)</td>
<td>2 (5.3)/1 (2.6)</td>
</tr>
<tr>
<td>PACU length of stay (min)</td>
<td>29.5 (22.8, 34.3)</td>
</tr>
<tr>
<td>Total remimazolam (mg)</td>
<td>71.5 (60.0, 91.5)</td>
</tr>
<tr>
<td>Total remifentanil (µg)</td>
<td>209.0 (170.8, 269.0)</td>
</tr>
</tbody>
</table>

Values are presented as mean ± SD, median (1Q, 3Q), or number (%). BMI: body mass index, ASA: American Society of Anesthesiologists, PACU: post-anesthesia care unit.

Table 2. The QoR-15K Scores

<table>
<thead>
<tr>
<th>QoR-15K items</th>
<th>Number of patients (n)</th>
<th>10-point score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score (1–3)</td>
<td>Score (4–7)</td>
</tr>
<tr>
<td>Able to breathe easy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Been able to enjoy food</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Feeling rested</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Have had a good sleep</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Able to look after personal hygiene unaided</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Able to communicate with family or friends</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Getting support from hospital doctor and nurse</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Able to return to work or usual home activities</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Feeling comfortable and in control</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Having a feeling of general well-being</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Moderate pain</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Severe pain</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Feeling worried or anxious</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Feeling sad or depressed</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Values are presented as number only or mean ± SD. QoR-15K: Korean version of 15-item Quality of Recovery.
good sleep in regards to physical comfort. Similarly no discernable difficulty (score of 1–3) was reported for QoR-15K items pertaining to physical independence and psychological support.

The inter-item and inter-dimension correlation matrices of QoR-15K are shown in Table 3 and Table 4, respectively. Inter-item Cronbach α and split-half reliability were 0.737 and 0.858 for 24-h QoR-15K, respectively. The test-retest ICC was 0.678 (95% confidence interval [CI], 0.506–0.810). Inter-dimension Cronbach α and split-half reliability were 0.722 and 0.769, respectively.

No significant correlation was found between total QoR-15K score and age (ρ = 0.094; 95% CI, –0.209 to 0.381; P = 0.573), PACU length of stay (ρ = –0.185; 95% CI, –0.439 to 0.137; P = 0.265) and duration of anesthesia (ρ = –0.223; 95% CI, –0.527 to 0.128; P = 0.178), thus excluding possible confounding effects.

Box-and-whisker plot and histogram of total QoR-15K score is shown in Fig. 4. Since patients scored on average 9 or above for each item, the total QoR-15K score did not show normal distribution. The skewness and kurtosis values of total QoR-15K score were –0.725 and –0.658, respectively. Out of the total 38 patients, 19 (50.0%) patients gave score range of 148 to 150 out of possible 150 for the total QoR-15K score.

**Discussion**

This is the first study to evaluate the QoR in patients receiving remimazolam-remifentanil TIVA. On average, the patients scored 9 and above for all QoR-15K items except for moderate pain, which averaged at 8.7. When categorizing and averaging the QoR-15 item scores into dimensions, all QoR-15-dimension scores exceeded 9 points. These results were obtained without the influence of confounding factors such as patient age, PACU length of stay, and anesthesia duration. Internal consistency, as measured by Cronbach’s α and split-half reliability, remained above recommended levels (0.70–0.90) [18]. In addition, throughout this study, no patient experienced severe pain, and only one patient reported a discernable post-discharge nausea and vomiting (PDNV).

While previous studies have investigated the effects of remimazolam on objective postoperative recovery parameters, such as physiologic endpoints, recovery time, and pos-
sible adverse events [2,7-10], there has been a gap in research regarding the QoR as perceived by patients who received remimazolam anesthesia. This study represents the first attempt to evaluate QoR as a primary endpoint in patients who underwent remimazolam-remifentanil TIVA. Furthermore, this study employed a widely used and validated psychometric assessment tool, the QoR-15, to thoroughly assess various aspects of recovery, including pain, physical comfort, physical independence, psychological support, and emotional state. These findings underscore the clinical significance of the study’s results.

In a prior study conducted by Shi et al. [15], cirrhotic patients undergoing endoscopic variceal ligation under general anesthesia were randomly assigned to either the remimazolam or propofol group. As a secondary endpoint, patient anesthesia satisfaction was assessed using a 10-point visual analog scale (VAS) [15]. While this scoring method was not as comprehensive as the QoR-15K questionnaire employed in this study, patients in the remimazolam group reported high satisfaction with their anesthesia experience, non-inferior to the propofol group [15]. Similar to Shi et al.’s study [15], we observed that the level of physical comfort, which encompasses factors such as the ability to breathe, have a good sleep, enjoy food, feel rested, and experience PDNV, demonstrated the strongest correlation with the total QoR-15K score. Particularly, the item ‘feel rested’ exhibited the highest correlation among all the QoR-15K items. These findings suggest that a significant portion of anesthesia satisfaction can be attributed to the quality of physical comfort experienced during remimazolam anesthesia.

In regards to postoperative nausea and vomiting (PONV), a prior study has reported that propofol possesses a direct antiemetic effect and can reduce the incidence of PONV [19]. Conversely, remimazolam lacks antiemetic properites, raising the possibility of a higher incidence of PONV with its use. However, a previous investigation comparing the frequency of PONV in craniotomy patients under either remimazolam or propofol found no significant difference in the incidence of PONV [9]. Furthermore, a study conducted by Zhang et al. [20], which involved patients undergoing hys-
Table 3. Inter-item Correlation for QoR-15K Scores Taken 24 h after Surgery

<table>
<thead>
<tr>
<th>QoR-15K Item</th>
<th>Total QoR-15K Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
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<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
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</thead>
<tbody>
<tr>
<td>Able to breathe easy</td>
<td>0.354†</td>
<td>-</td>
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<tr>
<td>Been able to enjoy food</td>
<td>0.169</td>
<td>0.403†</td>
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<tr>
<td>Feeling rested</td>
<td>0.676†</td>
<td>-0.005 – 0.145</td>
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<tr>
<td>Have had a good sleep</td>
<td>0.302</td>
<td>0.079, 0.099</td>
<td>0.301</td>
<td>-</td>
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<tr>
<td>Able to look after personal toilet and hygiene</td>
<td>0.258</td>
<td>-0.056 – 0.222</td>
<td>0.377†</td>
<td>-</td>
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<tr>
<td>Able to communicate with family or friends</td>
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<tr>
<td>Getting support from hospital doctors and nurse</td>
<td>0.264</td>
<td>0.302 – 0.081</td>
<td>0.074 – 0.111</td>
<td>-0.039</td>
<td>-</td>
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<tr>
<td>Able to return to work or usual home activities</td>
<td>0.483†</td>
<td>0.288, 0.269</td>
<td>0.108 – 0.046</td>
<td>0.322</td>
<td>-</td>
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<tr>
<td>Feeling comfortable and in control</td>
<td>0.370†</td>
<td>0.226 – 0.100</td>
<td>0.188 – 0.132</td>
<td>0.562†</td>
<td>-</td>
<td>0.805, 0.336†</td>
<td>-</td>
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<tr>
<td>Having a feeling of general well-being</td>
<td>0.534†</td>
<td>0.351 – 0.090</td>
<td>0.295 – 0.039</td>
<td>-0.128</td>
<td>-0.067, 0.152</td>
<td>-0.015</td>
<td>-</td>
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<tr>
<td>Moderate pain</td>
<td>0.599†</td>
<td>-0.015 – 0.101</td>
<td>0.514†</td>
<td>0.388†, 0.127</td>
<td>-</td>
<td>0.174, 0.022</td>
<td>0.216, 0.314</td>
<td>-</td>
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</tr>
<tr>
<td>Severe pain</td>
<td>0.218</td>
<td>-0.081 – 0.081</td>
<td>0.067 – 0.111</td>
<td>0.111 – 0.039</td>
<td>-</td>
<td>-0.486, 0.175</td>
<td>0.368†</td>
<td>-0.000, 0.250</td>
<td>-</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>0.520†</td>
<td>0.286, 0.024</td>
<td>0.326†</td>
<td>0.056 – 0.299</td>
<td>-0.111, 0.275</td>
<td>0.086, 0.361</td>
<td>0.008</td>
<td>0.159</td>
<td>-</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling worried or anxious</td>
<td>0.397†</td>
<td>-0.100 – 0.100</td>
<td>0.435†</td>
<td>0.132, 0.562†</td>
<td>-</td>
<td>0.379†, 0.336†</td>
<td>0.638†</td>
<td>-0.076, 0.216</td>
<td>0.368†</td>
<td>0.086</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling sad or depressed</td>
<td>0.234</td>
<td>0.282, 0.282</td>
<td>0.294 – 0.111, 0.039</td>
<td>-0.056, 0.143</td>
<td>-0.069, 0.257</td>
<td>0.023</td>
<td>-0.056, 0.159</td>
<td>0.368†</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

QoR-15K: Korean version of 15-item Quality of Recovery. *Following QoR-15K Item had zero variance because all patients gave a score of 10/10 and thus, the inter-item correlation could not be calculated. \( P < 0.05 \) was considered statistically significant.

---

Table 4. Inter-dimension Correlation for QoR-15K Scores Taken 24 h after Surgery

<table>
<thead>
<tr>
<th>QoR-15K dimension</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>0.60†</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical comfort</td>
<td>0.48†</td>
<td>0.82†</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional state</td>
<td>0.46†</td>
<td>0.46†</td>
<td>0.46†</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Support</td>
<td>0.36†</td>
<td>0.36†</td>
<td>0.36†</td>
<td>0.36†</td>
<td>-</td>
</tr>
</tbody>
</table>

\( P < 0.05 \) was considered statistically significant.
9.3 out of 10. Notably, these scores exceeded those of the propofol TIVA group. While the previous study focused on thyroid surgery, while ours was on hysteroscopic surgery, which may differ in invasiveness, these results still offer valuable insights into QoR after remimazolam general anesthesia and can provide a foundation for future controlled comparative studies. Second, our results were obtained from a single tertiary university hospital and study population was limited to patients receiving gynecologic day surgery, specifically hysteroscopic surgery. Some other effects of remimazolam including antiemetic effects as well as some aspects of QoR-15K scores may need to be verified through further studies involving various surgeries. Third, we used translated QoR-15K, which has been validated in a previous study [14] but there are other tools to evaluate patient recovery [11-14], some of which are more comprehensive such as QoR-40 [13]. Additionally, differences in questionnaires may have affected the measurement of recovery outcomes. Fourth, the QoR-15K questionnaire was only surveyed 24 h after surgery without further serial assessment. However, all of the patients had short postoperative hospital stay because of day surgery. Since patient’s mental and physical status can undergo rapid changes during acute postoperative phase, further investigation may be needed to evaluate changes in QoR-15K score for longer hospital stays after major surgeries.

In conclusion, patients receiving remimazolam-remifentanil TIVA showed satisfactory recovery, as indicated by 24-h postoperative QoR-15K scores, with no severe pain or PDNV. The results of this observational study suggest that remimazolam may be a suitable option for general anesthesia in day surgery, particularly in terms of patients’ QoR. However, further comparisons with other commonly used anesthetic agents, such as propofol, are warranted to better understand its comparative effectiveness.

**SUPPLEMENTARY MATERIALS**

Supplementary data is available at https://doi.org/10.17085/apm.23102.
FUNDING

None.

CONFLICTS OF INTEREST

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

DATA AVAILABILITY STATEMENT

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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REFERENCES

Charcot-Marie-Tooth disease (CMTD) is a genetic disorder characterized by progressive motor and sensory disorders [1,2]. It is the most commonly inherited neuromuscular disease, with mainly autosomal dominant (autosomal recessive or X-linked) inheritance [3]. The estimated prevalence of CMTD is 1:2,500 worldwide [4] and 1:19,230 in Korea [5]. Muscle weakness and atrophy typically develop in the distal lower limbs and slowly progress proximally, accompanied by motor and sensory deficits in all limbs over decades [2].

There are various types of CMTD: type 1 (demyelinating form) is characterized by a significant decrease in nerve conduction velocity (NCV); type 2 (axonal form) shows normal NCV with less severe clinical symptoms than those of type 1 and is a dominant intermediate type with variable NCV ranges [6,7]. The clinical manifestations are associated with various genetic anomalies and show different complications; however, distal muscle weakness and atrophy are typical clinical findings [1-3].

Background: Charcot-Marie-Tooth disease (CMTD) is a hereditary polyneuropathy associated with a life-threatening risk of pulmonary complications.

Case: A 61-year-old male with CMTD for 40 years was admitted for the drainage of an abscess in his left ankle. Total intravenous anesthesia was administered, and an electromyography device was attached to the hand for neuromuscular monitoring; however, the response was not measured. Kinemyography and acceleromyography devices were attached to both hands, and responses were obtained. After neuromuscular blockade (NMB) with rocuronium 0.6 mg/kg, the train-of-four (TOF) response on kinemyography was normally measured, but the post-tetanic count on acceleromyography consistently showed 0 during anesthesia. Sugammadex 200 mg was injected to reverse the NMB. After 5 min, the TOF ratios for kinemyography and acceleromyography exceeded 90%. The patient recovered without any complications.

Conclusions: For CMTD patients, acceleromyography or kinemyography is superior to electromyography, and sugammadex can be used to reverse NMB successfully.

Keywords: Anesthesia; Charcot-Marie-Tooth disease; Myography; Neuromuscular blockade; Neuromuscular monitoring; Sugammadex.
These clinical symptoms are mainly influenced by disease progression, specifically large axonal loss and decreased compound muscle action potential (CMAP) amplitude [7]. Despite the normal lifespan of CMTD patients, a severe clinical course can lead to life-threatening complications, such as vocal cord paralysis, pulmonary dysfunction due to respiratory muscle or diaphragm weakness, and respiratory failure [8,9].

The anesthetic management of CMTD patients should consider the possible risks of respiratory complications related to muscle weakness, autonomic dysfunction, and malignant hyperthermia [1,10,11]. Neuromuscular blockade (NMB) and its monitoring during general anesthesia are particularly challenging because CMTD is accompanied by motor weakness and peripheral polyneuropathy. After the use of neuromuscular blocking agents (NMBA), both prolonged NMB due to the loss of motor units [12-14] or denervation-like resistance [15] can occur. Therefore, adequate use of NMBA and continuous monitoring of NMB are essential in CMTD patients, and reversal of NMB to avoid postoperative pulmonary dysfunction should be considered [10,12,16,17].

This case report of abscess removal operation in a CMTD patient highlights anesthetic management from the perspective of neuromuscular transmission (NMT) monitoring, supplemented with an analysis of the literature. Written informed consent for publication of this case report was obtained from the patient after surgery. This case report is compliant.

**CASE REPORT**

A 61-year-old male (height, 178 cm; weight, 68 kg) visited our hospital complaining of pain and redness in the left ankle, which occurred without any specific cause. He was diagnosed with CMTD 1A in his early 20s and was not currently receiving treatment or medication. He had pes cavus foot deformity in both feet and atrophy of the peroneal muscle, which had worsened over 40 years (Fig. 1). He had a slight gait disturbance, but sensation and movement of the lower extremities remained normal. The patient’s family history revealed that his daughter also has a diagnosis of CMTD.

Although we recommended regional anesthesia or peripheral nerve block with sedation, the patient insisted on general anesthesia based on his experience. He was diagnosed with an intra-articular abscess, and surgical drainage was planned. The preoperative evaluation revealed no abnormalities on chest radiography or electrocardiography. Laboratory test results were normal except for a C-reactive protein level of 33 mg/L. Before the operation, his body tem-

![A](image1.png) ![B](image2.png)

**Fig. 1.** The patient exhibited weakness and atrophy of the peroneal muscle (A) with a pes cavus foot deformity (B), which are a characteristic feature of Charcot-Marie-Tooth disease.
perature was maintained at a slight fever above 37°C. The pulmonary function test results were within the normal range, without any respiratory symptoms. He did not complain of any other complications such as vocal cord paralysis, autonomic neuropathy, or neuropathic pain, except for diabetes, which was diagnosed approximately 10 years ago. At that time, the patient underwent lung biopsy under general anesthesia without any adverse events.

Total intravenous anesthesia with propofol and remifentanil was administered to avoid the risk of malignant hyperthermia. The patient was then transferred to the operating room without premedication. After attaching the monitoring devices, the patient was pre-oxygenated with 100% O₂. An electromyography (EMG) device (EMG-NMT module of Carescape® B850, GE Healthcare) was installed on the right arm appropriately according to the guideline [18]. Anesthesia was induced with propofol (Fresofol®, Fresenius Kabi) and remifentanil (Ultiva™, Mitsubishi Tanabe) using target-controlled infusion (TCI) pumps (Perfusor Space TCI, B. Braun). The target effect-site concentration (Ce) of propofol was increased to 3.0 μg/ml, and the values of state entropy and response entropy dropped below 60.

When the patient lost consciousness, mask ventilation with 6 L/min oxygen was administered, and NMT monitoring was initiated. A schematic overview of neuromuscular monitoring and blockade in the patient is shown in Fig. 2. An automatic calibration sequence was initiated to determine the supramaximal stimulation level for NMT monitoring. However, the response to supramaximal stimulation was not detected despite the movement of the thumb, and no train-of-four (TOF) response was monitored at a stimulation current of 70 mA. The EMG device was replaced with a

![Fig. 2. Schematic overview of neuromuscular monitoring and blockade of the patient. EMG: electromyography, AMG: acceleromyography, KMG: kinemyography, TOF: train-of-four, PTC: post-tetanic count.](image-url)
Device that used single-use surface electrodes (TetraGraph, Senzime AB); however, the TOF response could still not be measured. Owing to polyneuropathy, EMG was deemed unsuitable; therefore, the NMT monitoring device was switched to kinemyography (KMG; Carescaphe® B850, GE Healthcare) on the right hand and acceleromyography (AMG; TOFscan, IDMed) on the left hand. After an automatic calibration sequence, supramaximal stimulation was performed at a current of 70 mA in the KMG. The response in AMG was measured at 60 mA. Subsequently, 2-Hz TOF monitoring of the adductor pollicis muscles was performed every 12 s.

We planned to administer a small dose of rocuronium owing to the risk of delayed recovery from NMB [13], and 21 mg of rocuronium (0.3 mg/kg), a 95% effective dose, was administered. However, the TOF count (TOFc) remained at 4, and the amplitude of T4 was not reduced by more than 50% until 5 min. Thus, we administered an additional 21 mg of rocuronium, and the TOFc dropped to 0 after 2 min. The patient was then intubated, and TOF stimulations were administered every 1 min for monitoring TOFc or TOF ratio (TOFr) on the right hand using KMG. Simultaneously, the automatic post-tetanic count (PTC) mode of AMG was applied on the left hand. The TCI of propofol (Ce 2.0 to 4.0 µg/ml) and remifentanil (Ce 1.0 to 1.5 ng/ml) was used to maintain the anesthesia. The patient’s vital signs and hypnosis remained stable. His body temperature was maintained within normal limits using a forced air warmer (Bear Hugger®, 3M Company).

Thirty minutes after intubation, TOFc on KMG began to appear and reached 4 within 5 min. However, PTC on AMG consistently showed 0. Since it was difficult to objectively evaluate the degree of NMB and there was not much time left until the end of the surgery, we did not administer additional rocuronium. The surgery ended after approximately 60 min of intubation, and the TCI pump was turned off. At that time, the TOF ratios on the KMG was 0.34, whereas that of the AMG was 0. The AMG mode was converted to TOFr, and TOFr was 0. For the safe reversal from NMB, 150 mg (2 mg/kg) of sugammadex (Bridion®, MSD) was administered intravenously. Three min after sugammadex administration, TOFr began to appear on the AMG. After 10 min of sugammadex administration, TOFr was > 0.9 on both AMG and KMG, and self-respiration was restored. After the recovery of > 500 ml of tidal volume, the patient awakened. Exubation was carefully performed, and the patient was transferred to the recovery room. No respiratory depression or discomfort was reported in the recovery room. The next day, chest radiography and pulmonary function tests showed normal findings with forced vital capacity and forced expiratory volume in one second of 84.6% and 90.4% of the predicted normal values, respectively. The patient maintained stable hemodynamic and respiratory conditions in the ward. He was discharged without complications.

**DISCUSSION**

This case report presented a difficulty in obtaining reliable NMT monitoring results in a CMTD patient, which is essential for managing NMB. In this case, EMG could not detect the supramaximal stimuli or measure the TOF response, whereas KMG and AMG could be performed. These findings emphasize the need to employ appropriate NMT monitoring techniques for polyneuropathy patients such as CMTD.

Anesthetic management of CMTD patients can be challenging owing to the complex clinical characteristics of progressive motor and sensory deficits [1-3,8-11,19], as well as variable responses to NMBAs [12-15]. Choosing the correct rocuronium dose under these circumstances is a key difficulty. There is a potential for the development of prolonged postoperative NMB caused by a non-depolarizing NMB owing to the abnormal neuromuscular junction (NMJ) physiology of CMTD patients and impairment of the phrenic nerve and diaphragm [12-14,20]; however, resistance to NMB can be found after the use of NMBA despite muscle weakness [15]. Upregulation of acetylcholine receptors at the NMJ may be caused by denervation-like polyneuropathy, and as a consequence, a normal response or moderate resistance to NMBA can ultimately be shown [21]. As the initial dose of 0.3 mg/kg (21 mg) failed to induce adequate NMB in this case, an extra equivalent dose was necessary. These findings are consistent with those of a previous report showing a normal response to NMBA [15]. Moreover, if NMT monitoring is targeted to the chronically paralyzed muscle that shows resistance to NMB, there is a risk of administering excessive NMBA compared to the amount administered for the NMB of the respiratory muscles, which requires caution. Therefore, the effects of rocuronium in CMTD patients can be unpredictable, and adequate real-time NMT monitoring to titrate the dose of NMBAs is essential in these patients to balance the risk of inadequate muscle relaxation against prolonged paralysis.

However, monitoring NMT in CMTD patients presents unique challenges. **Table 1** presents previous case reports...
Table 1. Review of Case Reports That Describe Neuromuscular Monitoring during General Anesthesia in Charcot-Marie-Tooth Disease

<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>NMBAs</th>
<th>Reversal agents</th>
<th>Monitoring methods</th>
<th>Monitoring sites</th>
<th>Monitoring features</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al. (2019)[32]</td>
<td>Rocuronium</td>
<td>Pyridostigmine</td>
<td>None</td>
<td>-</td>
<td>Not mentioned.</td>
<td>Although the NMT module was prepared, the authors deemed it unnecessary.</td>
</tr>
<tr>
<td>Kappor et al. (2021)[33]</td>
<td>Atracurium</td>
<td>Neostigmine</td>
<td>None</td>
<td>-</td>
<td>Monitored visual notching of capnograph.</td>
<td>The authors thought PNS would be ineffective.</td>
</tr>
<tr>
<td>Naguib and Samarkandi (1998)[34]</td>
<td>Atracurium, Mivacurium</td>
<td>Neostigmine</td>
<td>AMG (TOF)</td>
<td>AP</td>
<td>Normal responses to both atracurium and mivacurium.</td>
<td>No evidence of prolonged response to atracurium and mivacurium.</td>
</tr>
<tr>
<td>Pogson et al. (2000)[12]</td>
<td>Vecuronium</td>
<td>Neostigmine</td>
<td>PNS (TOF)</td>
<td>AP</td>
<td>Only the T1 response showed at the PACU. All four responses were observed after additional use of neostigmine.</td>
<td>PNS was not utilized until the patient exhibited distress in the PACU because there were no issues during the previous anesthesia.</td>
</tr>
<tr>
<td>Gálvez-Cañellas (2013)[26]</td>
<td>Rocuronium</td>
<td>Sugammadex</td>
<td>AMG (ST, TOF)</td>
<td>AP and CS</td>
<td>Despite the absence of response in the AP, the response at the CS showed a 5 to 10% response.</td>
<td>CS could be useful and should be considered when access to the AP is challenging or impossible despite its inaccuracies.</td>
</tr>
<tr>
<td>Hiramatsu et al. (2022)[10]</td>
<td>Rocuronium</td>
<td>Sugammadex</td>
<td>AMG (TOF, PTC)</td>
<td>AP</td>
<td>Different response on both forearm. - Unable to monitor NMT at left arm while it was possible at right arm. - TOF ratio: &gt; 0.9 on right AP vs. 0 on left AP.</td>
<td>Prolonged respiratory paralysis refractory to sugammadex.</td>
</tr>
</tbody>
</table>


describing neuromuscular monitoring during general anesthesia for CMTD, showing various techniques, sites, and responses in NMT monitoring, indicating inter-individual variability. Although EMG-based NMT monitoring is gaining attention because of its accurate measurement and ability to overcome the problems of AMG-based equipment such as overestimation and postural limitations [22], muscle action potentials in CMDT patients may not be measurable using EMG because of its nature. In this case, supramaximal stimulation could not be obtained with EMG, and there was no TOF response despite a maximal stimulation current of 70 mA. EMG measures the CMAP, which can provide information on the number of functional fibers [22]. Demyelination neuropathy is associated with slowing of the NCV, prolongation of distal latency, and amplitude changes due to secondary axonal loss [23]. Moreover, the stimulation current required to produce minimal CMAP in CMTD type 1 patients is more than three times higher than that in normal patients [24]. Therefore, slowing of NCV, reduced CMAP of the muscles in CMT1, and a conduction block-like effect due to a high threshold for CMAP production may impair the EMG assessment of NMT [25]. Accordingly, AMG or KMG, which measures actual muscle contraction, may be more suitable for NMT monitoring in CMDT patients with muscle...
weakness and atrophy.

Interestingly, we monitored the TOF response using the KMG at 1 min interval on the right hand, while the automatic PTC mode using the AMG was applied to the left hand. The PTC remained at 0 throughout the monitoring period, although the TOFcs in the contralateral hand was 4. The response to TOF stimulation was absent, even though the AMG mode was converted from PTC to TOF. Although this discrepancy between the AMG and KMG might be caused by a difference in the progress of neuronal degeneration between the two hands [26], temporal depletion of acetylcholine release from nerve endings by PTC stimulation was suspected. During the calibration and initial administration of rocuronium, both AMG and KMG showed similar responses; however, AMG showed no response during PTC stimulation. Moreover, TOFr in the AMG was observed after the use of sugammadex. Therefore, the temporal dysfunction of NMJ associated with acetylcholine may have recovered after discontinuing PTC stimulation and administration of sugammadex. In an animal model of CMTD type 1, sustained nerve stimulation decreased acetylcholine release from nerve endings and temporarily impaired NMT [27]. Demyelinating polyneuropathy in CMTD is thought to be associated with structural and functional deficits in the NMJ. Moreover, it is possible that decreased acetylcholine release by stimulation of the PTC had an effect similar to that of increased sensitivity to NMBA at NMJ [28]; thus, no TOF response was observed until sugammadex administration. Therefore, the PTC mode may not be desirable for CMTD patients because it may cause errors in quantifying deep neuromuscular blockade.

In the present case, sugammadex was used to reverse NMB. In previous reports, sugammadex has been successfully used to reverse NMB in a CMTD patient without residual NMB [11,29]. However, prolonged respiratory paralysis has been reported despite the use of sugammadex [10]. The CMTD patient with severe restrictive pulmonary impairment showed resistance to high-dose sugammadex (17.3 mg/kg against rocuronium 0.73 mg/kg for a surgical duration of 273 min) with TOFr 0. Possible mechanisms for residual paralysis include reduced acetylcholine release from synapistic nerve endings and synaptic dysfunction of the respiratory muscles. Nonetheless, these perplexing results seem to originate from difficulties in NMB monitoring [10,26]. Reduced acetylcholine release from synapistic nerve endings or differences in the progression of neuropathy between the two hands may have led to unreliable NMT monitoring results [10,26]. It is assumed that the residual paralysis refractory to sugammadex was due to severe weakness of the diaphragm and respiratory muscles and not residual rocuronium in the NMJ. In the present case, the TOFr on KMG was 0.5 at the end of the surgery, and the patient recovered completely from NMB after using administration and showed normal postoperative pulmonary function. Therefore, sugammadex can provide reliable recovery from rocuronium-induced NMB in CMTD patients, and respiratory function can be restored if the patient’s neuropathy is not severe enough to induce life-threatening pulmonary dysfunction. In addition, Severe distal muscular weakness or atrophy may be accompanied by decreased NCV and CMAP, leading to the misinterpretation of NMT monitoring results [10,26]. Thus, confirmation of the applicability of the NMT device to the adductor pollicis muscle, whether the responses from both hands are similar or are supramaximal stimuli, can be obtained before using NMBA. In addition, NMT monitoring of the alternative muscles should be considered [26,30,31]. In the case of CMT patients with distal limb neuropathy, central muscles such as the corrugator supercilia or trapezius seem to provide information on adequate intubation and surgical conditions during surgery.

In summary, this case report highlights the complexities and nuances of NMT monitoring in CMTD patients. Given the complex nature of CMTD and the associated risks of postoperative pulmonary complications, it is imperative that anesthesiologists customize the NMB strategies for each patient. Adequate NMT monitoring using AMG or KMG is advisable; however, EMG has limitations in advanced polyneuropathy. The proper use of sugammadex according to NMT monitoring facilitates the rapid and safe reversal of NMB. The utility of employing alternative muscles to monitor NMT should be considered. Future research should focus on establishing evidence-based techniques for NMT monitoring in CMTD patients.

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**CONFLICTS OF INTEREST**

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

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Preoperative evaluation of systolic murmur with point-of-care echocardiography before an elective thoracic surgery
- A case report -

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Background: Systolic murmur suggesting the association of aortic valve (AV) stenosis or obstructive pathology in the left ventricular outflow tract (LVOT) usually requires preoperative echocardiographic evaluation for elective surgery.

Case: In a 63-year-old female patient undergoing elective thoracic surgery, the systolic murmur was auscultated on the right sternal border of the second intercostal space in the preoperative patient holding area. Point-of-care (POC) transthoracic echocardiography (TTE) demonstrated a systolic jet flow in the LVOT area. The peak systolic velocity of the continuous wave Doppler tracing, aligned to the LVOT and the AV, was approximately 1.5 m/s. The peak/mean pressure gradient was 11/6 mmHg for the AV and 9/5 mmHg for the LVOT. Anesthesia was induced under continuous TTE imaging. Intraoperative transesophageal echocardiography also confirmed the absence of any cardiac pathology.

Conclusions: POC echocardiography offered a thorough preoperative evaluation of an unexpectedly identified systolic murmur, avoiding a potential delay in the operation schedule for conventional preoperative echocardiographic evaluation.

Keywords: Echocardiography; Point-of-care testing; Systolic murmurs; Ventricular outflow tract, left.

CASE REPORT

A 63-year-old female with a 15-year history of well-controlled hypertension (height of 152.9 cm and weight of 74.5 kg) was scheduled for a video-assisted thoracic surgery for a slowly growing pulmonary nodule in the right upper lobe (RUL). While no cardiac symptoms had been noted during the routine pre-anesthetic evaluation, an intermittent systolic murmur was pointed out on the patient’s arrival at the pa-
tient-holding area. The murmur was pan-systolic in a conventional stethoscope and audible at the right sternal border of the second intercostal space in the supine position. Position change and the Valsalva maneuver did not affect the characteristics of the murmur. It was necessary to identify aortic valve (AV) stenosis, as well as to identify hypertrophic cardiomyopathy that could cause left ventricular outflow tract (LVOT) obstruction.

An attending anesthesiologist performed POC 2-dimensional (2D) transthoracic echocardiography (TTE, Epiq CVX\textsuperscript{TM} cardiovascular ultrasound system and X5-1\textsuperscript{TM} 3-dimensional [3D] transducer, Philips) to evaluate whether the systolic murmur had a potential association with severe AV stenosis or LVOT obstruction (Fig. 1A, Video 1A). The AV area was estimated as 2.11–2.33 cm\textsuperscript{2} and the LVOT was as 1.79–1.98 cm\textsuperscript{2}, respectively, by using the continuity equation. The peak/mean pressure gradient was 11/6 mmHg for the AV and 9/5 mmHg for the LVOT (figures were not presented).

In apical 4-chamber imaging, the left ventricle (LV) wall motion and Doppler analyses (mitral valve [MV] inflow and MV annular motion) suggested well-preserved systolic and diastolic performance: LV ejection fraction of 62%; the ratio of early diastolic MV inflow to early diastolic MV annulus motion (E/e’ ratio) was 4.5; and the LV 4-chamber longitudi-

![Fig. 1. Preoperative TTE imaging. (A) Apical 4-chamber view with poor nearfield delineation of LV wall motion. (B) Global longitudinal strain of LV and RV in apical 4-chamber view was -23.2% and -26.1%, respectively. (C) Continuous-wave Doppler tracing of LVOT and AV blood flows in the modified apical 4-chamber view is approximately 1.5 m/sec. (D) The distance between the MV coaptation and LV septum (C-Sept) is far greater than 2.5 cm in the parasternal long-axis view (two white dotted lines indicates the anterior and posterior MV leaflets). (E) In the absence of AV stenosis, SAM of anterior MV leaflet or LVOT obstruction, the systolic jet flow in the LVOT area is noted in the parasternal long-axis view. Ao: aortic valve opening, AV: aortic valve, C-sept: the distance between the mitral valve coaptation and left ventricular septum (yellow dotted line with reversed arrows in both ends), LA: left atrium, LV: left ventricular cavity, LV GLS A4C: LV global longitudinal strain in apical four-chamber view, LVOT: LV outflow tract, MV: mitral valve, RA: right atrium, RV: right ventricle, RV FWS: RV free wall strain, SAM: systolic anterior motion, TTE: transthoracic echocardiography.]
nal strain and right ventricular free-wall longitudinal strain, measured by on-cart software (Q-Lab™, Philips), were –23.2% and –26.1%, respectively (Fig. 1B, Video 1B).

The peak systolic velocity of the continuous wave Doppler tracing, aligned to the LVOT and AV in a modified apical 4-chamber view, was approximately 1.5 m/s and unaffected by applying the Valsalva maneuver (Fig. 1C).

The parasternal long-axis TTE image provided detailed information on the LVOT flow around the AV, MV apparatus, hypertrophied LV septum, and LVOT: no apparent pathology suggesting AV stenosis, such as calcification, fusion, or limited motion of AV leaflets, was noted (Fig. 1D, Video 1C). Despite systolic jet flow in the LVOT area, the geometry of the MV apparatus and the LVOT did not have risk factors for potentially developing systolic anterior motion (SAM) of the anterior MV leaflet or dynamic LVOT obstruction: the distance between the MV coaptation and the hypertrophied LV septum (C-Sept) was far greater than 25 mm, and the ratio of the length of the anterior to posterior MV leaflets was far greater than 1.5 [1].

The planned lobectomy proceeded without delay for performing a conventional preoperative echocardiographic evaluation. Two anesthesiologists induced general anesthesia under continuous monitoring of invasive arterial pressure and parasternal TTE imaging.

After anesthesia induction, real-time 3D transesophageal echocardiography (TEE, X8-2t xMatrix™ 3D transducer, Philips) confirmed the POC TTE findings. It provided much more detailed information about the origin and the nature of the murmur: the systolic jet flow arose from the narrow space surrounded by the anterior MV chordae tendineae (at the tip of the posteromedial papillary muscle) and the hypertrophied inferior LV wall (Fig. 2A and B, Video 2A and B). The jet traversed the LVOT area and reached the AV annulus, and its flow intensity was variable to the changes in the LV filling status (Fig. 2C, D).

The planned RUL lobectomy was completed, and the patient was discharged without any clinical event with hemodynamic instability. Before the discharge, a cardiologist performed a TTE due to an instantaneous aggravation of the murmur and concluded that the murmur was physiologic and required no further treatment.

Informed consent for publication of the present case was obtained from the patient.

DISCUSSION

The present case showed the value of POC TTE in providing an immediate cardiac evaluation in a patient presenting a sudden systolic murmur. POC TTE enabled the quick assessment of the systolic murmur and ruled out the current and potential association of severe AV stenosis or dynamic LVOT obstruction. The immediate and comprehensive cardiac evaluation prompted elective surgery without case cancellation for further echocardiographic evaluation.

Focused cardiac ultrasound performed by non-cardiologists (FOCUS, a similar definition of POC echocardiography) has provided essential information regarding associated cardiac pathologies and facilitated clinical decision-making in various critical scenarios [2]. FOCUS performed by anesthesiologists, especially during the preoperative period, can add enormous benefit to gaining insight regarding the associated pathologies, facilitating time-sensitive clinical decision-making in the surgical arena, and improving perioperative management [3,4].

Systolic murmurs are common in old ages [5,6], but its association suggests a higher likelihood of AV stenosis or obstructive pathology in LVOT. Therefore, proceeding or postponing the elective surgical case without further evaluation can be challenging in patients presenting systolic murmur. As in the present case, the dynamic nature of the murmur, as indicated by its absence of consistency, may complicate the complexity. Since perioperative anesthesia-induced vasodilation is critical to patients with severe AV stenosis and insufficiently attenuated noxious stimuli can induce catastrophic hemodynamic collapse in patients with dynamic LVOT obstruction, it is necessary to implement intense perioperative hemodynamic vigilance and thorough preoperative POC cardiac evaluation in a patient suddenly presenting a systolic murmur.

The peak velocity of the continuous-wave Doppler tracing aligned to the LVOT and AV was approximately 1.5 m/s (pressure gradient reaching about 9 mmHg) and not affected by applying the Valsalva maneuver. The peak pressure gradient and the discrete nature of the flow velocity enabled the exclusion of the possible association between AV stenosis and LVOT obstruction.

In the present case, in addition to the invasive BP monitoring, POC TTE monitoring was applied to detect and avoid dynamic LVOT obstruction due to relative hypovolemia and increased Venturi effect aggravating the risks during anesthesia induction [7,8]. In addition, the papillary muscle and
the LV inferior wall. The jet’s size and intensity were changing specifically to the LV filling status and contractility.

Meanwhile, the Venturi effect (sucking) is not the only factor developing SAM and dynamic LVOT obstruction. Unfavorable geometry of MV leaflet apparatus and LVOT reducing C-Sept, such as hypertrophied LV septum and a relatively longer posterior MV leaflet (compared to anterior MV leaflet) [1,9], can increase the risk of dynamic LVOT obstruction. In patients with shorter C-Sept, systolic LV flow can easily drag the anterior MV leaflet into LVOT [1,8,9].

In the present case, C-Sept, far longer than 25 mm, could exclude the potential risk of dynamic LVOT obstruction, even in unexpected LV filling status or intrathoracic pressure changes [1]. The variable intensity of the jet flow in 2D and 3D TTE and TEE imaging, specific to the changes in the LV dimension and filling status, may explain the inconsistency of the systolic murmur: preoperative fasting and dehydration might reduce LV dimension and exaggerate the systolic jet and murmur, which could be apparent in auscultation immediately before the start of the case [10,11].
In the meantime, there is no consensus regarding the extent of POC TTE. In most cases, the coverage may be limited to evaluating primary structural and functional cardiac problems because of the limited capabilities of hand-held devices. POC TTE can roughly detect SAM of anterior MV leaflet and dynamic LVOT obstruction, in addition to confirming the presence of valvular stenosis or regurgitation using Doppler [12]. A simple hand-held ultrasound device may be sufficient for POC TTE examination to assess murmurs, hemodynamic instability, ventricular function, and etiology of dyspnea [13]. In surgeries like hip fractures that are not emergencies but are essential, proceeding with the procedure can reduce the overall mortality rate [14] and prevent delays in treatment when necessary [15]. As in the present case, if a sophisticated and high-end TTE device (4-dimensional echo probe with sophisticated on-cart software analyzing LV wall motion, such as strain and tissue Doppler) can be applied by experienced anesthesiologists, the scope of POC TTE can be expanded to the thorough assessment of the valvular flow Doppler and cardiac wall motion.

SUPPLEMENTARY MATERIALS

Supplementary video is available at https://doi.org/10.17085/apm.23124.

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None.

CONFLICTS OF INTEREST

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DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

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AUTHORS’ REPLY: We thank Dr. Sethuraman for his interest in our case report [1]. We want to reply because we believe that organizing the concept of the intertransverse process block (ITPB) and discussing it in Anesthesia and Pain Medicine will help readers better understand the process.

In determining the nomenclature of regional anesthesia, the ITPB concept encompasses the multiple injection costotransverse block, the subtransverse process interligamentary plane block, the costotransverse foramen block (CTFB), and the midpoint transverse process to pleura block (MTPB) [2].

Please note that we performed a ‘costotransverse foramen block’ in case 1 [3], which is a faithful reproduction of the report by Shibata et al., and we did not perform a ‘multiple injection costotransverse block.’ In fact, there was a discussion between Dr. Shibata’s group and Dr. Nielson’s group regarding with the needle direction [4]; please refer to that as well. We performed CTFB in support of the opinion of Dr. Shibata et al that caudal to cephalad needle direction minimizes the risk of neurovascular injury. Therefore, we believe that the needle direction was correct.

We believe this point was caused by the confusion of nerve blocks with similar names and concepts, and that it is clear that procedures of ITPB need to be standardized.

Another point of interest in his letter was the representation of CTFB and MTPB as interfascial plane blocks. ITPB targets the tissue complex posterior to the superior costotransverse ligament (SCTL) [5] and is considered distinctly different from blocks that target the fascial plane, such as the erector spinae plane block.

This ‘intertransverse tissue complex’ comprises the intertransverse ligament, fatty tissue, the intertransverse and laversores costarum muscles, and the SCTL. Different from interfascial plane blocks, the feature of achieving analgesic efficacy by administration of local anesthetics into tissue complexes closer to the pathway to the paravertebral space is unique to ITPB.

In summary, the concept of ITPB has been established, but standardization of the technique is needed, as well as clarification of the mechanism and recommendations for appropriate clinical indications.

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Soiling of non operative lung during one lung ventilation using EZ blocker in a tracheostomised patient

TO THE EDITOR:

Sir,

Tracheostomy is a clinical scenario where a double-lumen tube can be difficult to insert and other methods of lung isolation are preferred. We would like to report a complication with the use of an EZ blocker (Teleflex Medical Incorporated), used for lung isolation in a patient with a tracheostomy. A 46 year old male patient presented to the hospital with complaints of altered sensorium and right-sided weakness. Noncontrast computed tomography of the head revealed left frontal and temporal intracranial haemorrhage with intraventricular extension. The patient was intubated because of a poor Glasgow coma scale and shifted to the intensive care unit (ICU). During the ICU course, he developed pleural effusion, for which an intercostal drain (ICD) was inserted and the patient was tracheostomised because of prolonged intubation. Because of the failure of the lung to expand despite an ICD, contrast enhanced computed tomography thorax was done which showed a left-sided hydropneumothorax with segmental collapse of the left lower lobe and a fistulous communication between left segmental bronchus and pleural cavity. The patient was considered for video-assisted thoracoscopic decortication and wedge resection of the left lower lobe segment. After induction of anaesthesia with injection fentanyl, propofol, and rocuronium, an EZ multiport adapter was connected to the tracheostomy tube 15 mm connector, and the tube was pulled out a little to allow for the Y-shaped limbs to open up considering the short distance of the tracheostomy site to the blocker. The EZ bronchial blocker was inserted under the guidance of a fiberoptic bronchoscope and the patient was positioned in the right lateral decubitus position for surgery with isolation of the left lung. Left sided empyema was noted on thoracoscopy, septations were removed and decortication done. Because of difficulty in the dissection of the posterior segments, surgery was converted to open thoracotomy. On the surgeon’s request for two lung ventilation to look for a fistula, the left lung was suctioned through the bronchial blocker port, and the cuff was deflated. The patient developed sudden increased peak airway pressures of 40 cmH₂O, and desaturation up to 80%. On auscultation, there was reduced air entry on the dependent side. Suction with 10 French suction catheter through bronchial blocker port was tried, but no improvement in peak airway pressure and saturation was noticed. A diagnostic fiberoptic guided visualisation of the right bronchus showed a mucus plugging of the right bronchus which could not be suctioned out with the 2.8 mm bronchoscope compatible with the EZ blocker. Bronchial blocker was then removed, a larger fiberoptic bronchoscope (FOB) of 4.6 mm was inserted and the mucus plug was suctioned out. The surgery was continued with two lung ventilation with low tidal volumes and low Positive end-expiratory pressure. A short apnoeic duration of 1 to 5 min was provided for the closure of the Broncho pleural fistula. The patient was shifted to ICU on ventilator support and weaned off the ventilator on the first postoperative day.

EZ blocker has been used successfully in patients with tracheostomy and its ease of positioning with minimal intraoperative displacement has been reported [1]. In a review by Moritz et al. [2] no serious complications were reported in 100 cases with EZ blocker. No reports of lung soiling have been reported with the use of EZ blocker but such complication should also be anticipated while deflation of the bronchial cuff as the secretion distal to the cuff can move into the trachea owing to the position of non-dependent lung. Also, larger size FOBs should be kept handy as smaller FOBs compatible with the EZ blocker do not allow for suction of larger clots and mucus plugs.

We suggest that increased airway pressures and desaturation on deflating cuff of the EZ blocker should raise a suspicion of dependent lung contamination. Also, all sizes of bronchoscope should be kept in the cart while using an EZ blocker for lung isolation.

Karthik Lakshmikantha, Tanvi M Meshram, Kamlesh Kumari, Darshana Rathod, and Ankur Sharma
Complications of using EZ blocker

Kamlesh Kumari, Darshan Rathod, Ankur Sharma. Supervision: Kamlesh Kumari, Darshan Rathod, Ankur Sharma.

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REFERENCES
1. Online manuscript review process and guidelines for submission

1) All manuscripts must be submitted through the online submission system (available at http://submit.anesth-pain-med.org). Any inquiries about the manuscripts should be posted on the “Contacting Author” page, which is available to the right upon logging in. Specify the manuscript number, author, and corresponding author when posting an inquiry.

2) The corresponding author should be a faculty. The corresponding author will be notified by e-mail whenever there is any change in the status of a submitted manuscript, and any resubmission can only be made by the corresponding author.

3) Once the manuscript has been submitted and placed under review, the content or author information cannot be changed.

4) Before submitting the reviewed manuscripts, please ensure that the title page contains the author names, affiliations, and corresponding author information.

5) Failure to submit responses to comments by reviewers and editors, along with the revised manuscript, within 60 days will be considered as “no intention to publish,” and the review process will be terminated.

2. Mandatory English editing for Korean authors

APM has made English editing mandatory for manuscripts submitted on or after September 1, 2013. Authors are responsible for the cost of editing. For English manuscripts, please submit them to a professional editing service after acceptance and upload the edited file and certificate of editing in the manuscript submission system. Manuscripts edited by an individual and not through a professional editing service will not be accepted. Manuscripts submitted in Korean will be translated into English by the Society after acceptance, and Korean version will be published only on the website (www.anesth-pain-med.org).
Instructions for Authors

Enacted: May 15, 2006
Recently revised (15th): January 16, 2023

Anesthesia and Pain Medicine (APM) is the official scientific journal of the Korean Society of Neuroscience in Anesthesiology and Critical Care (KSNACC), the Korean Society for Anesthetic Pharmacology (KSAP), the Korean Society of Obstetric Anesthesiologists (KSOA), the Korean Society of Pediatric Anesthesiologists (KSPA), the Korean Neuromuscular Research Society (KNRS), the Korean Society of Cardiothoracic and Vascular Anesthesiologists (KSCVA), the Korean Society of Transplantation Anesthesiologists (KSTA), the Korean Spinal Pain Society (KSPS), the Korean Society of Regional Anesthesia (KSRA), the Korean Society for Airway Management (KSAM), and the Korean Society of Geriatric Anesthesia and Pain (KSGAP). The abbreviated title is “Anesth Pain Med”. It is published in English four times a year on the last day of January, April, July, and October.

I. Editorial Policy

The Editor assumes that all authors listed in a manuscript have agreed with the following policy of the APM on submission of manuscript. Except for the negotiated secondary publication, the manuscript submitted to the APM must be previously unpublished and not be under consideration for publication elsewhere. Under any circumstances, the identities of the referees will not be revealed. Minimum publication charges and additional reprint fees will be due on every manuscript. All published manuscripts become the permanent property of the Korean Society of Anesthesiologists (KSA) and may not be published elsewhere without written permission. APM adheres completely to guidelines and best practices published by professional organizations, including Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (http://www.icmje.org/icmje-recommendations.pdf) from ICMJE and Principles of Transparency and Best Practice in Scholarly Publishing (joint statement by COPE, DOAJ, WAME, and OASPA; http://doaj.org/bestpractice) if otherwise not described below.

II. General Information

1. Publication types

APM focuses on clinical research, experimental research, case reports, reviews, letters to the editor, online images, and various introductions.

2. Language

APM publishes articles in English. The manuscript submitted in Korean will be translated into English by the society after acceptance. Korean version will be published only on the website (www.anesth-pain-med.org).

Spelling should abide by American spellings. Medical terminology should be written based on the most recent edition of Dorland’s Illustrated Medical Dictionary. Accepted manuscripts are requested to be proofread by professional English editors.

3. Submission of manuscripts

In addition to members of the Korean Society of Anesthesiologists, any researcher throughout the world can submit a manuscript if the scope of the manuscript is appropriate. Authors are requested to submit their papers electronically using the online manuscript submission system, available at: http://submit-apm.org. Authors, reviewers, and editors send and receive all correspondences through this system. Final revisions by authors should be submitted within 1 week of the request.

4. Data Availability Statement

Data sharing is encouraged by the APM, but a Data Availability Statement will be required and published with the manuscript. Authors will be provided the following options during submission or may use a draft of their own.

• The datasets generated during and/or analyzed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
• The datasets generated during and/or analyzed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
• The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.
• Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.
• All data generated or analyzed during this study are includ-
ed in this published article [and its supplementary information files].

- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of [third party name].

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Preprint submission will be processed through the usual peer-review process. In addition, the preprint’s history will be tracked by additional independent editor, with an emphasis on the posting procedure and format.

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Moreover, APM does not permit referencing a preprint as a reference unless there is an exceptional circumstance that the authors can justify.

If the authors of a submitted article differ from those of the preprint, the authors must explain the change in authorship and demonstrate that it complies with ICMJE recommendations.

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Artificial Intelligence (AI) programs (e.g. ChatGPT or other similar software) cannot be considered as authors of submitted manuscripts because they do not meet the requirements for authorship. For instance, they cannot understand the role of authors or take responsibility for the content of the paper. Additionally, AI cannot meet the authorship criteria set by organizations such as the International Committee of Medical Journal Editors (ICMJE). This includes having the ability to give final approval for publication and being accountable for the accuracy and integrity of the work.

Furthermore, AI lacks the capacity to comprehend a conflict of interest statement, and cannot legally sign such a statement. Additionally, AI does not have independent affiliation from its creators, nor can it hold copyright.

Therefore, when submitting a paper, authors should not include AI as authors but rather acknowledge the use of AI and provide transparent information about how it was used in writing the manuscript. As the field of AI is rapidly evolving, authors using AI should declare this fact and provide specific technical details about the AI model used, including its name, version, source, and the method of application in the paper. This is in line with the ICMJE recommendation of acknowledging writing assistance.

7. Peer review process

- The APM has an online submission and peer review system at http://submit.anesth-pain-med.org/. All submissions and peer review processes are done through the online submission system.
- Manuscripts to be reviewed: All submitted manuscripts are peer reviewed. Commissioned manuscripts are also reviewed. Research data or supplementary materials are subjected to peer review.
- Who conducts peer review: Submitted manuscripts will be reviewed by 2 or more external experts in the corresponding field. The editor selects peer reviewers according to the recommendation of the Editorial Board members or from the external expert database maintained by the editorial office. Some publication types, including editorials, errata, corrigenda, retraction, withdrawal, and letters to the editor, are reviewed by the editorial board member without external peer review.
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(Crosscheck). If a certain amount of the duplicate part is detected, it is returned to the authors.

- Duration for the first decision: The result of the first peer review is usually finished within two months. If there is no correspondence from the editorial office on the fate of the submitted manuscript two months after the submission, please get in touch with the editorial office at https://www.anesth-pain-med.org/about/contact.php.

- Revision process: The Editorial Board may request authors to revise the manuscripts according to the reviewer’s opinion. After revising the manuscript, the author should upload the revised files with a reply to each item of the reviewer’s opinion. Additions and amendments to the revised manuscript should be highlighted in red. The author’s revisions should be completed within 60 days after the request. If it is not received by the due date, the Editorial Board will not consider it for publication. To extend the revision period to more than 60 days, the author should negotiate with the Editorial Board. The manuscript review process should be finished with the second review. If the reviewers wish further review, the Editorial Board may consider it. Statistical editing is also performed if data need professional statistical review by a statistician. APM neither guarantees acceptance without review nor very short peer review times for unsolicited manuscripts.

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- The publication date is published with all published papers, including dates of submission, revision, and acceptance.

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The review and publication processes not described in the Instructions for Authors will be incorporated into the Editorial Policy Statements approved by the Council of Science Editor Board of Directors, available at www.councilscienceeditors.org/.

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III. Research and Publication Ethics Guidelines

For the policies on research and publication ethics, the “Good Publication Practice Guidelines for Medical Journals” (https://www.kamje.or.kr/board/view?b_name=bo_publication&boid=13) or the “Ethical Guidelines on Good Publication” (http://publicationethics.org/resources/guidelines) or “Ethical Considerations in the International Committee of Medical Journal Editors” (http://www.icmje.org/recommendations) are applied.

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The corresponding author is required to summarize all authors’ conflicts of interest disclosures. The disclosure form shall be same with ICMJE Uniform Disclosure Form for Potential Conflicts of Interest (www.icmje.org/conflicts-of-interest). A conflict of interest may exist when an author (or the author’s institution or employer) has financial or personal relationships or affiliations that could influence (or bias) the author’s decisions, work, or manuscript. All authors should disclose
their conflicts of interest, i.e., (1) financial relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony), (2) personal relationships, (3) academic competition, and (4) intellectual passion. These conflicts of interest must be included as a footnote on the title page or in the Acknowledgements section.

All funding sources should be declared on the title page or in the Acknowledgements section at the end of the text. If an author’s disclosure of potential conflicts of interest is determined to be inaccurate or incomplete after publication, a correction will be published to rectify the originally published disclosure statement, and additional action may be taken as necessary.

If one or more editors are involved as authors, the authors should declare conflict of interest.

Ex) AAA has been an editor of the Anesthesia and Pain Medicine since 2017; however, he was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

2. Statement of informed consent

Copies of written informed consents and Institutional Review Board (IRB) approval for clinical research are recommended to be kept. The editor or reviewers may request copies of these documents to clarify potential ethical issues.

3. Protection of privacy, confidentiality, and written informed consent

Identifying details should not be published in written descriptions, photographs, or pedigrees unless it is essential for scientific purposes and the patient (or his/her parents or guardian) provides written informed consent for publication. Additionally, informed consent should be obtained in the event that the anonymity of the patient is not assured. For example, masking the eye region of patients in photographs is not adequate to ensure anonymity. If identifying characteristics are changed to protect anonymity, authors should assure that alterations do not distort scientific meaning. When informed consent has been obtained, this should be indicated in the published article.

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In the reporting of experiments that involve human subjects, it should be stated that the study was performed according to the Helsinki Declaration of 1975 (revised 2013) (Available from https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/) and approved by the Institutional Review Board (IRB) of the institution where the experiment was performed. Clinical studies that do not meet the Helsinki Declaration will not be considered for publication. Identifying details should not be published (such as name, initial of name, ID numbers, or date of birth).

In the case of an animal study, a statement should be provided indicating that the experimental processes, such as the breeding and the use of laboratory animals, were approved by the Research Ethics Committee (REC) of the institution where the experiment was performed or that they did not violate the rules of the REC of the institution or the NIH Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, https://www.nap.edu/catalog/5140/guide-for-thecare-and-use-oflaboratory-animals). The authors should preserve raw experimental study data for at least 1 year after the publication of the paper and should present this data if required by the Editorial Board.

5. Registration of the clinical research

It is recommended that all clinical trials be registered in the primary registry before submission. APM accepts registration in any of the primary registries that participate in the World Health Organization (WHO) International Clinical Trials Portal (http://www.who.int/ictrp/en), NIH ClinicalTrials.gov (http://www.clinicaltrials.gov), or Korea Clinical Research Information Service (CRiS, http://cris.nih.go.kr).

6. Reporting guidelines

The APM recommends that a submitted manuscript follow reporting guidelines appropriate for various study types. Good sources for reporting guidelines are the EQUATOR Network (www.equatornetwork.org) and the NLM's Research Reporting Guidelines and Initiatives (www.nlm.nih.gov/services/research_report_guide.html).

7. Author and authorship

An author is considered to be an individual who has made substantive intellectual contributions to a published study and whose authorship continues to have important academic, social, and financial implications.

Authorship credit should be based on: (1) substantial contributions to the conception or design of the work, or to the acquisition, analysis, or interpretation of data for the work; (2)
the drafting of the article or revising it critically for important intellectual content; (3) final approval of the version to be published; and (4) agreement on taking accountability for the accuracy or integrity of the work. Authors should meet these four criteria, and these criteria distinguish the authors from other contributors.

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3) Plagiarism for scientific English
   Copying of verbatim text, often from multiple sources

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IV. Manuscript Preparation

APM recommends compliance with some or all of the following guidelines (https://www.equator-network.org).

CONSORT for reporting of randomized controlled trials (http://www.consort-statement.org)

STARD for reporting of diagnostic accuracy studies (http://www.stard-statement.org)

STROBE for reporting of observational studies in epidemiology (http://www.strobe-statement.org)

PRISMA for reporting of systematic reviews (http://www.prisma-statement.org)

MOOSE for reporting of Meta-analyses of observational studies (https://jamanetwork.com/journals/jamasurgery/article-abstract/2778476)

CARE for reporting of clinical cases (https://www.care-statement.org)

AGREE for reporting clinical practice guidelines (http://www.agreetrust.org/resource-centre/agree-reporting-checklist/)

ARRIVE for reporting of animal pre-clinical studies (https://arriveguidelines.org/arrive-guidelines)

1. Word processors and format of manuscripts

A manuscript must be written in proper and clear English or Korean. Our preferred file format is DOCX or DOC. Manuscripts should be typed double-spaced on A4-sized paper, using 12 point font in English, using 10 point font in Korean.
2. Abbreviation of terminology

Abbreviations should be avoided as much as possible. When they are used, a full expression of the abbreviated words should be provided at the first use, with the abbreviation following in parentheses.

Ex) target controlled infusion (TCI)
After that, “TCI” can be used instead of “target controlled infusion.”

Common abbreviations may be used, however, such as DNA. Abbreviations can be used if they are listed as a MeSH subject heading (https://www.ncbi.nlm.nih.gov/mesh).

3. Word spacing

1) Leave 1 space on each side when using arithmetic marks such as +, −, ×, etc.
Ex) $24 \pm 2.5$

Leave no space when using a hyphen between words.
Ex) intra-operative

2) When using parentheses, leave 1 space on each side in English, and leave no space in the Korean manuscript.

3) When using brackets in parentheses, apply square brackets.
Ex) ([ ])

4) Manuscripts in Korean should obey the rules of Korean spelling (www.korean.go.kr).

4. Citations

1) If a citation has 2 authors, write as “Hirot a 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) Citations should be applied after the last word.
Ex) It is said that hypertension can be induced [1] and the way to injure the brain [2] is...
Ex) Choi and Kim [1] reported...

3) Apply citations before a comma or period.
Ex) ...is reported [1],

4) Several or coupled superscripts can be written as [1–5] or [1,3,5].

5. Arrangement of manuscript

The manuscript should be organized in the order of title, abstract, introduction, methods, results, discussion, acknowledgments, references, tables, figures, and figure legends. Figures should be uploaded as separate files. The title of each new section should begin on a new page. The conclusion should be included in the discussion section. Number pages consecutively, beginning with the first page of the manuscript. Page numbers should be placed in the middle of the bottom of the 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 included as a supplement in an appendix.

6. Organization of manuscript

1) Original article (Clinical or Experimental research)

1) Cover page (upload separately)

1) Title
   Title should be concise and precise. The first word should be capitalized. Drug names in the title should be written with generic names, not brand names. For the title, only the first letter of the first word should be capitalized.

Ex) Effect of smoking on bronchial mucus transport velocity under total intravenous anesthesia .........

[○]
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Provide drug names as generic names, not product names.

Ex) In CPR, Isosorbide Dinitrate is, ......... [○]

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3) 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.

4) Previous presentation at conferences
   Title of the conference, date of presentation, and the location of the conference may be described.

5) Funding statement
   Disclosure of all financial support for the work, including departmental or institutional funding/support, is mandatory.
Conflicts of interest
Any conflicts of interest for any or all authors within the 36 months of submission. If there are no competing interests, please add the following statement: "The authors declare no competing interests." 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 (without author information)
It should be the same as the Cover page.

② Abstract
All manuscripts should contain a structured abstract that is written only in English. Authors should provide an abstract of no more than 250 words. It should contain 4 subsections: Background, Methods, Results, and Conclusions. Citation of references is not permitted in the abstract. A list of key words at least 6, with a maximum of 10 items, should be included at the end of the abstract. Key words should be selected from MeSH (https://www.ncbi.nlm.nih.gov/mesh), and these should be written in small letters with the first letter capitalized. Separate each word with a semicolon (;), and include a period (.) at the end of the last word.
Ex) Keywords: Carbon dioxide; Cerebral vessels; Oxygen; Spinal analgesia.

③ Introduction
The introduction should address the article’s purpose concisely and include background information relevant to the paper’s purpose.

④ Methods
The methods section should include sufficient details regarding the design, subjects, and methods of the research in order, as well as methods used for data analysis and control of bias in the study. Sufficient details must be provided in the methodology section of an experimental study so that others can further replicate it.

Institute and author names should be avoided.
When reporting experiments with human or animal subjects, the authors should indicate whether they received approval from the Institutional Review Board for the study. When reporting experiments with animal subjects, the authors should indicate whether the Institutional Board supervised the handling of the animals for the Care and Use of Laboratory Animals. Demographic data should be included in the materials and methods section if applicable. As a rule, subsection titles are not recommended. If several study designs were used, then subtitles can be used without assigning numbers.

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). Authors should define how they determined race or ethnicity and justify their relevance.

● Units Laboratory information should be reported using the International System of Units [SI], available at: https://www.nist.gov/pml/special-publication-811
<Exceptions>
A. The unit for volume is “L”, while others should be written as “dl, ml, μl”.
Ex) 1 L, 5 ml
B. The units for pressure are mmHg or cmH₂O, instead of Pascal.
C. Use Celsius for temperature. °C
D. Units for concentration are M, mM, μM.
Ex) μmol/L; [ × ]
E. When more than 2 items are presented, diagonal slashes are acceptable for simple units.
Negative exponents should not be used.
Ex) mg/kg/min [O], mg · kg⁻¹ · min⁻¹ [ × ]
F. Leave 1 space between number and units, except %, °C.
Ex) 5 mmHg
Ex) 5%, 36°C
G. Units of time
Ex) hour: 1 h = 60 min = 3,600 s, day: 1 d = 24 h
= 86,400 s

● Machines and equipment
According to the 11th edition of the American Medical Association, provide model name and manufacturer’s name. Do not present the country.
For drug names, use generic names. If a brand name should be used, insert it in parentheses after the generic name. Provide® or ™ as a superscript and the manufacturer’s name.
Ions
Ex) Na⁺[O], Mg²⁺[O], Mg⁺²[×], Mg⁺[×]
Ex) Premedicated magnesium [O]
Ex) Premedicated Mg⁺² [O]

5. Results
Results should be presented in a logical sequence in the text, tables, and figures, giving the main or most important findings first. Do not repeat all the data provided in the tables or figures in the text; emphasize or summarize only the most important observations. Results can be sectioned by subsection titles but should not be numbered. The citation of tables and figures should be provided as Table 1 and Fig. 1. Type or print each table on a separate page. Figures should be uploaded as separate tif, jpg, pdf, gif, ppt files.

6. Statistics
Precisely describe the methods of statistical analysis and computer programs used. Mean and standard deviation should be described as mean ± SD, and mean and standard error should be written as mean ± SEM. Median and interquartile should be described as median (IQR, 3QR). When displaying P values, use a capital P and do not put a “.” between “P” and “value”.
A. Describe the statistical tests employed in the study in enough detail so readers can reproduce the same results if the original data are available. The name and version of the statistical package should be provided.
B. 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.
C. 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. 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.
D. When analyzing a categorical variable, an exact test or asymptotic method with appropriate adjustments should be used if the number of events and sample is small. The standard chi-squared test or difference-in-proportions test may be performed only when the sample size and the number of events are sufficiently large.
E. The APM strongly encourages authors to show confidence intervals, and 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.
F. 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 (ex. P = 0.160, not as P = 0.16 or 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.
G. A priori 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. 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.
H. When reporting a randomized clinical study, a CONSORT type flow diagram, as well as all the items in the CONSORT checklist, should be included. If limited in terms of the space of the manuscript, this information should be submitted as a separate file along with the manuscript.
I. 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 (SD) of cardiac indices in patients measured on a scale that is accurate to 0.1 L/min/m² should be expressed as 2.42 (0.31) L/min/m².
J. Except when otherwise stated herein, authors should conform to the most recent edition of the American Medical Association Manual of Style.

7. Discussion
The discussion should be described to emphasize
the new and important aspects of the study, including the conclusions. Do not repeat in detail the results or other information that is provided 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.

Funding
Financial support, including foundations, institutions, pharmaceutical and device manufacturers, private companies, intramural departmental sources, or any other support, should be described.

Acknowledgments
Persons or institutes that contributed to the manuscript but not sufficiently to be coauthors may be recognized.

References
- References should be obviously related to documents and should not exceed 50 in number. The number of references should not exceed 100 in reviews. However, the number of references has no limitation in systematic review and meta-analysis. References should be numbered consecutively in the order in which they are first mentioned in the text. Provide citations in the body text. All references should be listed in English, including author, title, name of journal, etc.
- The format for references 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 2015 Oct 2; cited Year Month Day]. Available at: www.ncbi.nlm.nih.gov/books/NBK7256/).
- If necessary, the Editorial Board may request original documents for the references.
- Six authors can be listed. If there are more than 6 authors, only list 6 names with “et al.”
- Provide the start and final page numbers of the cited reference.
- Abstracts of conferences may not 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 article. Name of journal published year; volume: start page-final page.


Journal article volume with supplement

Journal article issue with supplement

B. Monographs
- If reference page is only 1 page, mark ‘p.’
- Note if it is beyond the 2nd edition.


- Translated documents cannot be used as references. The original documents should be provided as references.

C. Chapter
Any separate author of a chapter should be provided.

D. Electronic documents

E. Online journal article

F. Advance access article

The reference style for APM is conveniently available as an out-of-the-box style within both EndNote and RefWorks.

⑪ Tables
- Only one table is to be drawn per page in the order cited in the text.
- The title of the table is to be in English and written at the top of the table in the form of a phrase.
- Words in the table excluding the title should use capital letters for the first word, and the following words are to be written in small letters.
- For demographic data, gender is recorded as M/F, age as yr, (if necessary, use days or months in children) without decimal point. The “±” sign within the table is to be aligned with the rows above and below.
- Footnotes are to be written in the following order: “Values are mean ± SD (or SEM) or median (1Q, 3Q)”, the explanations for the groups and the abbreviations in order of appearance, and statistics. Abbreviations apart from internationally recognized abbreviations are to be explained with their full spellings at the bottom of the table. Full spellings are to be presented even for repeated abbreviations for each table in order of appearance.
- Significance marks are to conform to the Vancouver style (Uniform Requirements for Manuscripts Submitted to Biomedical Journals. JAMA 1997; 227: 927-34). In other words, these must be in the order of “∗, †, ‡, §, ∥, ¶, **, ††, ‡‡” and written as superscripts.

⑫ 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 Photographs
① APM 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 frame the image clearly. 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, or ppt files. The width of figure should be 84 mm (one column). The contrast of photos or graphs should be at least 600 dpi. The 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 Fig. 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 An individual should not be recognizable in photographs or X-ray films unless written consent has been obtained from the subject and is provided at the time of submission.
⑧ Pathological samples should be pictured with a measuring stick.

(4) Video (movie) clip(s)
The APM publishes supplemental video (movie) clip(s) that will be available online. Authors should submit videos according to our video submission guidelines.
① Each video clip should clearly illustrate the primary
findings within an adequate amount of viewing time and should 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 names and/or ID numbers, hospital names, and dates of the procedures, should be removed.

(2) 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.

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

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

(5) The maximum number of video clips is 20.

(6) The video clip(s) should be playable on Microsoft Windows OS. The video clip(s) should be tested for playback before submission, preferably on computer not used for their creation, to check for compatibility issues.

(7) Individual video files should be a minimum of 480 × 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 > 2 GB files will be made at the end of the review process.

(8) 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).

(9) The author will be able to find additional information in the Figures and photographs section.

2) Systematic review and meta-analysis

Systematic review and meta-analysis are considered as an original article. 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 original article, except,

- All systematic reviews and meta-analyses should be registered at an appropriate online public registry (e.g., 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/.
- Number of references has no limitation in systematic review and meta-analysis.

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. Copies of written informed consents should be kept. If necessary, the editor or reviewers may request copies of these documents. If these steps are impossible, Institutional Review Board approval should be obtained prior to submission. The rarity of a disease condition is itself not an acceptable justification for a case report.

(1) Cover page: Same as that for clinical and experimental studies.

(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 3 and maximum
of 10 items, should be included at the end of the abstract.

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

(4) Case report: Describe only the clinical information that is directly related to the 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: The number of references should be less than 20. However, if necessary, the number of reference can be added in accordance with the decision of the editorial committee.

(7) Tables and figures: Proportional to those for 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 are invited only by editorial board. If authors want to submit an unsolicited review article, please contact editorial office (apm@anesthesia.or.kr). Review articles should include unstructured abstracts written in English equal to or less than 250 words. The organization should be in order of abstract, introduction, text following each title, conclusion and references. Figures and tables should be provided in English. Body text should not exceed 30 A4-sized pages, and the number of figures and tables should each be less than 6. However, if necessary, the number of pages, the number of figures, and tables can be added in accordance with the decision of the editorial committee.

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Letters to the Editor should include brief constructive comments that concern previously published articles and interesting cases. Letters to the Editor should be submitted no more than 3 months after the paper has been published.

(1) Cover pages should be formatted in the same way as those of clinical research papers. The corresponding author should be the first author. A maximum of five authors is allowable.

(2) The body text should not exceed 1,000 words and should have no more than 5 references. A figure or a table may be used.

(3) Letters may be edited by the Editorial Board, and if necessary, responses by the author of the subject paper may be provided.

6) Editorial
Editorials are invited by the editorial committee and should be commentaries on articles recently published in the APM, and can be described in free style.

7) Book reviews and announcements
Book reviews as well as news of scientific societies and scientific meeting dates in Korea or abroad can be included. Their formats will be the same as those of Letters to the Editor.

8) Images and Videos in APM
(1) The title should contain no more than 8 words. No more than 2 authors should be listed.

(2) The legend should contain no more than 250 words.

(3) If there is more than one panel, please label them Panel A, Panel B, etc.

(4) The legends to the images and videos should briefly present relevant clinical information, including a short description of the patient’s history, relevant physical and laboratory findings, clinical course, response to treatment (if any), and condition at the last follow-up.
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(In identical order to the electronic submission and the corresponding author should be underlined)

Journal: Anesthesia and Pain Medicine

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Clinical Research

General instructions

1. Please note that it is unethical to submit the same manuscript to two different journals simultaneously. The paper should not have been submitted to the Anesthesia and Pain Medicine either.
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3. The pages should be numbered, starting with the first page.
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5. Should be a brief running title.

Abstract

6. The abstract should be in structured format (Background; Methods; Results; and Conclusions)
7. Should include at least six and no more than ten keywords.
8. Should be fewer than 250 words.

Contents: (Introduction-Discussion)

9. Background (referenced), objective. The introduction should give a concise account of the background and purpose of the investigation.
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11. Figures and photographs should be submitted as jpg, gif or tif files, separately from the text of the paper.
12. Legend of figure should be described on a separate page following references in sentences of present tense.
13. Tables should be included in the text.
14. Follow the instructions for citing references.
15. Conclusion or summary should be the last section.

References

16. Follow the reference format.
17. Number references (as brackets; [ ]) in the sequence they appear in the text.
18. If you cite accepted manuscripts “In Press” as references, please provide one electronic copy.

Others

19. Raw data should be presented if the committee requests.
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Abstract

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7. Should only include less than 6 keywords.
8. Should be fewer than 250 words.

Contents: (Introduction-Discussion)

9. Background (referenced), objective. The introduction should give a concise account of the background and purpose of the investigation.
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12. Tables should be included in the text.
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References
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Title of the manuscript
6. The diagnosis or intervention of primary focus followed by the words “case report”
7. Only the first letter of the first word should be capitalized.

Abstract
8. Should not include references
9. Should only include less than 5 keywords (at least 2).
10. Should be fewer than 150 words.

Contents: (Background-Case-Conclusion)

Introduction & Case report & Discussion
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13. Legend of figure should be described on a separate page following references in sentences of present tense.
14. Tables should be included in the text.
15. Follow the instructions for citing references.
16. Discussion should be the last section.

References
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8. Tables should be included in the text.

References

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10. Number references (as brackets; [ ]) in the sequence they appear in the text.
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13. The names or affiliations of the authors should be concealed in the manuscript and figures.

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2. Please note that it is unethical to submit the same manuscript to two different journals simultaneously. The paper should not have been submitted to the Anesthesia and Pain Medicine either.
3. Please fill in the manuscript number that was originally assigned to your submission.
4. The Anesthesia and Pain Medicine holds the copyright of published manuscripts.
5. The pages should be numbered.
6. Manuscripts should be written in 10 point or larger, double-spaced, with a wide margin.
7. Manuscript should address a single topic chosen only among original articles or case reports under review by editorial board of APM.
8. A maximum of five authors is allowable.
9. Please specify the word count of the body text, and make sure the letter is fewer than 1,000 words.

Content

10. A figure or a table may be used.
11. Figures and photographs should be submitted as jpg, gif or tif files, separately from the text of the paper.
12. Legend of figure should be described on a separate page following references in sentences of present tense.
13. Tables should be included in the text.

References

14. Follow the reference format.
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16. If you cite accepted manuscripts “In Press” as references, please provide one electronic copy.
17. The references should not be more than 5 references.

Others

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