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Turkish Journal of Anaesthesiology & Reanimation

Contents

Review Article

Original Articles

Case Reports

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Review Article
Paediatric Anaesthesia

Turkish Journal of Anaesthesiology & Reanimation

Turk J Anaesthesiol Reanim 2025;53(2):34-41

Anaesthesia Considerations on Paediatric Neurosurgery

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Abstract

Paediatric neurosurgery has seen significant increases and improvements because of advancements in technology and monitoring techniques. This type of surgery presents unique challenges to the anaesthesiology team because of the general characteristics of paediatric patients and the complexity of the procedures. Managing paediatric patients undergoing complex neurosurgery requires profound knowledge of age-related normal physiology and the principles of common paediatric neuroanaesthesia. This review focuses on updated information about various critical topics in paediatric neurophysiology, bleeding management, acute pain treatment, intraoperative neuromonitoring, the specifics of the sitting position, and the general principles of paediatric neuroanaesthesia.

Keywords: Bleeding, neurosurgery, neurotoxicity, paediatric anaesthesia, positioning

Main Points

- Paediatric neurosurgical anaesthesia requires dedicated staff with comprehensive and profound knowledge.
- Specific "hot" points include paediatric neurophysiology, tumor-specific characteristics, intraoperative bleeding, sitting position, postoperative pain treatment, neuromonitoring, and extubation-related differences in neurosurgery.
- Advances in monitoring and endoscopic surgery have improved patient prognosis.

Introduction

Paediatric neuroanaesthesia presents a unique challenge to paediatric and adult neuroanaesthesiologist. Children undergoing neurosurgical procedures have different physiological and morphological features, making this type of surgery and patient population very special.[1] Children present with specific challenges in physiology, pharmacology, anaesthesia care, intensive care unit (ICU) monitoring and treatments, and neurological follow-up. Nowadays, paediatric neurosurgery is becoming more common in practice, so every anaesthesiologist must be aware of its important specifics and the skills required.[2] Neuroanaesthesia principles in children are the same as in adults and include neuromonitoring, decreased perioperative intracranial pressure, brain tissue oxygenation and perfusion, adequate haemodynamics, and early evaluation after the procedure.[3] There are several key challenges in neurosurgical anaesthesia care that anaesthesiologists must address. Childhood tumors are often localized in the posterior fossa, thereby making the sitting position and its consequences a concern. Anatomical and physiological parameters vary with the age of the child. Perioperative neurological evaluation presents age-related difficulties owing to poor communication. Important aspects such as airway management, vascular access, anaesthesia induction, anaesthesia maintenance, blood loss, and recovery from anaesthesia differ significantly between neurosurgical procedures in adults and children. Table 1 summarizes the most important anaesthesia care concepts for paediatric neurosurgery. This review provides updated knowledge on paediatric neurosurgical anaesthesia, with a focus on new developments.

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Table 1. Specific anaesthesia concepts for common paediatric neurosurgical procedures	
Brain tumors	• Prone/sitting/supine position • Hormonal/non-hormonal secreting • Brainstem tumor (bradycardia, cardiac arrest) • Cranial nerve damage (especially mixed nerves) • Increased intracranial pressure • Maintain adequate MAP and CPP • Avoid hypotension and hypercapnia • Delayed extubation • Reinforced endotracheal tube • Endotracheal tube position (head movement during positioning) • Diabetes insipidus in craniopharyngiomas (hypernatremia, polyuria) • Sodium balance during the third and lateral ventricles
Hydrocephaly	• Open vs. endoscopic • Local vs. general anaesthesia (depend on age, metal status, and procedure) • If external drainage: local anaesthesia may be performed • If available, local anaesthesia can minimize hypotension, hypoxia, and delayed extubation. • Hypothermia prevention (warm fluids and blankets) • Arrhythmias resulting from ventricular distention • Bradycardia (from increased intracranial pressure, fast and large cerebrospinal fluid amount evacuation) • Antibiotic prophylaxis
Craniosynostosis	• Other abnormalities (cardiac, Crouzon, Apert, Pfeiffer, metabolic) • Careful preoperative cardiac evaluation • Increased intracranial pressure (if hydrocephaly associated) • Difficulty in airway management (large head, temporomandibular joint stiffness) • Increased incidence of bleeding, hypothermia, and infections
Chiari malformations	• Brainstem compression • Difficulty/careful airway management • Severe bradycardia/cardiac arrest • Sitting position (hypotension, venous air embolism)
Epilepsy surgery	• Chronic antiepileptic therapy • Neurodevelopment problems • Increased liver metabolism (larger anaesthetic dose) • Inhalators may be epileptogenic • Unexplained tachycardia may include seizures • Intraoperative seizures (propofol, lorazepam, local iced water irrigation)
Encephalocele	• Microcephaly and external herniation • Careful positioning (accidentally rupture) • Other congenital malformations • Difficult airways • Antibiotic prophylaxis
Meningomyelocele	• Often associated with Chiari type 2 • Careful airway manipulation (brainstem stimulation) • Antibiotic prophylaxis • Bleeding • Hypothermia
MAP, mean arterial pressure; CPP, cerebral perfusion pressure.	

Neurological and Haemodynamic Features of Paediatric Patients

In paediatric neurosurgery, the clinical scenario requires careful attention to both paediatric-specific physiology and the intricacies of neurosurgical care, demanding a tailored approach from the anaesthesiologist. Children, particularly infants and younger age groups, present unique challenges due to developmental differences in cerebral hemodynamics. Baseline cerebral blood flow and autoregulation parameters are generally lower in paediatric patients than in adults, although these values progressively increase and align with adult norms as children age. Autoregulation, typically within a range of 20-60 mmHg in paediatric patients, can be easily disrupted, necessitating careful blood pressure management to maintain stable cerebral perfusion.

A significant factor to consider is the elevated cerebral metabolic rate of oxygen ($CMRO_2$) in children, which makes them more vulnerable to adverse effects from hypoxia, hypotension, and hypoglycemia.[4] These risks stem from children's high metabolic demands and limited physiological reserve compared with adults. Consequently, any compromise in oxygen supply can rapidly lead to cerebral ischemia and neuronal injury. Therefore, anaesthesiologists must vigilantly monitor oxygenation and circulation to prevent hypotension and hypoxemia. This involves careful titration of anaesthetic agents, fluid management, and frequent assessment of hemodynamic status.

Additionally, the anaesthesiologist must be familiar with age-specific normal ranges for vital signs because children's heart rates and blood pressure significantly vary across developmental stages. Precise control of these parameters is essential to maintain optimal cerebral perfusion and minimize the risk of intraoperative complications.[4] Understanding these age-related variations is critical in adapting anaesthesia plans to support neurological outcomes in paediatric neurosurgery.

Anaesthetic Technical Challenges in the Paediatric Patients

Preoperative evaluation is a critical element in paediatric neuroanaesthesia. Depending on the child's age, the anaesthesiologist may encounter challenges in obtaining information directly from the patient, making the input from relatives essential. Another significant aspect of the procedure is assessing the patient's level of consciousness and potential increased intracranial pressure. Preoperative neurologic evaluation is crucial for documenting any existing deficits.[5] If the patient has a congenital disease, other associated congenital conditions may be present, necessitating a cardiac evaluation. Additionally, it is important to carefully assess the volume status and dehydration to optimize preoperative vascular bed filling.[6]

Airway and vascular access management can be challenging. If the patient is agitated, inhalation sedation is suitable for inserting a peripheral venous cannula; however, it is not recommended for patients with reduced consciousness who require rapid induction sequence to prevent aspiration. Central lines are generally inserted when a peripheral cannula is not feasible or significant volume and blood transfusion are anticipated. The femoral route for the central line may be suitable and must be removed asap to minimize thrombosis. The echo-guided insertion approach is a common practice and increases procedure success and safety.[7] Airway management and intubation are critical steps in caring for these patients. Babies with hydrocephalus (Figures 1-3) often have increased head circumference, thereby complicating ventilation and intubation. In cases

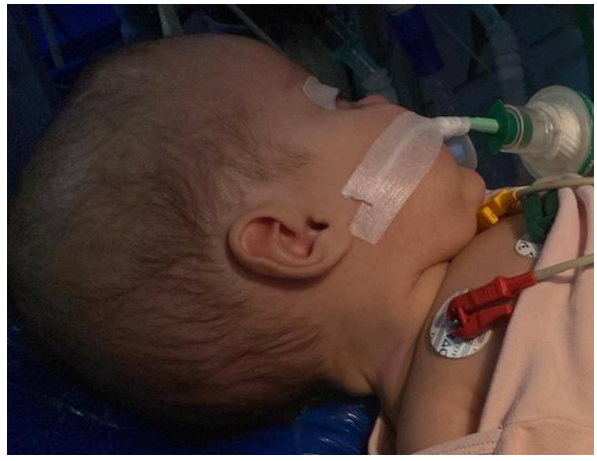

Figure 1. Large head in a hydrocephalus baby (original photo)

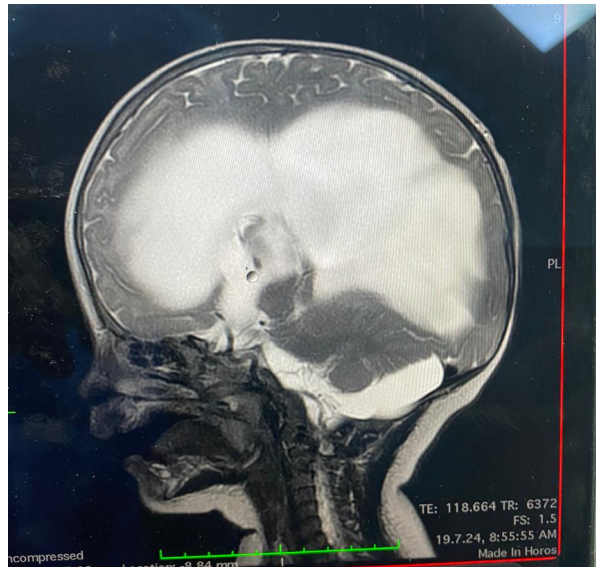

Figure 2. Characteristic imaging images of a patient with hydrocephalus (original photo)

of Chiari malformation (Figure 4), any head movement during ventilation and intubation can lead to brainstem damage.[8] Patients with craniosynostosis may experience temporomandibular joint ankylosis, which is associated with reduced mouth opening and intubation difficulties.[8,9] Further increases in intracranial pressure, hypoxemia, severe hypotension, and gastric aspiration must be avoided as much as possible.

Anaesthesia maintenance can be done using inhalator anaesthetic agents, total intravenous anaesthesia, or an inhalator-intravenous combination approach. Sevoflurane appears to be safer for paediatric patients than for adults because it does not cause significant cerebral vasodilation. Sevoflurane is used not only for sedation to obtain vascular access but also for anaesthesia maintenance. Total intravenous anaesthesia is preferred when vascular access is already established in the ward and the patient is not agitated, allowing for easier manipulation. No data show a clear advantage of one technique over the other.[10]

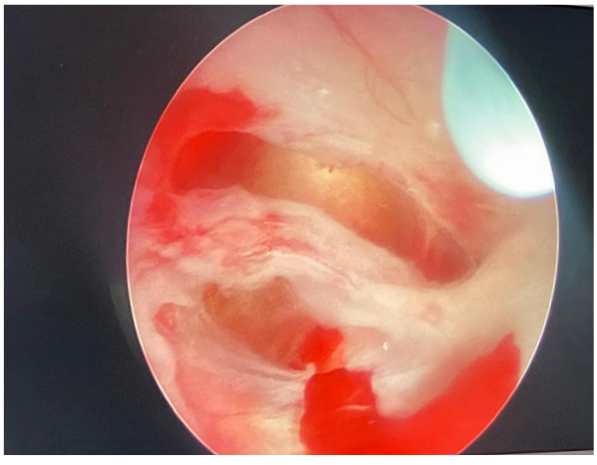

Figure 3. Intraoperative endoscopic treatment views (original photo)

Emergency anaesthesia and child extubation requires special attention and is often associated with complications mainly respiratory.[11] Paediatric neurosurgery is considered an intermediate-risk procedure for extubation because of an increased risk of reintubation due to impaired airway and respiratory control.[11,12] Two techniques have been reported: awake extubation and sleep extubation.[13] Extubation after paediatric neurosurgery differs significantly from extubation after other paediatric surgeries. Several predictors of delayed extubation in children undergoing neurosurgical procedures have been proposed. Various authors have identified factors such as preoperative mental status, surgery duration exceeding six hours, extensive resection, cranial nerve damage, brain edema, hypothermia, and significant blood loss as predictors of delayed extubation.[14] Sangtongjaraskul et al.[15] conducted a study involving 539 paediatric neurosurgical patients and found a 10% incidence of delayed extubation. The primary causes of this delay were blood loss exceeding 40% of the total blood volume, preoperative oxygenation status, and intracranial surgery.[15] Thus, extubation after paediatric neurosurgery may present challenges due to not only general paediatric complications but also decreased consciousness, new postoperative deficits, cranial nerve damage, and neurosurgical postoperative complications, such as cerebral edema, pneumocephalus, and intracranial bleeding.

Anaesthetic Physiological Challenges in Paediatric Patients

Intraoperative bleeding during paediatric neurosurgery often occurs during specific procedures, such as craniosynostosis (Figures 5, 6), but can also occur in large tumor resections.

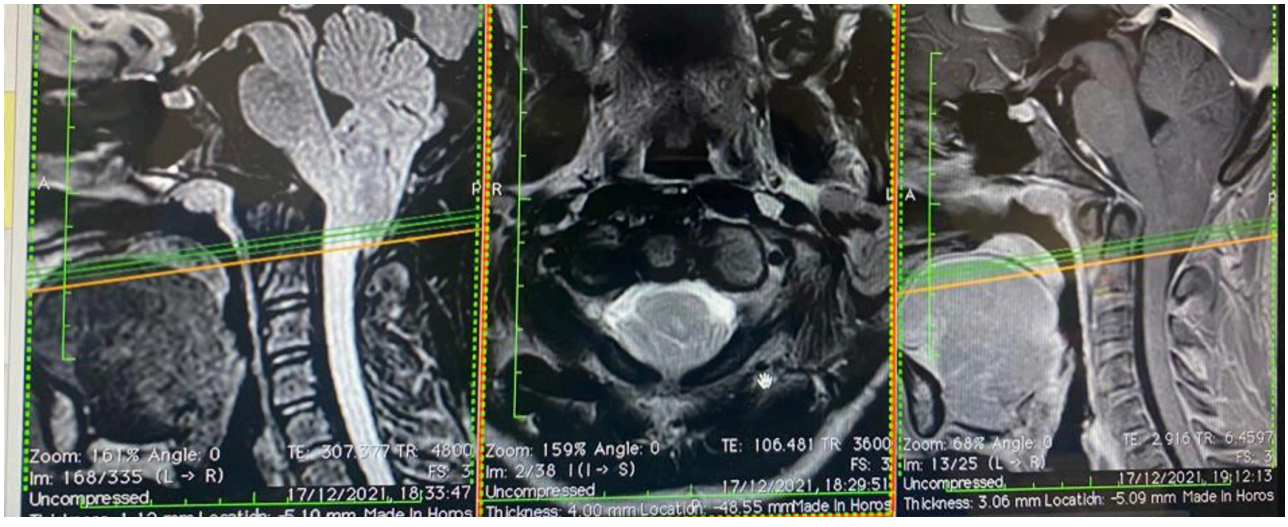

Figure 4. Chiari malformation (original photo)

The principles of management are the same as those in adults and include hemodynamic and hypoperfusion management, as well as the prevention of coagulopathy. In children, blood loss may be insidious and can seriously compromise tissue perfusion. It is essential to evaluate blood loss according to age, weight, brain condition, and preoperative hemoglobin level.[16] Blood transfusions are more frequently associated with complications (allergy, hemolysis) than in adults.[17] Recognizing risk factors is crucial for developing a detailed management approach. Recently, several predictor factors for poor prognosis have been reported, including low weight, large tumors, prolonged surgical duration, and perioperative anaemia.[18] The volume of bleeding is generally correlated with hemodynamic disturbances, reduced brain perfusion, reduced tissue oxygenation, a large volume of fluid administration, and complications from blood transfusions.[19] A hemoglobin level >8 g dL^{-1} may ensure normal cerebral tissue oxygenation.[20] King et al.[21] reported data from 6,583 patients who underwent craniosynostosis surgery and found no side effects of tranexamic acid, such as seizures or thrombosis. Several studies have reported that tranexamic acid is effective in reducing intraoperative bleeding and the need for transfusions.[22,23] de Faria et al.[24] found no benefits of tranexamic acid in brain surgery, but noted its effectiveness in brain and spine trauma. Interesting results have been published by Goobie et al.[25] They compared the effects of low and high concentrations of tranexamic acid. They concluded that a loading dose of 10 mg kg^{-1}, followed by a maintenance dose of 5-10 mg kg^{-1} h^{-1}, could reduce the need for transfusions without adverse effects.

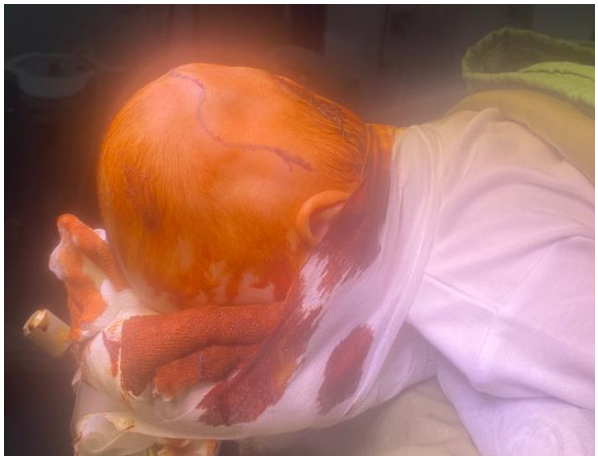

Figure 5. Patient in the prone position undergoing craniosynostosis surgical correction (original photo)

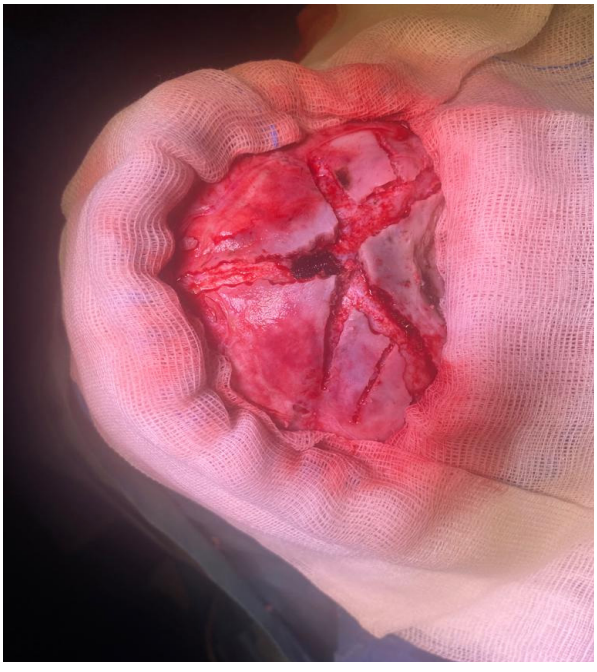

Figure 6. Surgical correction of craniosynostosis (original photo)

Pain treatment following neurosurgery is a cornerstone in postoperative period. It is generally accepted that opioids for acute pain treatment after neurosurgery may be effective, with close monitoring of side effects. Non-steroidal anti-inflammatory drugs are often used as adjuvants because of the risk of bleeding, even in the absence of evidence. However, Xing et al.[26] published data on 320 paediatric neurosurgical patients and found that opioids such as tramadol, fentanyl, and morphine may be safe. Multimodal analgesia has gained popularity in recent years. A meta-analysis by Kulikov et al.[27] recently reported the efficacy of this analgesic technique and the use of regional analgesia after neurosurgery. The systematic review (PROSPECT) was published, including 53 randomized controlled trials.[28] The authors found that multimodal analgesia, combining non-steroidal anti-inflammatory drugs, dexmedetomidine, paracetamol, and scalp blocks, was effective in treating acute postoperative pain. They concluded that opioids should be considered if non-opioid treatments fail. Regional analgesia is now performed in many centers as part of multimodal analgesia.[29] This can reduce systemic drug administration and side effects. It is important to consider patient characteristics and the type of neurosurgical procedure when selecting the appropriate analgesia regimen.

Intraoperative neuromonitoring is crucial in various neurosurgical procedures. The most common neuromonitoring techniques are motor evoked potentials and somatosensory evoked potentials. These techniques enhance the quality of the procedure, ensure patient safety, and reduce the risk of further brain damage.[30] Several intraoperative factors, including hypotension, hypoglycemia, antiepileptic drugs, inhalants, and muscle relaxant use, can affect neuromonitoring results. Inhalators (sevoflurane, isoflurane, nitrous oxide) can trigger epileptic episodes, especially if the minimum alveolar concentration is >0.5,

and can modulate motor-evoked potential results.[30,31] Total intravenous anaesthesia appears to be safe. If the use of muscle relaxants is necessary, the anaesthesiologist may choose a short-acting agent and monitor neuromuscular blockade using TOF. Thus, in small infants, the anaesthesiologist can start with inhalational sedation, secure vascular access, and continue with total intravenous anaesthesia after intubating the patient's trachea without muscle relaxants.

The sitting position is often used in children because brain tumors are predominantly located in the posterior fossa (Figure 7). Surgeons may prefer the sitting position based on their personal preferences and institutional protocols. This position offers surgical advantages, including better exposure through direct access and improved drainage of blood and cerebrospinal fluid. However, this approach introduces several physiological changes that are of particular concern to anaesthesiologists. Complications associated with the sitting position include hypotension, severe jugular vein obstruction, brain edema, facial and pharyngeal edema, and venous air embolism. Hypotension can result from gravitational pooling of blood in the abdomen, reduced venous return, preoperative hypovolemia due to mannitol, vomiting, or fasting, use of positive end-expiratory pressure to prevent venous air embolism, and the vasodilatory effects of anaesthetics.[32] To manage hypotension, the anaesthesiologist must optimize vascular bed filling by administering fluids, using intermittent pneumatic compression stockings, administering vasopressors, and correcting the patient's position. To ensure adequate cerebral perfusion, the arterial invasive monitoring transducer should be positioned at the level of the external auditory meatus (Figure 8). Venous air embolism is a significant complication associated with the

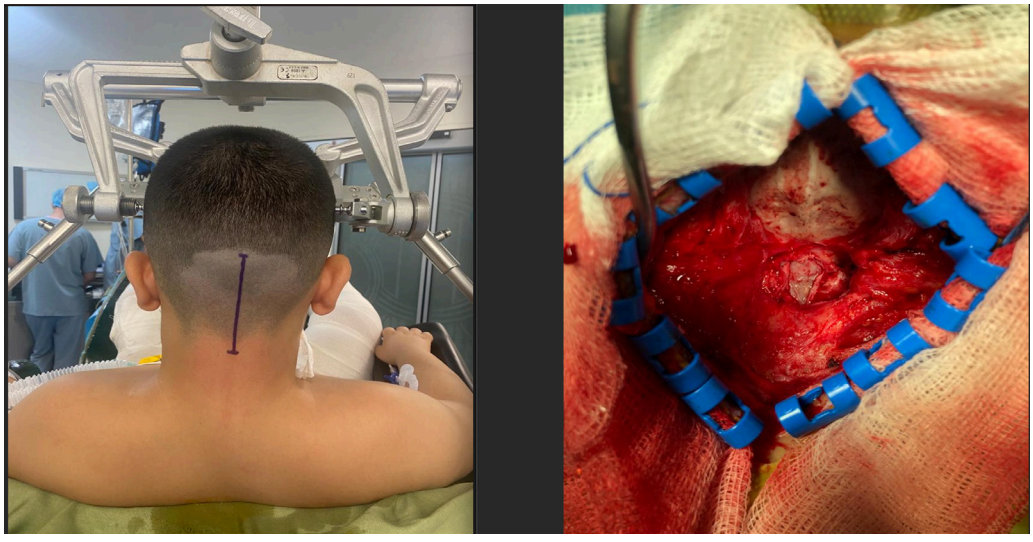

Figure 7. Patient in the sitting position for posterior fossa surgery and scull exposure (original photo)

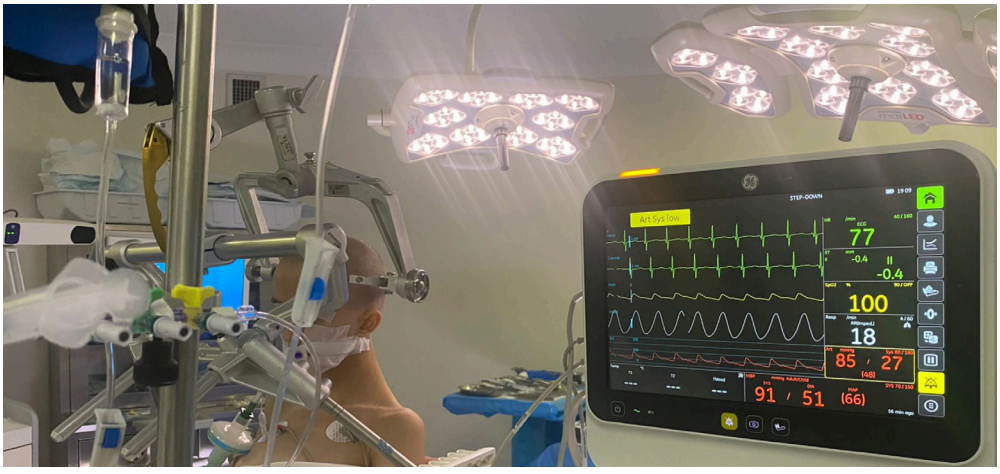

Figure 8. Arterial line transducer positioned in the external auditory meatus for accurate invasive blood pressure monitoring (original photo)

sitting position.[33] This typically occurs when the surgical site is approximately 10 cm above the right atrium, allowing venous air to enter the right atrium. This can cause air embolism, right heart failure, impaired cardiac output, hypotension, hypoperfusion, and potentially death if not promptly and aggressively treated, especially if a large amount of air (5 mL kg^{-1}) enters.

Sudden decreases in $ETCO_2$, hemodynamic disturbances (such as hypotension and arrhythmias), and hypoxemia strongly suggest venous air embolism. The diagnosis is confirmed by echocardiography (either transthoracic or transesophageal). Treatment includes reversing the patient's position, aspirating air from a central catheter (if one has been previously inserted), administering fluids, and using vasopressors or inotrope to support hemodynamics.[33]

Several studies have examined the incidence of venous air embolism in children. Bithal et al.[34] found that the incidence and severity of venous air embolism in children are comparable to those in adults when they are in the sitting position. The authors concluded that the sitting position is safe for children undergoing posterior fossa surgery. Harrison et al.[35] published data for 16 years of experience, reporting a 9.3% incidence of venous air embolism with no perioperative consequences. In a retrospective analysis, Dilmen et al.[36] included 601 adults and 91 children who underwent surgery in the sitting position. They reported an incidence of venous air embolism of 20.4% in adults and 26.3% in children, with no related complications. Thus, they found the sitting position to be safe for both adults and children.[36] Teping et al.[37] studied the semi-sitting position in paediatric neurosurgery and reported their data for 10 years of experience. They enrolled 42 patients who underwent posterior fossa surgery and found an 11.9% incidence of venous air embolism, but without hemodynamic instability. The authors concluded that the semi-sitting position is safe if performed by a dedicated and experienced anaesthesiology staff. Therefore, every paediatric anaesthesiologist or neuroanaesthesiologist must have profound knowledge and experience regarding the physiological consequences of the sitting position to ensure safe and successful posterior fossa surgery.

Conclusion

Paediatric neurosurgical anaesthesia requires a dedicated and experienced staff. A multidisciplinary team, including paediatricians, neurologists, neurosurgeons, anaesthesiologists, and nurses, can ensure patient safety and improve treatment outcomes. In addition to new developments in paediatric research, a profound understanding of the physiological and anatomical features of paediatric patients is crucial.

Footnotes

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Perioperative Practice Patterns of Anaesthesiologists Surrounding Glucagon-Like Peptide-1 (GLP-1) Agonist Medications

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Abstract

Objective: Aspiration of gastric contents during induction of anaesthesia is a rare but well-recognized complication with high morbidity and mortality risk. Patients at highest risk include those with full stomachs, diabetes, hiatal hernias, gastrointestinal obstructions, severe gastroesophageal reflux, and known delayed gastric emptying. Recently, the use of glucagon-like peptide-1 (GLP-1) agonists has expanded rapidly, including their application in cosmetic weight loss. This drug class suppresses glucagon release after meals, thereby delaying gastric emptying over an undefined duration. For patients taking these medications in the perioperative period, the effect on overall aspiration risk is unknown. This survey details the current practice pattern of anaesthesiologists regarding GLP-1 agonists.

Methods: An IRB-approved 30-question, uncompensated survey was distributed to 30,096 self-reported actively practicing United States members of the American Society of Anesthesiologists (ASA). The survey collected demographic information, practice information, and included questions about the management of patients taking GLP-1 agonists. To ensure participant confidentiality, no identifiable information was collected.

Results: The survey response rate was 5.98%, with 1,801 surveys returned. Ninety-seven percent of respondents indicated familiarity with GLP-1 agonists, and eighty-one percent indicated they had not personally witnessed complications in patients taking GLP-1 agonists. Most respondents indicated perioperative aspiration as the largest concern and the most commonly reported witnessed complication. 62% reported having "some" to "a lot" of experience providing anaesthesia to patients taking these medications. Most respondents reported NPO guidelines consistent with current ASA practice guidelines.

Conclusion: The majority of anaesthesiologists report perioperative aspiration as their highest concern for patients taking this class of medications.

Keywords: Anaesthesiologists, glucagon-like peptide-1, off-label use, physicians, practice patterns

Main Points

- A nationwide survey of anaesthesiologists indicated their main concern for patients taking glucagon-like peptide-1 agonists, is increased risk of delayed gastric emptying and subsequent increased risk of aspiration on induction of general anaesthesia.

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Introduction

Management of type 2 diabetes (T2DM) and obesity has changed dramatically with the increased use of glucagon-like peptide-1 (GLP-1) agonists.[1-9] Originally approved for the treatment of T2DM, GLP-1 agonists were found to have profound effects on weight loss, surpassing what was previously achievable with medication management alone (average <5% reduction in weight).[5] Currently, semaglutide [brand name Ozempic (Novo Nordisk, Bagsværd, Denmark)] and tirzepatide [brand name Mounjaro (Eli Lilly and Company, Indianapolis, IN)] hold Food and Drug Administration (FDA) approval limited to the treatment of T2DM.[2,4] However, Wegovy (Novo Nordisk, Bagsværd, Denmark), a "sister" semaglutide, and Zepbound (Eli Lilly and Company, Indianapolis, IN), a "sister" tirzepatide, gained FDA approval for medical management of obesity in 2021 and 2023, respectively.[6-8] In the past five years, these medications have increased in popularity, greatly.[10] Additionally, a rising number of app-based weight loss programs with questionable screening and patient follow-up have raised patient safety concerns with the FDA and other governing bodies.[5]

GLP-1 agonists depress appetite by delaying gastric emptying and suppressing post-prandial glucagon release. Because this class of drugs has a longer half-life than endogenous GLP-1, the durations of these side effects related to long half-life and its weekly dosing regimen is uncertain. Given the potential for gastroparesis and retained gastric contents, anaesthesiologists are justified in their concerns about the significant risk of perioperative regurgitation and pulmonary aspiration syndrome, even when patients follow standard preoperative fasting times.[7] The American Society of Anesthesiologists (ASA) issued a consensus statement that advocated discontinuing weekly-dosed GLP-1 medications 1 week prior to surgery. In cases where discontinuation of pre-operative GLP-1 agonists is not possible or if gastrointestinal symptoms (e.g., nausea, vomiting) are present, the ASA recommends a gastric ultrasound to assess stomach contents or proceeding with rapid sequence intubation (RSI) at induction.

Given the relative youth of these compounds and rapidly expanding indications, there are few published data on their utilization, anaesthetic implications, and subsequent perioperative management. In a recent letter to the anaesthesiology editor, Ushakumari and Sladen[12] expressed that the current ASA guidelines lack the evidence to support them; however, the European Society of Anaesthesiology and Intensive Care (ESAIC) has recently updated guidelines with further evidence for preoperative considerations, for anaesthesiologists.[11-13] To better understand how anaesthesiologists are navigating the ubiquitous use of GLP-1 agonists, this survey aims to explore their current practice patterns. As the use of GLP-1 agonists increases, this study seeks to enhance understanding of GLP-1 agonists' effects on perioperative physiology and contribute to the development of evidence-based guidelines for safer anaesthetic management.

Methods

Survey Design

Institutional Review Board University of Florida exemption was obtained (approval no.: IRB202301912, date: 21.06.2024). The survey was based on a review of existing literature and included a pilot survey of 76 anaesthesiologists at a single academic tertiary care center. The study aimed to investigate current anaesthetic practice patterns and familiarity with GLP-1 agonists among practicing anaesthesiologists in the United States. The 30-question electronic survey included questions about gender, age range, race, years in practice, fellowship training, practice demographic and geographic area, anaesthesia-specific preoperative clinic status, and existing perioperative institutional guidelines surrounding GLP-1 agonists. Primary outcomes assessment was based on self-reported familiarity with GLP-1 agonists and experience and comfort providing anaesthesia to patients taking them. Respondents were also asked about complications, adverse events, management, NPO guidelines, and intubation strategy for patients taking GLP-1 agonists. No identifiable information was collected.

Participant Selection

This uncompensated survey was disseminated to all actively practicing members in the United States of the ASA. The survey was sent out twice via email, with a two-week period between the initial survey email and the follow-up email.

Data Analysis

Incomplete survey responses, as well as responses from those who indicated they were "Retired", were excluded from analysis. Responses that were left blank were not included in the descriptive outcomes or analyses. The practice demographics were simplified to describe primarily inpatient or outpatient practice. Those who reported 50% or more outpatient practice were classified as having a primary focus on outpatient practice, with the others classified as having a primary focus on inpatient practice. Respondents who reported "some" or "a lot" of comfort with GLP-1 agonists were identified as "more experienced," and the others were described as "less experienced."

Statistical Analysis

Statistical analysis was conducted using JMP Pro, Version 15 (SAS Institute Inc., Cary, NC). Responses to all questions were summarized. Chi-square tests were used to assess associations between demographic and clinical data and outcome responses. An alpha level of 0.05 was used for significance for all tests.

Results

Overall

The survey was sent to 30,096 actively practicing anaesthesiologists in the United States. 18,234 of the emails were opened, and 1,801 responses were received. This resulted in a response rate of 5.98% of the total and 9.9% from those who opened the email. Of those responses, two reported they were retired, and their responses were withheld from study analysis. Twenty-seven surveys were started, but the majority of responses were left blank and were removed from the study analysis as well, resulting in 1,772 responses being included in the analysis. Responses that were left blank for individual questions were not included in the study analysis.

Demographics

Complete demographic data from the survey respondents are shown in Supplementary Table 1. Sixty-three percent of respondents were male, and 72% reported they identified as White or Caucasian. Sixty-three percent were less than 55 years old, and fifty-four percent reported they had been in practice for less than 10 years. Twenty-eight percent of respondents (496/1764) reported they worked in the Southeast region (AL, AR, FL, GA, KY, LA, MS, NC, SC, TN, VA, WV); 22% in the Midwest (IA, IL, IN, KS, MI, MN, MO, ND, NE, OH, SD, WI), and 21% in the Northeast (CT, DE, MA, MD, ME, NH, NJ, NY, PA, RI, VT). Over half of respondents reported working in an urban, (28%, 487/1759) or a major metropolitan (32%, 559/1759) area. Forty-one percent (726/1768) reported they had completed fellowship training. Fifty-eight percent (1031/1765) reported they worked in a private or group-owned practice. The majority reported they supervised residents or midlevel providers (78%, 1378/1761). Thirty-six percent of respondents (631/1767) reported a 50/50 split between inpatient and outpatient practice. Few (3%, 70/1767) reported they worked at a 100% inpatient practice, while 12% reported a 100% outpatient surgery practice. Twenty-six percent (454/1761) of respondents indicated their patients were evaluated in a preoperative anaesthesia clinic 100% of the time; 20%, (355/1761) reported their patients were never evaluated in a preoperative anaesthesia clinic.

Patient Populations

Respondents indicated that diabetes was the most common indication (59%, 903/1532) for using GLP-1 agonists, followed by obesity management (23%, 350/1532). Ten percent, (151/1532) reported they were unaware of the prescription indication, and 8% (128/1532) reported a primary indication of cosmetic weight loss. Regarding the management of bridging medications in the perioperative period, 61% (261/426) of patients were managed by primary care providers, 30% (128/426) by the endocrinologist, and 6% (21/426) by the surgeon. Further details are shown in Table 1.

Table 1. Patient Population/Practice Information

Percent of time patients are evaluated at a preoperative anaesthesia clinic	**n**	**% of total**
<25% of the time	332	18.85%
25-50% of the time	265	15.05%
50-75% of the time	355	20.16%
75-100% of the time	454	25.78%
Never	355	20.16%
Supervision of midlevel providers (residents, nurse anaesthetists, anaesthesia assistants)	**n**	**% of total**
No	383	21.75%
Yes	1378	78.25%
Average BMI in practice region	**n**	**% of total**
<25	21	1.20%
>40	29	1.66%
25-30	219	12.53%
30-35	1021	58.41%
35-40	458	26.20%
BMI cut-off for elective surgical procedures	**n**	**% of total**
No BMI cut-off	1360	77.36%
Yes, <30	3	0.17%
Yes, <35	8	0.46%
Yes, <40	56	3.19%
Yes, <45	102	5.80%
Yes, <50	229	13.03%
Familiarity with a class of drugs called GLP-1 agonists (i.e., Ozempic, Wegovy, Mounjaro)	**n**	**% of total**
No	56	3.18%
Yes	1703	96.82%
Experience level providing anaesthesia to patients who take GLP-1 agonists	**n**	**% of total**
No	219	12.39%
Yes, a little	448	25.35%
Yes, a lot	296	16.75%
Yes, some	804	45.50%
Comfort level with providing anaesthesia to patients taking GLP-1 medications	**n**	**% of total**
Extremely comfortable	406	26.50%
Extremely uncomfortable	21	1.37%
Neither comfortable nor uncomfortable	391	25.52%
Somewhat comfortable	496	32.38%
Somewhat uncomfortable	218	14.23%

Table 1. Continued		
Most common indication for which patients have been prescribed a GLP-1 agonist	**n**	**% of total**
Cosmetic weight loss	128	8.36%
Primary diabetes management	903	58.94%
Primary obesity management	350	22.85%
Unknown	151	9.86%
BMI, body mass index; GLP-1, glucose-dependent insulinotropic peptide.		

NPO Guidelines/Practice Patterns

Most respondents (75%, 1066/1418) indicated their NPO guidelines for patients taking GLP-1 agonists did not differ from the standard ASA preoperative NPO guidelines for all patients. Five percent (72/1418) reported that patients were required to be NPO for 24 hours prior to surgery, and 3% (44/1418) indicated patients were excluded from "enhanced recovery after surgery" drinks. When asked if they altered intubation strategy for these patients, 39% of respondents (558/1418) reported using RSI or RSI with nasogastric tube suctioning, 15% (213/1418) reported altered intubation strategy by excluding laryngeal mask airway use, and 40% (563/1418) reported no alteration in intubation strategy.

Eighty-eight percent of respondents (1210/1383) reported that the type of surgery did not alter the duration patients were required to hold GLP-1 agonists prior to the day of the procedure. Eighty-seven percent of respondents (1208/1385) indicated that medication management for GLP-1 agonists did not differ between patients undergoing planned general anaesthesia and monitored anaesthesia care. For those patients taking GLP-1 agonists for primary diabetes management, 43% (612/1430) of respondents indicated they did not require their patients to hold the medication prior to undergoing elective surgery, 16% (224/1430) required holding for less than 1 week, 15% (214/1430) deferred to the primary care physician or endocrinologist, and 12% (180/1430) required holding the medication for 1 to 2 weeks. For those patients taking GLP-1 agonists for non-diabetic indications, 39% (545/1415) continued taking GLP-1 agonists before elective surgery, 18% (256/1415) held the medications between 1 and 2 weeks, and 15% (219/1415) held the medications for less than 1 week. Further details are shown in Table 2.

Outcomes and Complications

Ninety-seven percent (1703/1759) of respondents answered that they were familiar with GLP-1 agonists. Sixty-two percent (1100/1767) answered that they had "some" to "a lot" of experience providing anaesthesia to patients taking

Table 2. NPO Guidelines/Practice Patterns		
In patients taking GLP-1 medication for DIABETIC indications, how long do you advise patients to hold GLP-1 medications prior to undergoing elective surgery?	**n**	**% of total**
<1 week	224	15.66%
>2 weeks	40	2.80%
1-2 weeks	180	12.59%
Defer to PCP or endocrinologist	214	14.97%
Defer to surgeon	39	2.73%
I do not have them hold it	612	42.80%
I temporarily decrease the dosage	4	0.28%
Other	117	8.18%
In patients taking GLP-1 medication for DIABETIC indications with HELD medications, do you temporarily transition the patient to another medication?	**n**	**% of total**
No	953	62.29%
Yes, defer to other provider	467	30.52%
Yes, other	18	1.18%
Yes, transition to insulin	92	6.01%
Management of bridging medications	**n**	**% of total**
Endocrinologist	128	30.05%
Other	16	3.76%
PCP	261	61.27%
Surgeon	21	4.93%
In patients taking GLP-1 medication for NON-DIABETIC indications, how long do you advise patients to hold GLP-1 medications prior to undergoing elective surgery?	**n**	**% of total**
<1 week	219	15.48%
>2 weeks	92	6.50%
1-2 weeks	256	18.09%
>3 Weeks	7	0.49%
>4 weeks	12	0.85%
Defer to PCP or endocrinologist	141	9.96%
Defer to surgeon	48	3.39%
I do not have them hold it	545	38.52%
I temporarily decrease the dosage	5	0.35%
Other	90	6.36%

Table 2. Continued

Does the duration of how long you recommend patients hold the medication differ whether the anaesthesia plan is monitored anaesthesia care versus general anaesthesia?	**n**	**% of total**
No	1208	87.22%
Yes	177	12.78%
Does the duration of how long you recommend patients hold the medication differ based on surgery type?	**n**	**% of total**
No	1210	87.49%
Yes	173	12.51%
Does the duration of how long you recommend patients hold the medication differ whether the patient will be admitted or be discharged home the day of surgery?	**n**	**% of total**
No	1315	95.29%
Yes	65	4.71%
Do your NPO guidelines differ from the recommended ASA guidelines for patients taking this medication?	**n**	**% of total**
No	1066	75.18%
Other	103	7.26%
Yes, they are excluded from ERAS drinks	44	3.10%
Yes, they are required to be NPO for 12 hours prior to surgery	133	9.38%
Yes, they are required to be NPO for 24 hours prior to surgery	72	5.08%
Do you alter your intubation strategy for patients who have been taking GLP-1 agonists?	**n**	**% of total**
No	563	39.70%
Other	84	5.92%
Yes, excludes patient as LMA candidate	213	15.02%
Yes, rapid sequence intubation	427	30.11%
Yes, rapid sequence intubation and nasogastric tube to suction	131	9.24%
Does the duration of how long you recommend patients hold the medication differ whether the anaesthesia plan is monitored anaesthesia care versus general anaesthesia?	**n**	**% of total**
No	1208	87.22%
Yes	177	12.78%

Table 2. Continued

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Do you alter your intubation strategy for patients who have been taking GLP-1 agonists?	**n**	**% of total**
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Other	84	5.92%
Yes, excludes patient as LMA candidate	213	15.02%
Yes, rapid sequence intubation	427	30.11%
Yes, rapid sequence intubation and nasogastric tube to suction	131	9.24%
Is management affected by surgery type	**n**	**% of total**
No	1210	87.49%
Yes	173	12.51%
Is management affected by postoperative discharge plans	**n**	**% of total**
No	1315	95.29%
Yes	65	4.71%

ASA, American Society of Anesthesiologists; ERAS, enhanced recovery after surgery; GLP-1, glucose-dependent insulinotropic peptide; LMA, laryngeal mask airway; PCP, primary care provider.

GLP-1 agonists. Twenty-seven percent (406/1532) answered that they were extremely comfortable providing anaesthesia to patients taking GLP-1 agonists, while 16% reported they were "somewhat uncomfortable" or "extremely uncomfortable" most respondents (81%, 1243/1532) had not personally witnessed any perioperative complications in patients taking GLP-1 agonists. Aspiration was the most common complication reported (57%, 165/289) by those who witnessed perioperative complications. For those who had not personally witnessed a perioperative complication, the majority, (60%, 1001/1674) reported their biggest concern was related to higher perioperative aspiration risk from delayed gastric emptying. Further details are shown in Table 3.

Comments From Respondents

Respondent comments regarding the need for increased guidance and education, aspiration concerns, uses and opinions on gastric ultrasound, airway management, and coordination of care concerns are shown in Table 4.

Analyses

Experience with GLP-1 agonists

To evaluate if there was any association between the demographic and clinical variables collected and those who reported "some" or "a lot" of comfort with GLP-1 agonists,

Table 3. GLP-1 Complications

What is the most common indication for which patients have been prescribed a GLP-1 agonist?	**n**	**% of total**
Cosmetic weight loss	128	8.36%
Primary diabetes management	903	58.94%
Primary obesity management	350	22.85%
Unknown	151	9.86%
Personally witnessed complications	**n**	**% of total**
None	1243	81.14%
Perioperative aspiration	165	11%
Perioperative ketoacidosis or non-diabetic normoglycemic ketoacidosis	51	3%
Other	92	6%
Highest perceived complication risk	**n**	**% of total**
Higher perioperative aspiration risk from delayed gastric emptying	1370	82%
Perioperative ketoacidosis or non-diabetic normoglycemic ketoacidosis	450	27%
Other	199	12%
None	30	2%

GLP-1, glucose-dependent insulinotropic peptide.

Table 4. Survey Responses

Need for increased guidance/ education from the ASA	I am very concerned about this class of medications and delayed gastric emptying. We have no ability at my center to advise patients to alter their medications other than [on the] day of surgery. I am interested in an official ASA guideline on this so we can circulate to surgeons to be considered when scheduling patients at our ASC.
	Very interested in updated practice guidelines. We are at a constant battle with GI physicians for outpatient endoscopy and patients taking this medicine for weight loss. Help from ASA would be greatly appreciated.
	Intubation strategy changes and NPO guidance is needed. Also, a strong recommendation for ERAS exemption is also needed given the observed gastric emptying delays.
	I am very interested to see what the ASA has to say about this drug and potential statements. My group would be willing to change NPO status/induction management and work with our preoperative clinic for these patients.
	I am acutely aware of this concern and have alerted our providers to watch for this class of medications and consider altering practice. We have not recommended holding these drugs preoperatively at this point, but will consider this going forward.
	Many concerns regarding aspiration risk especially when NPO for minimum recommended time per ASA guidelines. Would like more direction on gastric emptying, aspiration risk, and if [there is a] difference between patients taking for DM vs weight loss.
	We recently initiated changes to include a two-week discontinuation of these medications because of increased aspiration risk. We primarily do sedation anaesthesia for cosmetic procedures, and I do not feel comfortable sedating patients that have been on this medication because of the possibility of having a full stomach despite the NPO normal guidelines.
	I would like to see guidelines for all types of anesthetics especially for outpatient endoscopies (EGD and colonoscopy). We need to have a guideline to show GI docs specifically the requirement, otherwise I am very concerned for increased aspiration frequency.
Aspiration concerns	I have colleagues with a GI practice that see significant retained gastric contents on patients on GLP-1 agonists. I strongly feel their aspiration risk is increased, so thank you for trying to get clarity on proper management.
	We are hearing anecdotal reports of fasted EGD patients with undigested food seen in their stomachs. Anxiously awaiting some specialty specific guidelines, and in the meantime, taking a case by case conservative approach.

Table 4. Continued	
	I see stomachs full of food in EGDs in patients on these drugs. Disaster waiting to happen. For obesity treatment should be stopped preop[eratively]. Diabetics have gastroparesis anyway, so maybe they are not tolerating these as well; I don't see as many people on it just for diabetes.
	From what I've read, the delayed gastric emptying is a concern but not consistent; severe aspiration has been rare but those instances are concerning to me - would be great if the ASA came out with a practice advisory.
	Wondering if these patients should be excluded from a MAC case or even an LMA. Aspiration is obviously a major complication but definitely one we want to avoid at a stand alone surgery center.
Gastric ultrasound uses/options	I typically gastric ultrasound patients prior to the OR to assess gastric volume.
	Would like to see a study where point of care ultrasound (POCUS) is used to evaluate these patients for gastric contents under routine ASA fasting guidelines.
	It would be interesting to see research either with residual stomach content or ultrasound for stomach volumes.
	I extensively assess patients satiety, nausea or fullness. My goal is POCUS soon.
	Would like to see a study where pocus is used to evaluate these patients for gastric contents under routine ASA fasting guidelines.
	Most common instance we see is GI work-up for side effects related to medication (e.g., nausea). In these patients, our group is recommending 2 days [of] clears with 12 hours NPO. We are trying to schedule them at a facility with anaesthesia machines and ultrasound available. The thought is to do gastric ultrasound in pre op. Some partners are planning to intubate all of these patients due to prior "possible aspiration" events.
	Little direction from ASA regarding appropriate practice; will occasionally use gastric ultrasound if curvalinear probe available at facilities; have heard of several incidences of delayed gastric emptying in the region- but none at our practice.
Airway management	Several institutions have increased the pre-surgical NPO time for solids for these patients (our institution has not yet), but the exact data is unknown. I know a few institutions that are working on clinical studies right now to further explore this issue. I don't trust the patients to be NPO under the normal ASA guidelines if they have taken their medication in the past week, so I strongly prefer ETT + RSI for them over MAC or LMA.
	My current management of patients taking GLP-1 agonists include intubation with RSI and exclude the use of LMAs. With reference to MAC cases, I make it a point of keeping the patients lighter and maintain upper airway reflexes/protection. I solidly believe that these patients should be treated as an increased aspiration risk just as we would for gastroparesis patients.
	As a private practice anesthesiologist, we are seeing a spike in the number of patients taking these medications for weight loss and we are struggling how to manage these patients since there is very little guidance. We are now intubating patients that normally we would perform a TIVA or LMA's on to reduce the risk of aspiration.
	I do not have them hold it because of its long half life. I treat them as full stomach precautions. If MAC, I keep them much lighter. If GA, I will RSI and not use an LMA. I am very concerned about aspiration and very much waiting for some practice guidelines to standardize our practice surrounding these medications.
	I have not yet modified my intubation strategy but I am very seriously considering doing RSI for all these patients.
	I inform the patient that there may be a higher risk of aspiration and I am more likely to intubate a patient in cases that I would have used an LMA or avoided intubation when patients are on this medication.
	To summarize, we currently have no policies in place changing our practice, though some individual providers have made some practice changes (as noted). None of my patients have had complications (that I know of), but some of my CRNAs have [had] first-hand issues at other institutions (e.g., aspiration). As the popularity of these drugs spread, we are facing a big problem, so thank you for doing this. I'm looking forward to your results.
Coordination of care concerns	We don't have really any official guidelines for these medications right now at our institution, which is why we generally defer to the PCP for perioperative management. That being said, the PCP does not know of the emerging risks/issues we are seeing with these patients in the perioperative period. In discussions with colleagues, we have SO MANY experiences with seeing delayed gastric emptying with these patients.
	Glad to see someone is working on guidelines for this population. Not only anesthesiologist, but surgeons and PCPs seem to be unaware of the risks associated to these medications. They are still been managed as any other patient and included in ERAS protocols. Very worrisome and dangerous.
	Hopefully the ASA can partner with endocrine societies for some formal recommendations.

ASA, American Society of Anesthesiologists; ASC, ambulatory surgery center; CRNAs, certified registered nurse anesthetists; EGD, esophagogastroduodenoscopy; ERAS, enhanced recovery after surgery; ETT, endotracheal tube; GA, general anaesthesia; GI, gastrointestinal; GLP-1, glucagon-like peptide-1; LMA, laryngeal mask airway; MAC, monitored anaesthesia care; NPO, nil per os; OR, operating room; PCP, primary care provider; POCUS, point-of-care ultrasound; RSI, rapid sequence intubation; TIVA, total intravenous anaesthesia.

experience with GLP-1 agonists was condensed from 4 categories into 2 categories: those who reported "some" or "a lot" of experience with GLP-1 agonists and those who reported "a little" or "none."

A significant association was found between experience with GLP-1 agonists and the proportion of patients evaluated at a preoperative anaesthesia clinic (χ^2: 11.1, P=0.0255). Those who reported their patients were evaluated at a preoperative anaesthesia clinic 75% to 100% of the time were 1.38 times more likely to report "some" or "a lot" of experience with GLP-1 agonists than those who reported <25% of patients were seen in a preoperative anaesthesia clinic; they were also 1.52 times more likely [Odds ratio (OR) 1.52 (1.12, 2.08), P value 0.0081] to report "some" or "a lot" of experience than those who reported their patients were seen 25% to 50% of the time in a preoperative anaesthesia clinic. Those who reported their patients were never seen in a preoperative anaesthesia clinic, were 1.48 times more likely [OR 1.48 (1.07, 2.06), P value 0.0184] to report "some" or "a lot" of experience with GLP-1 agonists than those who reported their patients were seen in a preoperative anaesthesia clinic 25% to 50% of the time.

Overall, there was no association between experience with GLP-1 agonists and changes to intubation strategy. However, when the data were examined across practice types, we found that those in private practice or group-owned practice who reported "some" or "a lot" of experience with GLP-1 agonists were 1.44 times more likely [OR 1.44 (1.06, 1.95), P value 0.0195] to alter their intubation strategy than those who reported "little" or "no" experience with GLP-1 agonists.

Comfort with GLP-1 agonists

A significant association was found between comfort with GLP-1 agonists and the proportion of patients being seen at a preoperative anaesthesia clinic (χ^2 11.71, P value 0.0197). Those who reported that patients are seen in a preoperative anaesthesia clinic 75% to 100% of the time were (1) 1.54 times more likely [OR 1.54 (1.01, 2.12), P value 0.0115] to report "some" or "a lot" of comfort with GLP-1 agonists than those who reported their patients are seen 25% to 50% of the time; (2) 1.6 times more likely [OR 1.6 (1.18, 2.17), P value 0.0026] to report "some" or "a lot" of comfort with GLP-1 agonists than those who reported their patients are seen 50% to 75% of the time in a preoperative anaesthesia clinic; and (3) 1.41 times more likely [OR 1.41 (1.04, 1.91), P value 0.0262] to report "some" or "a lot of" comfort than those who reported their patients are never seen in a preoperative anaesthesia clinic.

Complications related to GLP-1 agonists

A significant association was found between those who reported witnessing complications in patients taking GLP-1 agonists and their experience level with GLP-1 agonists (χ^2 30.65, P < 0.0001). Those who reported "some" or "a lot" of experience with GLP-1 agonists were 2.38 times more likely [OR 2.38 (1.72, 3.30), P < 0.0001] to report having witnessed complications in patients taking GLP-1 agonists. There was a significant association found between comfort level with GLP-1 agonists and witnessing complications in patients using these drugs: those who reported less comfort with GLP-1 agonists were 1.41 times more likely [OR 1.41 (1.09, 1.82), P value 0.0094] to report having witnessed complications in their use.

There was no association found between those who reported witnessing complications in patients taking GLP-1 agonists and practice demographic (>50% outpatient vs. inpatient) (χ^2 1.04, P value 0.3069). No association was found between witnessing complications in patients taking GLP-1 agonists and geographic location (urban vs. suburban) (χ^2: 0.48, P value 0.4899).

Altered Intubation Strategy Related to GLP-1 Agonists

No significant association was found between experience level with GLP-1 agonists and alterations in intubation strategy in patients on such treatment (chi-square 2.83, P value 0.0927). Those who reported less comfort with GLP-1 agonists were 1.65 times more likely [OR 1.65 (1.33, 2.06), P value < 0.0001] to report altering their intubation strategy than those who reported "some" or "a lot" of comfort with GLP-1 agonists.

Those who reported having witnessed complications in patients taking GLP-1 agonists were 3.22 times more likely [OR 3.22 (2.34, 4.44), P value < 0.0001] to report they alter their intubation strategy than those who have not witnessed complications in these patients.

Different NPO Guidelines for GLP-1 Agonists

A significant association was found between practice type and alterations in NPO guidelines for those taking GLP-1 agonists. Those who reported being in a private or group-owned practice were 1.53 times more likely [OR 1.53 (1.13, 2.09), P value 0.0067] to report using different NPO guidelines for patients taking GLP-1 agonists (compared to ASA standard guidelines) than those who reported being in academic practice. Similarly, they were 1.52 times more likely [OR 1.52 (1.07, 2.18), P value 0.0198] than those who reported being in hospital-employed practice. Of note, at the time of this survey, the ASA had not yet released its consensus statement and providers' guidelines required longer NPO times than ASA standard guidelines.

Discussion

GLP-1 agonists have soared in popularity due to their significant effects on weight loss. Our group previously

demonstrated the exponential rise in internet search interest for "Ozempic," "Wegovy," and "Mounjaro" in a Google Trends analysis.[10] In 2023, new GLP-1 agonist prescriptions for diabetes increased by 128% and prescriptions for obesity increased by 352%.[14] The growing trend is likely to continue as researchers explore indications beyond diabetes and obesity for this drug class, including polycystic ovarian syndrome, Alzheimer's disease, Parkinson's disease, and nonalcoholic fatty liver disease.[15-19] With increasing use, it is imperative to better understand how these medications can affect patients' physiology in the perioperative setting.

Anaesthesiologists in our study indicated their highest concern for patients taking GLP-1 agonists, was increased aspiration risk on induction of anaesthesia, which was also the most witnessed complication. Delayed gastric emptying is most pronounced within the first 3 months of use, and may subside after 20 weeks according to one study.[20] Other data on patients undergoing upper endoscopy suggest no predictability regarding the interval of GLP-1 agonists (e.g., semaglutide) discontinuation period and the prevalence of finding retained gastric contents at the time of endoscopy.[21] In the setting of diabetes, patients already present with an elevated baseline risk of gastroparesis,[22] and it is uncertain how GLP-1 agonists may further affect this risk.

The most recent ESAIC guidelines recommend to hold GLP-1 agonists at least one week, prior to scheduling procedures that require sedation or anaesthesia for patients who inject weekly.[11] Furthermore, the guidelines specify that if the medications are given for obesity, then two weeks (i.e, three half-lives) are recommended. If the medication is prescribed as daily oral or subcutaneous administration, they recommend discontinuing GLP-1 agonists on the day of the procedure. Similarly, the current ASA consensus-based guidance statement on preoperative management of patients taking GLP-1 agonists advocates for patients undergoing elective procedures to hold these medications 1 week preoperatively and to evaluate patients for symptoms that could put them at increased risk of gastroparesis (e.g., nausea, bloating, or abdominal pain). If those symptoms are present, it is advised to treat patients as if they have a "full stomach" and to discuss these risks with the patient/surgical team or to consider delaying the procedure.[13] However, from a pharmacologic standpoint, in order to avoid the aspiration risk induced by delayed gastric emptying, the medication would need to be held for at least 5 half-lives prior to surgery, and, depending on the specific GLP-1 agonist, could need to be held up to 2 or more weeks.[23] This time interval raises practicality concerns, especially in settings without routine preoperative surgical, anaesthesia clinics. In the current study, only 26% of participants reported attending an anaesthesia preoperative clinic, while 20% reported attending none. Preoperative anaesthesia clinics have been shown to reduce patient morbidity and mortality.[24] Therefore, facilitating preoperative care with additional precautions (i.e., medication bridging, collaboration with primary care providers, additional clearance) may thereby avoid potential perioperative complications. Given the increasing use of GLP-1 agonists, earlier evaluation by an anaesthesiologist or preoperative-specific team is likely beneficial for aspiration risk reduction, and in the case of diabetics, for improved glycemic control for optimal surgical outcomes if bridging medications are needed.

Other safety concerns include the broader availability via app-based prescription and pharmacy services, as a result, several deaths related to compounded GLP-1 agonists have been reported.[25,26] Preoperative anaesthesia clinics would enable a degree of quality control at least prior to surgery.

This survey illustrates considerable variation in respondents' comfort levels with patients taking GLP-1 agonists and perioperative management of this population. Less than one-third of respondents felt extremely comfortable providing anaesthesia to patients taking GLP-1 agonists, while 16% felt "somewhat uncomfortable" or "extremely uncomfortable." Those who were less comfortable were 1.65 times more likely to report altering their intubation strategy for patients taking these medications ($P < 0.0001$) and 1.41 times more likely to report witnessing complications ($P = 0.0094$). While these findings do not demonstrate causality, a general sense of apprehension regarding the perioperative management of this patient population is evident, in conjunction with other findings of this and other studies. Anaesthesiologists who have witnessed complications are 3.22 times more likely, to report altering their intubation strategy than those who have not ($P < 0.0001$). Respondents in a private or group-owned practice setting with more experience with GLP-1 agonists were 1.44 times more likely to report altering their intubation strategy compared to those with little experience. Similarly, anesthesiologists who practice in a private or group-owned practice setting were 1.53 times more likely to report using different NPO guidelines for patients on GLP-1 agonists (compared to ASA standard guidelines).

Education for physicians and physician extenders in providing anaesthesia to patients taking these drugs is imperative. The ASA has indicated that increased research is needed to elucidate the effects of GLP-1 agonists on gastric emptying and aspiration risk. Our group is currently conducting a prospective study using ultrasonography to investigate gastric contents in the preoperative setting.

Study Limitations

Our survey provides new insight into the perioperative practice patterns of anesthesiologists in patients taking GLP-1 agonists. However, there are several limitations. Overall,

the response rate was low. Only 5.98% of those listed as actively practicing United States members who are ASA members responded to the survey. Therefore, the results of this survey may not be representative of the true population. Several questions required subjective assessments as well as self-reporting. The ASA has announced consensus-based guidance for preoperative management of patients taking GLP-1 receptor agonists since the survey was completed, those who requested increased guidance from the ASA may be satisfied with this statement.

Conclusion

A primary concern held by the ASA members surveyed was that patients taking GLP-1 agonists may have delayed gastric emptying and subsequently an increased aspiration risk. Moreover, free-text responses indicated providers wanted further guidance from the ASA, as current guidelines may be insufficient regarding the NPO as well as medication cessation recommendations. As the use of these drugs ubiquitous, widespread implementation of preoperative anaesthesia clinics should be considered, and excellent communication with the surgical team is essential. Further mechanistic research in the perioperative setting is needed.

Ethics

Ethics Committee Approval: Institutional Review Board University of Florida exemption was obtained (approval no.: IRB202301912, date: 21.06.2024).

Informed Consent: Survey study.

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Footnotes

Author Contributions: Surgical and Medical Practices - S.C.S.-V., M.B., S.H.H.,; Concept - S.C.S.-V., M.B., S.H.H., A.K., P.M., S.D.M., H.J.F., F.H.; Design - S.C.S.-V., M.B., S.H.H., F.H.; Data Collection and/or/Processing - S.C.S.-V., K.O., M.B., S.H.H., F.H.; Analysis and/or/Interpretation - S.C.S.-V., K.O., M.B., S.H.H., F.H.; Literature Review - S.C.S.-V., K.O., M.B., S.H.H., F.H.; Writing - S.C.S.-V., K.O., M.B., S.H.H., F.H.

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Original Article
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The Effect of Prone Position on Right Ventricular Functions in CARDS: Is Survival Predictable when Evaluated Through Transesophageal Echocardiography?

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Abstract

Objective: To evaluate the cardiopulmonary effect during prone position (PP) on right ventricular (RV) recovery in coronavirus disease-2019 related acute respiratory distress syndrome (C-ARDS) through transesophageal echocardiography (TEE).

Methods: This prospective study included 30 moderate-to-severe C-ARDS patients who were treated with PP in the first 48 h of invasive mechanical ventilation support. It was evaluated with TEE three times: before PP (T_0), the first hour of PP (T_1), and the first hour of returning to the supine position (T_0 + 24 h) (T_2) after 23 hours of PP treatment. RV end-diastolic area/left ventricular (LV) end-diastolic area (RVEDA/LVEDA), tricuspid annular plane systolic excursion (TAPSE) and LV end-systolic eccentricity index were preferred RV evaluations as primary outcomes. Pulmonary effects of PP were evaluated as a secondary outcome, including PaO_2/FiO_2, driving pressure (dP), static compliance (Cstat), mechanical ventilation parameters, and their association with 28-day survival. Tissue DO_2 was examined as a secondary outcome, and it was calculated using the measured cardiac output through TEE.

Results: With the cardiopulmonary effect of PP, the decrease in RVEDA/LVEDA, the increase in TAPSE, PaO_2/FiO_2, and Cstat, and the decrease in dP were statistically significant ($P < 0.05$). The Cstat value associated with 28-day survival showed decreased mortality for each unit increase. The Cstat cut-off value, which was statistically significant for survival, was 37.

Conclusion: PP can improve RV recovery and oxygenation, but it isn't always accompanied by increased survival. An increase in the Cstat may improve survival without the development of RV dysfunction while maintaining heart-lung interaction.

Keywords: ARDS, lung compliance, prone position, respiratory mechanics, right ventricular, transesophageal echocardiography

Main Points

- Prone position (PP) can improve right ventricular (RV) recovery and oxygenation but it isn't always accompanied by increased cardiac output and DO_2.
- The left ventricular (LV) curative effect of PP can be observed when LV function worsens secondary to RV dysfunction.
- The importance of the compatible lung can be explained both by its protective effect on the lung, preventing pressure and volume damage, and by its protective effect on the heart through the heart-lung interaction.

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Introduction

Non-coronavirus disease-19 (non-COVID-19) associated acute respiratory distress syndrome (ARDS) patients in the prone position (PP) showed improved right ventricular (RV) function by reducing RV pressure with effects on ventilation and gas exchange.[1] In COVID-19 related ARDS (C-ARDS), especially in the severe form, increased shunt rate, impaired ventilation/perfusion ratio (V/Q), hypoxic pulmonary vasoconstriction inhibition, and increased immune microthrombosis may have similar effects on the RV.[2] The cardiopulmonary pathophysiology and outcomes of C-ARDS vary, and this variability requires monitoring to follow the diagnosis and treatment process. This study aimed to increase the treatment success of the PP in C-ARDS and to provide a prognostic factor for survival by analyzing and monitoring heart-lung interactions. Therefore, we used transesophageal echocardiography (TEE) to evaluate the cardiopulmonary effects of PP.

The primary outcome of the study was that in patients with moderate/severe C-ARDS, improvement was observed in the RV with PP, i.e., there was a decrease in the RV end diastolic area/left ventricular (LV) end diastolic area (RVEDA/LVEDA) values at PP+1 h (T_1) and PP+24 h (T_2) compared to the pre-PP (T_0) values, and this decrease can be used as a prognostic factor for survival. The secondary outcomes of this study were to analyze the cardiopulmonary effects of PP; to determine the changes in cardiac output (CO), LV end systolic eccentricity index (LVESEI), tricuspid annular plane systolic excursion (TAPSE), PaO_2/FiO_2, static compliance (Cstat), and dynamic compliance (Cdyn); and to investigate the relationship between these variables and prognostic factors.

Methods

Study Design and Population

This study had a prospective, cross-sectional, single-center design. After obtaining ethical approval for the study, moderate/severe C-ARDS patients admitted to the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Anaesthesiology and Reanimation Clinic Intensive Care Unit, who received invasive mechanical ventilation support and applied PP in the first 48 h, between February and May 2022, were included. The number of patients in the study was determined to be 30 based on the power analysis. The inclusion criteria were: i) age greater than 18 years; ii) patients diagnosed with polymerase chain reaction/computed tomography (PCR/CT) results, with moderate/severe severity class according to the Berlin ARDS classification, with prone positioning applied within the first 48 hours after orotracheal intubation; and iii) obtaining an informed consent form. A total of 30 patients were included. Exclusion criteria were as follows: relative, absolute contraindications for PP, and TEE, and a diagnosis of pulmonary embolism. It is shown in the flow chart (Figure 1).

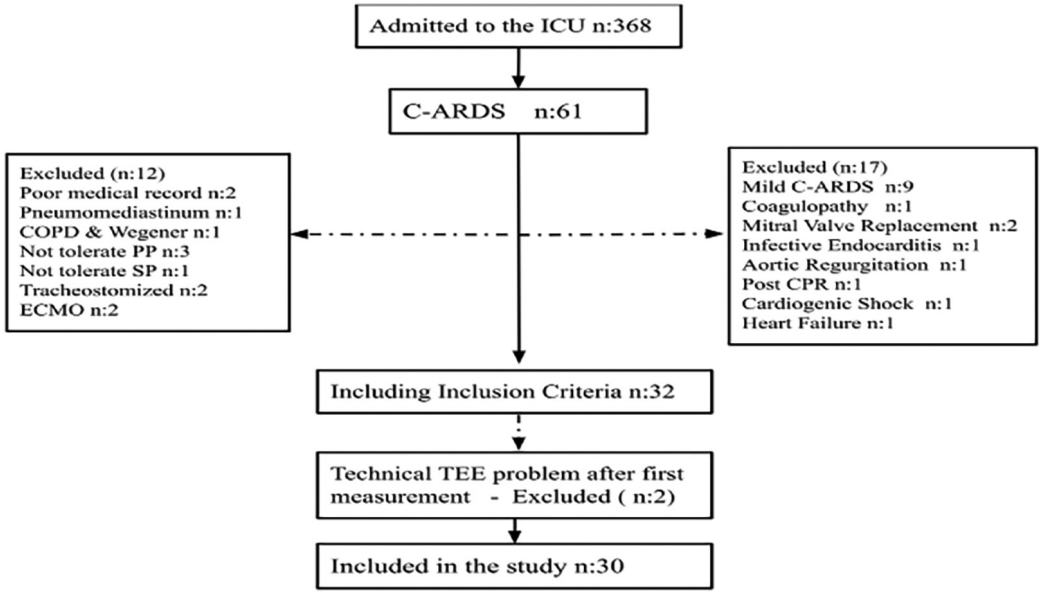

Figure 1. Flow diagram for the study

ICU, intensive care unit; C-ARDS, coronavirus disease-2019 related ARDS; CPR, cardiopulmonary resuscitation; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; TEE, transesophageal echocardiography

Ethical Consideration

This study was approved by the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinical Research Local Ethics Committee with the decision number 2022-03-03, dated 07.02.2022, following the approval of the Ministry of Health Clinical Research Board form'-2022-01-30T12_22_28' and was registered at clinical trials.gov (no: NCT06456606, protocol ID: 2022/40) by the principal investigator and was conducted in accordance with the Declaration of Helsinki, 2013.

Data Collection

The patients were evaluated with TEE (x7-2t transducer with Philips Affiniti 30 System-Philips Healthcare, andover, MA, USA) in the supine position at three different times: before PP (T_0), at the first hour of PP (T_1, T_0+1 h), and at the first hour of returning to supine after 23 h of PP (T_2, T_0+24 h). Each measurement was repeated three times by the same doctor, and the average values were recorded. TEE was performed by D.B. who has 5 years of experience using echocardiography in the intensive care unit and F.N.Ç.T. who is a cardiologist. It was applied for each measurement, and the probe was removed after the measurements. Measurements were conducted in accordance with the European Society of Cardiology guidelines.[3] The TAPSE value shown in Figure 2A was calculated using transthoracic echocardiography (TTE) from the lateral annulus of the tricuspid valve in the apical four chamber view, using the MM mode, at the time of T_0 and T_2 (S-4 transducer with Philips Affiniti 30 System-Philips Healthcare, Andover, MA, USA).

RVEDA/LVEDA is shown in Figure 2B, and RV end diastolic volume (RVEDV) and LV end diastolic volume (LVEDV) are shown in Figure 2C, in mid esophageal four chamber image. The LV outflow tract (LVOT) diameter and area were measured and calculated on the mid-esophageal aortic valve long-axis image, as shown in Figure 2D. In Figure 2E, the LVOT velocity time integral (VTI) was measured with anteflexion in the deep transgastric (TG) axis using pulsed Wave Doppler. Stroke volume (SV) was calculated using the LVOT VTI and LVOT areas. CO was calculated using SV and heart rate (HR), as CO=(HRxSV).[4,5] LVESEI was calculated in the TG mid-papillary short axis image shown in Figure 2F provided with anteflexion in the TG axis.[6,7]

During each measurement, mechanical ventilation parameters were recorded, vital signs were recorded, arterial blood gas analysis was performed, and Cstat and driving pressure (dP) values were measured. Using the PaO_2:FiO_2 to Horowitz ratio, DO_2 values, $COx(Hb\times1.34\times SaO_2+PaO_2\times0.003)$ were recorded.

Statistical Analysis

Statistical analyses were performed using the statistical software packages R (R Core Team, 2020) and Jamovi. Conformity of data to the normal distribution was evaluated using the Shapiro-Wilk test and Q-Q marking. Descriptive

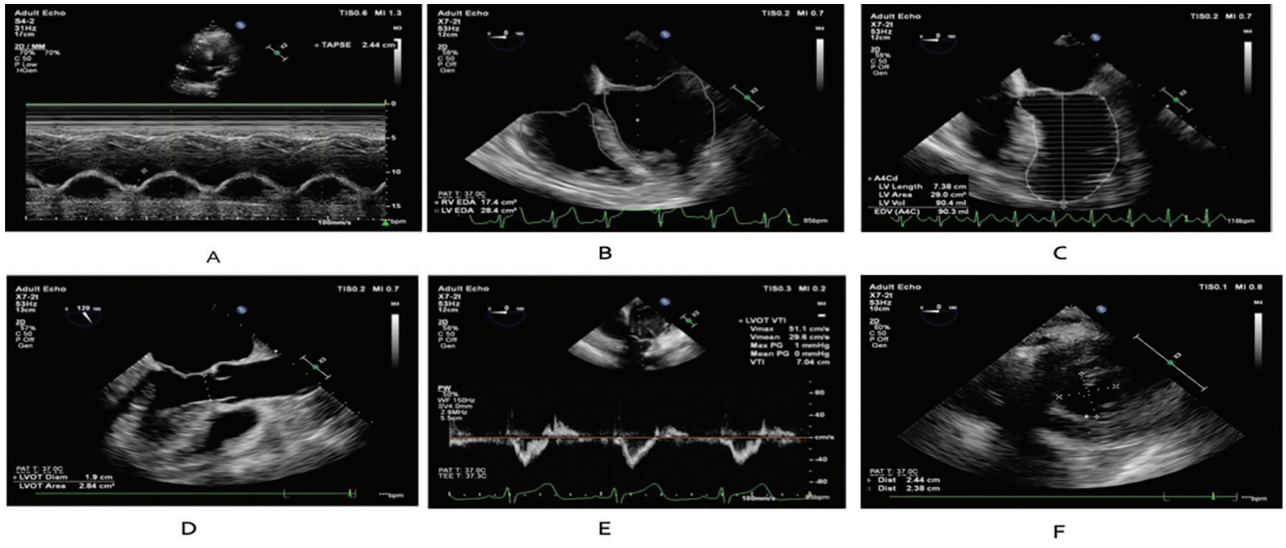

Figure 2. Transthorasic and transesophageal measurements

A) TAPSE, B) LVEDA/RVEDA, C) LVEDV, D) LVOT diameter, E) LVOT-VTI, F) LVESEI

TAPSE, tricuspid annular plane systolic excursion; LVEDA, left ventricular end diastolic area; RVEDA, right ventricular end diastolic area; LVEDV, left ventricular end diastolic volume; LVOT, left ventricular outflow tract; LVOT-VTI, left ventricular outflow tract velocity time integral; LVESEI, left ventricular end systolic eccentricity index

statistics are expressed as mean (standard deviation) for normally distributed numerical variables, median (interquartile range) for non-normally distributed numerical variables, and frequency (percent) for categorical variables. Numerical variables of two independent subgroups were compared using the Mann-Whitney U test for numerical data and the chi-square test for categorical data, with the Fisher's exact test used as appropriate. The numerical variables of the two dependent groups were compared using the paired t-test, and the variables that did not fit the normal distribution were compared using the Wilcoxon test. Comparison of three dependent groups was made with repeated measures analysis of variance test, and the η^2G value was used as the effect size.[8] Paired comparisons were made with Student's t-test, and *P* values were corrected by Holm's method. A *P* value of < 0.05 was considered statistically significant. Pearson's correlation coefficients were calculated to determine the direction and strength of the relationship between the normally distributed numerical variables. A Kaplan-Meier analysis was used to evaluate the survival difference between two independent subgroups, and the log-rank test was used for comparisons between the two groups.

Results

Patient Population

Of the 61 patients with C-ARDS, 29 were excluded based on the exclusion criteria. Two patients were excluded because TEE deteriorated after T_0 measurement and the measurements could not be continued. Thirty patients were included in the study, Figure 1. This study included 18 female (60%) and 12 male (40%) patients. The mean age was 65.5±10.9 years. Ninety percent of the patients were PCR positive and 100% had CT findings. According to the Berlin ARDS severity classification, 53.3% (n = 16) were moderate, 46.7% (n = 14) were severe. Intensive Care Unit (ICU) admission scores sequential organ failure assessment: 9.87±2.45, acute physiology and chronic health evaluation II: 28.5±7.12, charlson comorbidity index: 4.17±2.17, pneumonia severity index score: 88.9±27.3 are shown in Table 1. The comorbidities of patients on ICU admission are shown in Table 1; analysis of the parameters evaluated at T_0-T_2 and analysis of the cardiopulmonary parameters evaluated at T_0-T_1-T_2 is shown in Table 2.

When the relationship between T_0, T_1, and T_2 times of RVEDA/LVEDA was evaluated, it was determined that the decrease in values was significant (*P*=0.012). While the decrease in the 1st hour after PP compared to pre-PP (*P*=0.025) and the decrease after the 24th hour after PP (*P*=0.042) were significant, the difference between the 1st and 24th hours was not significant. A graph showing the mean values for T_0: 0.56, T_1: 0.51, T_2: 0.53 (n = 29) is shown. The mean Horowitz value pre-PP was 107.2 and post-PP was 178.6 (*P* < 0.001). The increase occurred in all stages, with an average increase of 45 (units) from T_0 to T_1 and 26.4 (units) from T_1 to T_2. There was a significant increase in all the measurements (T_0-$_1$ *P*=0.001, T_0-$_2$ *P*=0.001, T_1-$_2$ *P*=0.027) (Figure 3).

A statistically significant correlation was found between the Cstat value and 28-day survival. According to the Kaplan-Meier calculation, the cut-off Cstat value was found to be 37, and the 28-day survival was lower in patients, with a

Table 1. Patient's Characteristics and Comorbidities on ICU Admission

	Total n = 30
	$\overline{X}$ (SD)
Age (years)	64.5 (10.9)
PBW (kg)	57.6 (10.5)
BMI (kg m^{2-1})	33.4 (9.03)
BSA (m^2)	1.93 (0.144)
SOFA score	9.87 (2.45)
APACHE II score	28.5 (7.12)
CCI score	4.17 (2.17)
PSI score	88.9 (27.3)
ACP risk score	3 [1]
Timing of OTI (days from diagnosis)	11.5 (9.45)
Duration of IMV (days)	15.1 (8.55)
LOS in ICU (days)	18.5 (9.31)
LOS in hospital (days)	26.1 (14.2)
Survival (days)	20.8 (9.67)
Total PP hours	135 (83.3)
	n (%)
Severe ARDS	14 (46.7)
Diabetes mellitus	11 (36.7)
Hypertension	15 (50)
Coronary artery disease	6 (20)
Lymphoma	4 (13.3)
Asthma	3 (10)
Solid tumor	4 (13.3)
Chronic kidney disease	2 (6.7)
Leukemia	6 (20.0)
No smoke	17 (56.7)
Mortality-28 day	18 (60)

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

PBW, predicted body weight; BMI, body mass index; BSA, body surface area; SOFA, sequential organ failure assessment; APACHE II, acute physiology and chronic health evaluation II; CCI, Charlson comorbidity index; PSI, pneumonia severity index; ACP, acute care pathway; OTI, orotracheal intubation; IMV, invasive mechanical ventilation; LOS, length of stay; ICU, intensive care unit; PP, prone position; ARDS, acute respiratory distress syndrome

Table 2. Analysis of the Cardiopulmonary Parameters Evaluated in T_0-T_2 and T_0-T_1-T_2

	T_0 (pre-PP)	T_2 (T_0+24 h)				
	$\overline{X}$ (SD)	$\overline{X}$ (SD)	t	P	d	
TAPSE (mm) (n = 25)	19.2 (3.53)	20.4 (2.31)	-2.13	**0.044**	0.425	
	Median (IQR)	**Median (IQR)**	**W**	***P***	**rbc**	
Troponin (ng L^{-1})	27.8 [43.6]	33.3 [42.9]	132	0.066	0.393	
pro-BNP (ng L^{-1}) (n = 29)	1122 [2222]	1074 [2895]	199	0.701	-0.085	
CK (U L^{-1})	118 [228]	80 [84.8]	316	**0.035**	0.451	
	T_0 (pre-PP)	T_1 (T_0+1 h)	T_2 (T_0+24 h)			
	$\overline{X}$ (SD)	$\overline{X}$ (SD)	$\overline{X}$ (SD)	F	***P***	η^2G
RVEDV (mL) (n = 27)	42.3 (16.5)	31.8 (11)	33.4 (13.6)	15.6	**<0.0001**	0.091
LVEDV (mL) (n = 29)	96.0 (33.2)	84.4 (24.8)	88.6 (24.9)	4.07	**0.022**	0.033
LVESV (mL)	50 (19.7)	43.4 (12.3)	46.8 (15.1)	3.8	**0.028**	0.036
SAP (mmHg)	133 (26.6)	124 (17.0)	135 (23.8)	2.27	0.112	0.041
DAP (mmHg)	65.3 (13.8)	62.5 (11.0)	65.3 (9.46)	0.969	0.386	0.014
MAP (mmHg)	88.7 (16.7)	84.4 (14.3)	90.4 (14.6)	1.58	0.215	0.028
Heart rate (beat mn)	89.6 (26.4)	88.7 (20.8)	87.6 (22.1)	0.147	0.864	0.001
Norepinephrine (µg kg^{-1} min)	0.100 (0.061)	0.108 (0.074)	0.156 (0.183)	0.066	0.936	0.002
Balance (mL)	286 [662]	367 [969]	568 [1138]	12.2	**0.002**	
SPO_2 (%)	93.4 (3.26)	94.7 (2.48)	94.1 (2.05)	1.41	0.257	0.036
FiO_2 (%)	0.782 (0.114)	0.689 (0.141)	0.617 (0.162)	24.5	**<0.001**	0.193
PaO_2 (mmHg)	81.9 (19.8)	98.6 (28.6)	99.3 (26.5)	5.1	**0.009**	0.095
$PaCO_2$ (mmHg)	50.6 (13.6)	50.8 (10.6)	56.6 (21.8)	1.46	0.241	0.031
MV (L mn)	7.10 (1.34)	7.31 (1.18)	6.99 (1.32)	0.891	0.416	0.011
TV (mL)	468 (82.4)	470 (62.8)	454 (68.8)	1.14	0.326	0.011
Peep (cmH_2O)	9.00 [2.00]	9.50 [2.00]	10 [2.00]	1.08	0.582	
dP (cmH_2O) (n = 29)	17.0 (3.89)	17.3 (3.50)	15.7 (2.93)	4.39	**0.017**	0.030
Cdyn (mL cmH_2O)	29.4 (9.13)	28.0 (6.21)	30.2 (9.47)	4.19	**0.020**	0.010
Cstat (mL cmH_2O)	33.0 (9.85)	30.7 (8.92)	34.0 (10.1)	7.72	**0.001**	0.020
pH	7.36 (0.106)	7.35 (0.101)	7.34 (0.120)	0.325	0.724	0.005
BE (mmoL L^{-1})	2.36 (4.52)	1.76 (4.42)	3.47 (4.34)	4.06	**0.022**	0.026
Lactate (mmoL L^{-1})	1.75 [0.950]	1.70 [0.650]	1.60 [0.875]	2.75	0.252	
SO_2 %	94.2 [4.77]	96.4 [4.25]	96.4 [2.25]	14.6	**<0.001**	
Bicarbonate (mmoL L^{-1})	26.1 (4.27)	25.4 (4.19)	26.8 (4.34)	2.92	0.062	0.020

Values are presented as mean ± SD or median.

t, Paired samples t-test; d, Cohen's d effect size; P, Probability, $P < 0.05$

TAPSE, tricuspid annular plane systolic excursion; IQR, interquartile range, rbc, rank biserial correlation; BNP, B-type natriuretic peptide; W, Wilcoxon; CK, creatine kinase; PP, prone position; F, F test; η^2G, Effect size; RVEDV, right ventricular end diastolic volume; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; MV, minute volume; TV, tidal volume; dP, driving pressure; Cdyn, compliance of dynamic; Cstat, compliance of static; BE, base excess.

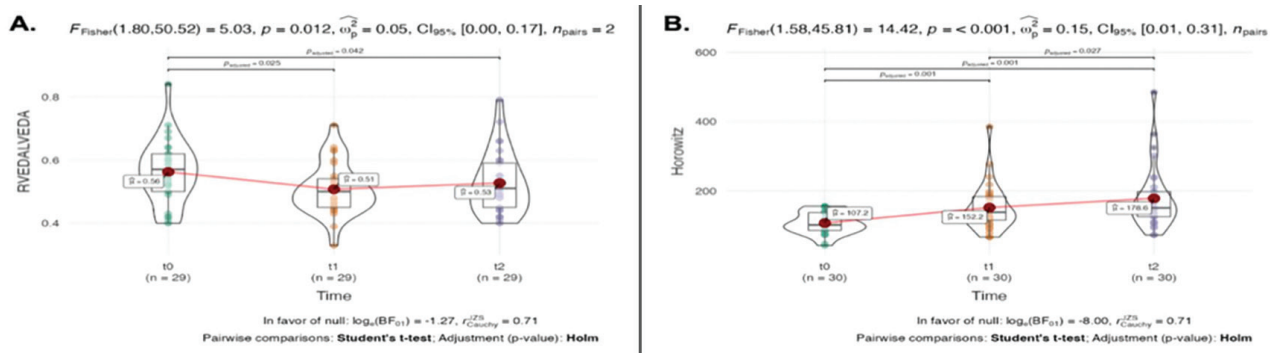

Figure 3. Change of RVEDA/LVEDA and Horowitz ratio with prone position

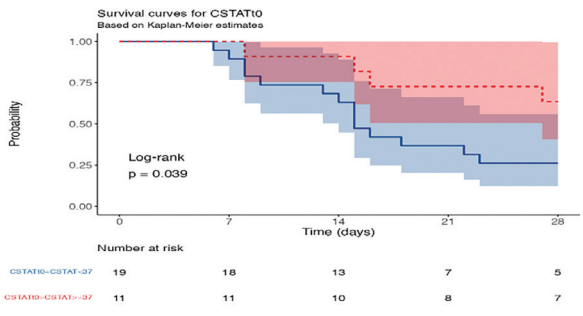

Figure 4. Survival curves for static compliance

value <37. At the end of 28 days, 5 of 19 patients with Cstat at T_0 <37, and 7 of 11 patients with Cstat ≥37, survived. Each Cstat value from T_0, T_1, and T_2 was found to be significant in terms of survival. It was determined that an increase of 1 unit according to Cstat at T_0 value increases the probability of 28-day survival with an HR of 0.91 (0.86-0.98, *P*=0.007), (T_0 t=2.913 *P*=0.007, T_1 t=2.796 *P*=0.009, T_2 t=3.267 *P*=0.003) (Figure 4).

Changes in the CO, confidence interval (CI), ejection fraction, LVOT VTI, LVESEI, DO_2 values were not significant (Figure 5). There was no significant difference between patients

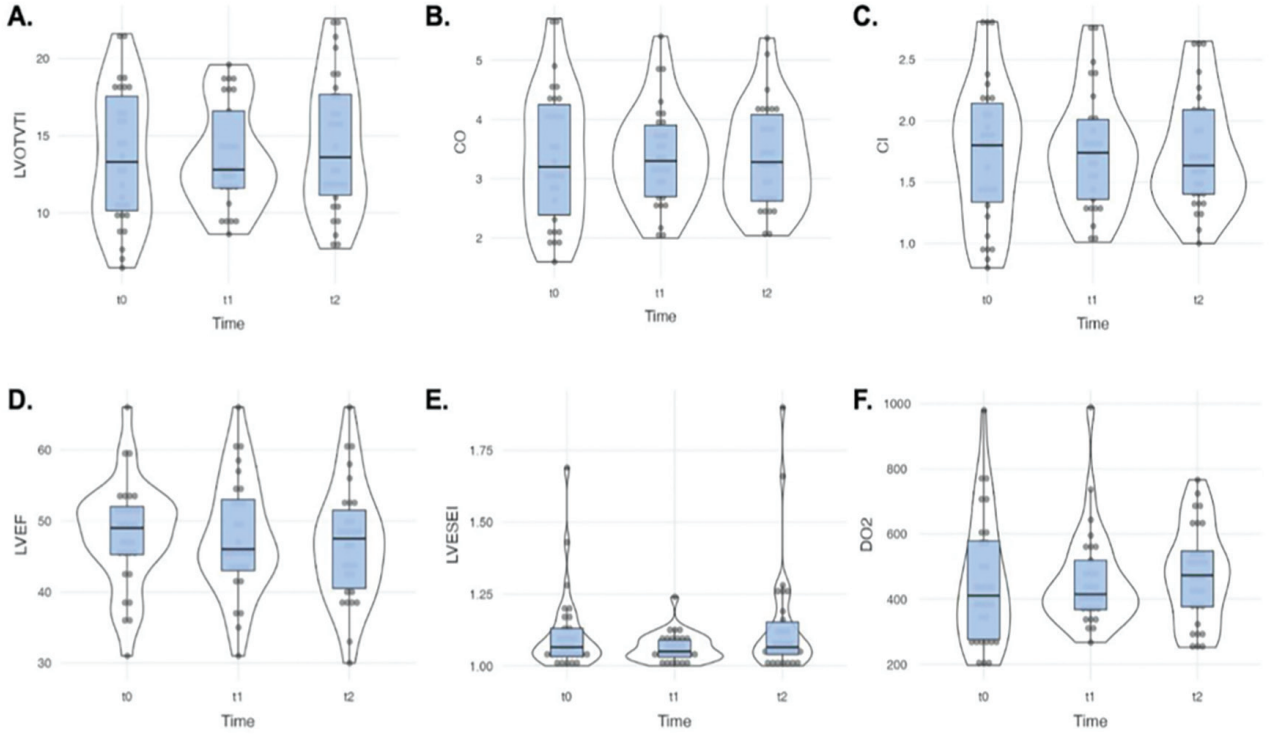

Figure 5. Change of LVOT-VTI, CO, CI, LVEF, LVESEI, DO_2 with prone position

CO, cardiac output; CI, cardiac index; LVEF, left ventricular efection fraction; LVESEI, left ventricular eccentricity index

who survived and those who did not in terms of the total number of PP hours applied over 28 days. Although lower T_1 Horowitz and delta Horowitz between T_0-T_1 and T_0-T_2 were observed in the mortality group, these values were not significant.

Discussion

In studies evaluating the heart-lung interaction in C-ARDS, the use of echocardiography has been recommended, with an emphasis on the importance of evaluating RV dysfunction (RVD) to reduce mortality.[9-11] For the definition of RVD, among the parameters specified by the PRICES study published by the European Society of Intensive Care Medicine, the values of RVEDA/LVEDA and TAPSE were preferred.[12] The recommended value of 0.6 (<0.6 normal, 0.6-1 dilated, >1 severe) is used as the RVEDA/LVEDA cut-off value for RVD definition.[13] In the case series, which included nine C-ARDS patients with a Horowitz mean of 77, evaluations were conducted using TEE and three-dimensional (3D) before PP, at the first hour after PP, and in the supine position (PP+16 h). The RVEDA/LVEDA ratio did not increase; the LVESEI improved with PP; and the LVOT VTI decreased. The CI remained in balance with the increase in HR secondary to a decrease in LVOT VTI. RVEDV and LVEDV were observed to decrease significantly with the use of 3D.[14]

There was a small increase in LVOT VTI due to the effect of PP, which was not statistically significant. Reflecting the RVD recovery, RVEDA/LVEDA decreased, and TAPSE increased significantly. However, no increase in the CO was observed. This might be the result of LV worsening, concomitant with an improvement in the RVD. Chotalia et al.[15] also showed that there are different cardiovascular sub-phenotypes in COVID-19 pneumonitis and that the PP response is different in sub-phenotypes. The significant increase in Horowitz was not sufficient to provide a significant change in the DO_2 value. This showed that PP would not be sufficient to increase tissue oxygen supply, only by oxygenation, which could be possible with the combination of positive cardiac and pulmonary effects. Despite the severe C-ARDS, no significantly advanced RVD was observed. The median value of acute cor pulmonale (ACP) risk score was 3, but only 12 patients had a baseline RVEDA/LVEDA ≥0.6. Unless RVD causes LV dysfunction, its curative effect may not be sufficient to increase the DO_2. The curative effect of PP on LV is observed when LV worsens secondary to RVD.

In a study evaluating the pulmonary circulation effects of inhaled nitric oxide (iNO) therapy in 12 C-ARDS patients with TTE, concomitant RV dilatation and dysfunction were demonstrated in only one-third of patients, despite baseline Horowitz values <150.[16] The baseline Horowitz mean of our sample group of 30 was 107.2, and there were 12 patients with RVEDA/LVEDA ≥0.6. The improvement in RVD and oxygenation with PP shown in this study contrasts with findings from another RVD study, which did not show improvement with iNO treatment. RVD cannot be estimated using the Horowitz value, and the importance of echocardiography in diagnosis is clear. In improving oxygenation in C-ARDS patients, improvement in V/Q may contribute more than pulmonary vasodilatation. In another study in which sildenafil was used in the treatment of patients with C-ARDS, no significant improvement was found in oxygenation.[17] The etiology of hypoxemia in C-ARDS varies and does not always cause increased pulmonary vascular resistance. Sometimes, pulmonary vasodilation is also a cause of hypoxemia.[18] In a study stating that there is a relationship between an increase in CI and hypoxemia, a pulmonary artery catheter was used in the analysis, and increased shunt flow was stated as the cause of hypoxemia.[19]

In the study by Vieillard-Baron et al.[1] with 42 ARDS patients, Vieillard-Baron et al.[1] divided the patients into two groups, ACP and non-ACP, and evaluated them with TEE twice, before and after PP (PP+18 hours). In the ACP group, RVEDA/LVEDA improvement, CI increase, and LVESEI improvement were significant. Working on homogeneity with Horowitz <100 has proved advantageous. Had the patient group been divided into multiple groups according to the RVEDA/LVEDA value in our study, a better relation could have been observed by evaluating during PP, just before returning to the supine position, in addition to our assessments.

An analysis of the relationship between C-ARDS and RVD in 90 patients showed that longitudinal contraction of the RV was preserved, but there was radial damage.[20] Similarly, the increase in TAPSE values with PP was significant, but the mean value of the baseline was 19.2±3.53, which was already preserved. Not measuring tricuspid regurgitation, systolic pulmonary artery pressure, or TAPSE's inability to evaluate radial damage may have affected the result of TAPSE not being associated with survival.

RV free wall strain was evaluated in a study of 32 C-ARDS patients, and abnormal strain was observed in them. The compliance, and mechanical ventilation parameters were better in patients with low strain values. They concluded that RVD in C-ARDS develops from cardiac damage or vascular thrombosis rather than from pulmonary causes.[21] They found a significant correlation between RVD and mortality in a cohort study using TEE, and examined the longitudinal shortening fraction as a prognostic factor in C-ARDS.[22] Temperikidis et al.[23] analyzed nine C-ARDS patients before PP, 18 hours after PP, and 1 hour after returning to supine. Abnormal onset strain values are a poor prognostic indicator.

In a multicenter cohort study by Vandenbunder et al.[24] that included 1st day and 14th day values and was conducted with 372 patients, no 28-day survival relationship was observed, although there was a significant decrease in the value on the 14th day. In a study examining the effect of PP on Horowitz and Cstat in C-ARDS and non-C-ARDS patients, the effects of the first PP were effective in predicting the prognosis.[25] In the other study, they concluded that low Cstat and high D-dimer levels were associated with mortality.[26] Here, a significant correlation between Cstat in the first 48 h after orotracheal intubation and 28-day survival in C-ARDS was observed.

Fossali et al.[27] used electrical impedance tomography during PP, in a survival analysis of increased oxygenation in 21 patients with moderate/severe C-ARDS. They showed increased oxygenation, lung area gain in the dorsal areas, and a decrease in the dead space shunt ratio in the ventral areas, but found no significant correlation between increased lung area and either disease severity or improvement in oxygenation.[27] Despite the increase in oxygenation, we did not see a significant increase in DO_2 in our study. Among the pulmonary parameters affected by PP, dP decreased, and Cstat and Cdyn increased. Cstat, a cardiopulmonary parameter that we found to be significantly related to survival, draws attention to the importance of a compatible lung. The importance of the compatible lung can be explained both by the protective effect on the lung by preventing pressure and volume damage, and by its protective effect on the heart through the heart-lung interaction.

Study Limitations

Limitations of this study; two-dimensional was used in volume evaluation, the number of our patient group and it was single-centered. The effect of the PP on the RV in C-ARDS is better evaluated in comparison to patients without PP. In this study, where the relationship between RVD and survival was examined, we believe that the presence of additional factors affecting the results. Indeed, in most patients, secondary infections and the development of septic shock were causes of mortality.

Conclusion

The cardiopulmonary pathophysiology and outcomes of C-ARDS are variable, and this variability requires monitoring throughout the diagnosis and treatment process. PP can improve RV recovery and oxygenation; however, it does not always lead to increased survival. The use of echocardiography is important in evaluating the mechanism of cardiopulmonary injury and treatment process in C-ARDS patients with frequent RVD and high mortality, and its use is becoming common. The fact that the increase in Cstat has been shown to be associated with 28-day survival suggests that a better-functioning lung will interact more effectively with the heart and improve survival. Randomized, multicenter studies are needed on this subject. It could be said that holistic recovery and individualized treatment strategies should be targeted instead of improvement in a single parameter.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinical Research Local Ethics Committee with the decision number 2022-03-03, dated 07.02.2022.

Informed Consent: Informed consent was obtained.

Footnotes

Author Contributions: Surgical and Medical Practices - D.B, S.A., G.S.; Concept - Z.Ç., D.Ö., F.N.Ç.T.; Design - D.B., Z.Ç., G.S.; Data Collection and/or/Processing - D.B., S.A., D.Ö., F.N.Ç.T.; Analysis and/or/Interpretation - Z.Ç., S.A., D.Ö., G.S.; Literature Review - D.B., Z.Ç., S.A., F.N.Ç.T.; Writing - D.B., Z.Ç., D.Ö., G.S., F.N.Ç.T.

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Validation and Translation of the 3D-CAM to Turkish in Surgical Intensive Care Patients

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Abstract

Objective: Delirium is a common condition that can significantly worsen a patient's clinical status. Timely and accurate detection of this often-overlooked condition is essential for effective prevention and treatment. This study aims to validate the Turkish version of the 3-Minute Diagnostic Interview for Confusion Assessment-defined Delirium (3D-CAM-TR), which has been culturally adapted for surgical intensive care patients.

Methods: This study was conducted in surgical intensive care units and wards at three academic hospitals, including 133 surgical intensive care patients. The 3D-CAM was culturally adapted and translated into Turkish. The 3D-CAM-TR was administered by trained clinicians from the first to the third postoperative day. During this period, delirium diagnosis was made by experienced psychiatrists using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria as the reference standard. All assessors were blinded to each other's assessment results. The 3D-CAM delirium diagnosis was compared with the reference standard in all patients.

Results: A total of 133 adult patients were assessed over three consecutive days, findings in 399 paired assessments. Compared to the DSM-5-based reference standard, the sensitivity and specificity of the 3D-CAM-TR assessment were found to be 95% and 97%, respectively, for rater 1, and 93% and 99%, respectively, for rater 2, with good inter-rater reliability (Kappa coefficient=0.898, confidence interval=0.84, 0.96).

Conclusion: Our resultings indicate that the 3D-CAM-TR is a dependable and precise instrument for assessing delirium in postoperative intensive care patients.

Keywords: 3D-CAM, Delirium, Intensive Care, Turkish Version, Validation

Main Points

- The sensitivity of the Turkish version of the 3-Minute Diagnostic Interview for Confusion Assessment-defined Delirium (3D-CAM-TR) assessment was found to be 95% for rater 1 and 93% for rater 2.
- The specificity of the 3D-CAM-TR assessment were found to be 97% for rater 1, and 99% for rater 2.
- Assessment was have good inter-rater reliability.

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Introduction

Postoperative delirium (PD) is a common complication in geriatric surgical patients. As defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), delirium is a transient condition marked by disturbances in attention, awareness, and cognition, with symptoms that develop suddenly and fluctuate over time.[1] Delirium is associated with accelerated cognitive decline, although there is ongoing debate about whether it serves as a marker or a risk factor for subsequent persistent cognitive impairment.[2,3]

The exact etiology of PD remains unclear. However, it is recognized as an acute disturbance in cognitive function and/or spatial-temporal perception, which can be diagnosed at the bedside using specific diagnostic tools. PD typically presents with an abrupt onset and a fluctuating course, and without systematic screening, it may be easily overlooked. The condition is characterized by three core features: altered consciousness, changes in cognitive abilities, and a rapid onset.[4]

The DSM-5 is used to establish the definitive diagnosis of delirium. Nevertheless, utilizing it correctly necessitates specialized psychiatric training and education. The most commonly used tool developed for use by non-psychiatric practitioners to help diagnose delirium is the Confusion Assessment Method (CAM). Other tools described include the CAM for intensive care units (CAM-ICU) and the CAM-defined 3 Minute Diagnostic Interview for Delirium (3D-CAM).[1]

The 3D-CAM can be completed in an average of three minutes and has excellent diagnostic test properties with 95% sensitivity and 94% specificity compared to a reference standard based on a comprehensive clinical evaluation.[5] The 3D-CAM is a concise interview that utilizes verbal responses complete the CAM diagnostic algorithm.[6] By providing a short, repeatable method for detecting delirium, the 3D-CAM facilitates case finding among hospitalized frail elderly patients.

Although the 3D-CAM has been translated and validated into many languages, there is currently no Turkish translation or validation available. The aim of our study is to translate the 3D-CAM into Turkish and validate the Turkish version 3D-CAM (3D-CAM-TR) in surgical patients.

Methods

This study was conducted prospectively to translate and validate the reliability of the Turkish version of the 3D-CAM in surgical intensive care patients. The research protocol received approval from the Aydın Adnan Menderes University Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee (date: 28.01.2021, approval no.: 2021/28). The study was registered with Clinical Trials under the number NCT04853706. The multicenter study was carried out. All enrolled patients or their proxies provided written informed consent.

Translation and Back Translation

The forward translation process, which involves translating the original version into the target language, was carried out independently by two bilingual experts: a specialist doctor of Turkish descent who has lived in the United States for an extended period (AT), and a medical student, also of Turkish descent, who was born and raised in the United States (OT). Both translators independently translated all items of the 3D-CAM, including response options and instructions, into Turkish. The initial translation was then reviewed by Dr. Edward R. Marcantonio, the original developer and validator of the 3D-CAM. After incorporating the revisions he suggested, the translation received his formal approval.

To identify potential conceptual inaccuracies, a back-translation process was employed, whereby the translated text was retranslated from the target language back into the source language. Any back-translations that deviated from the intended meaning were revised in the Turkish version, back-translated again, and subjected to further review. This iterative process continued until the principal developer gave final approval for the reverse translation (Figure 1).

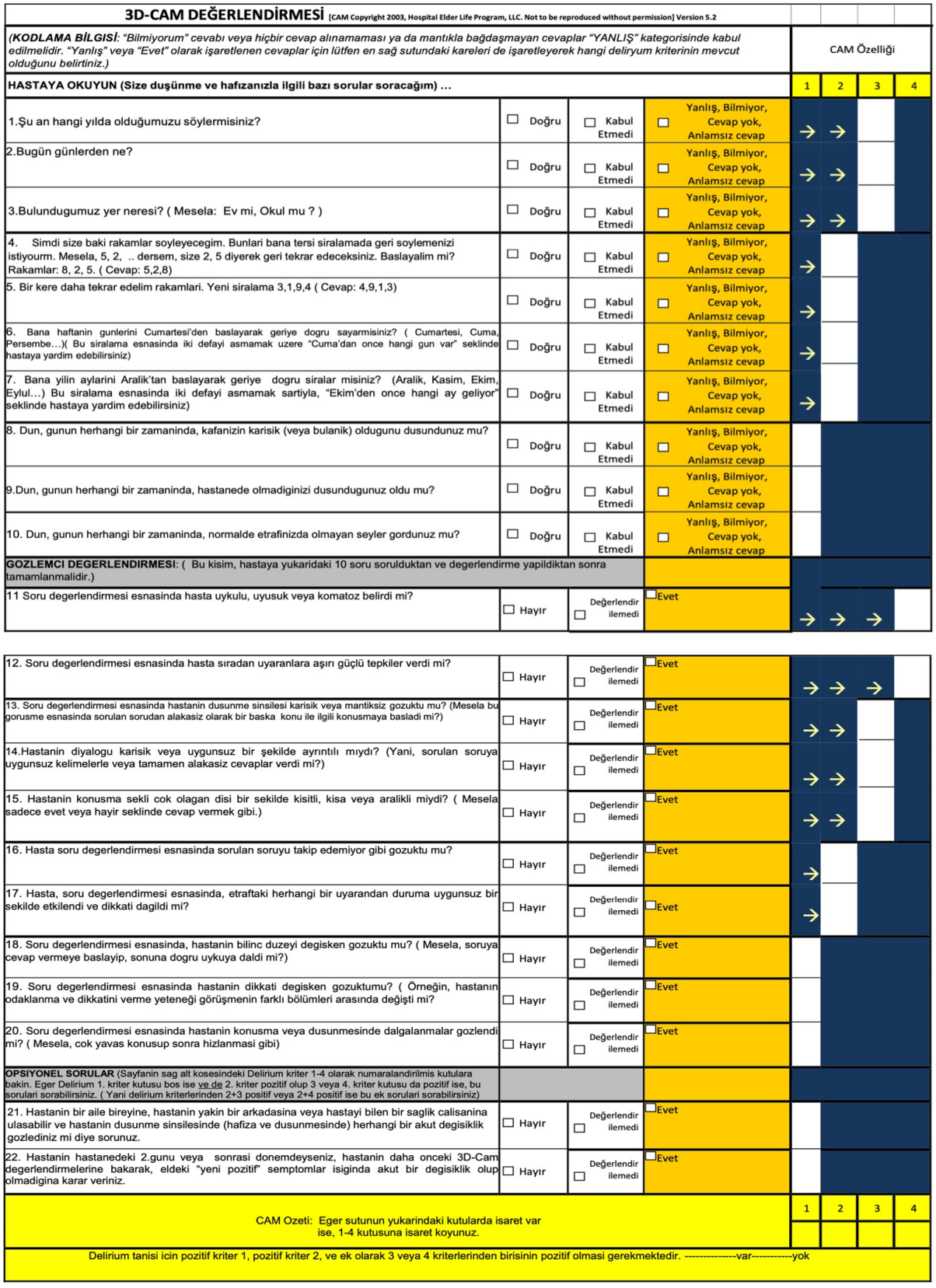
Participants

To be eligible for participation, individuals met the following inclusion criteria: (a) be at least 18 years of age and (b) have an American Society of Anesthesiologists (ASA) classification. Physical status 1-3. (c) admitted to the postoperative critical care unit and are expected to stay in the hospital for more than 48 hours. Additionally, patients with an Mini-Mental State Examination (MMSE) score of 20 or higher are included, while those with dementia are excluded.

Exclusion criteria: (a) Patients who declined to participate, (b) Patients with significant visual or auditory impairment/disability or the presence of endotracheal intubation that may impede communication, (c) The presence of a significant psychiatric condition, such as bipolar disorder, major depression, schizophrenia, Alzheimer's disease, dementia, or parkinsonism, and (d) profound sedation or unconsciousness. ASA physical status IV or V refers to patients who have severe systemic disease posing a continuous threat to life (IV) or patients who are not expected to survive without the surgery (V). (e) Patients receiving surgical procedures with a duration of less than one hour.

Enrollment and Baseline Data Collection

The assessment of eligibility and obtaining patient consent were conducted during the preoperative consultation. Demographic and historical medical information, including medication use, was obtained during this appointment.



3D-CAM DEĞERLENDİRMESİ [CAM Copyright 2003, Hospital Elder Life Program, LLC. Not to be reproduced without permission] Version 5.2							
(KODLAMA BİLGİSİ: "Bilmiyorum" cevabı veya hiçbir cevap alınamaması ya da mantıkla bağdaşmayan cevaplar "YANLIŞ" kategorisinde kabul edilmelidir. "Yanlış" veya "Evet" olarak işaretlenen cevaplar için lütfen en sağ sutundaki kareleri de işaretleyerek hangi deliryum kriterinin mevcut olduğunu belirtiniz.)				CAM Özelliği			
HASTAYA OKUYUN (Size duşünme ve hafızanızla ilgili bazı sorular soracağım) …				1	2	3	4
1.Şu an hangi yılda olduğumuzu söylermisiniz?	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→	→		
2.Bugün günlerden ne?	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→	→		
3.Bulunduğumuz yer neresi? (Mesela: Ev mi, Okul mu ?)	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→	→		
4. Simdi size baki rakamlar soyleyecegim. Bunlari bana tersi siralamada geri soylemenizi istiyourm. Mesela, 5, 2, .. dersem, size 2, 5 diyerek geri tekrar edeceksiniz. Baslayalim mi? Rakamlar: 8, 2, 5. (Cevap: 5,2,8)	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→			
5. Bir kere daha tekrar edelim rakamlari. Yeni siralama 3,1,9,4 (Cevap: 4,9,1,3)	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→			
6. Bana haftanin gunlerini Cumartesi'den baslayarak geriye dogru sayarmisiniz? (Cumartesi, Cuma, Persembe…)(Bu siralama esnasinda iki defayi asmamak uzere "Cuma'dan once hangi gun var" seklinde hastaya yardim edebilirsiniz)	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→			
7. Bana yilin aylarini Aralik'tan baslayarak geriye dogru siralar misiniz? (Aralik, Kasim, Ekim, Eylul…) Bu siralama esnasinda iki defayi asmamak sartiyla, "Ekim'den once hangi ay geliyor" seklinde hastaya yardim edebilirsiniz)	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap	→			
8. Dun, gunun herhangi bir zamaninda, kafanizin karisik (veya bulanik) oldugunu dusundunuz mu?	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap				
9.Dun, gunun herhangi bir zamaninda, hastanede olmadiginizi dusundugunuz oldu mu?	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap				
10. Dun, gunun herhangi bir zamaninda, normalde etrafinizda olmayan seyler gordunuz mu?	☐ Doğru	☐ Kabul Etmedi	☐ Yanlış, Bilmiyor, Cevap yok, Anlamsız cevap				
GOZLEMCI DEGERLENDIRMESI: (Bu kisim, hastaya yukaridaki 10 soru sorulduktan ve degerlendirme yapildiktan sonra tamamlanmalidir.)							
11 Soru degerlendirmesi esnasinda hasta uykulu, uyusuk veya komatoz belirdi mi?	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→	→	→	
12. Soru degerlendirmesi esnasinda hasta sıradan uyaranlara aşırı güçlü tepkiler verdi mi?	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→	→	→	
13. Soru degerlendirmesi esnasinda hastanin dusunme sinsilesi karisik veya mantiksiz gozuktu mu? (Mesela bu gorusme esnasinda sorulan sorudan alakasiz olarak bir baska konu ile ilgili konusmaya basladi mi?)	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→	→		
14.Hastanin diyalogu karisik veya uygunsuz bir şekilde ayrıntılı mıydı? (Yani, sorulan soruya uygunsuz kelimelerle veya tamamen alakasiz cevaplar verdi mi?)	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→	→		
15. Hastanin konusma sekli cok olagan disi bir sekilde kisitli, kisa veya aralikli miydi? (Mesela sadece evet veya hayir seklinde cevap vermek gibi.)	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→	→		
16. Hasta soru degerlendirmesi esnasinda sorulan soruyu takip edemiyor gibi gozuktu mu?	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→			
17. Hasta, soru degerlendirmesi esnasinda, etraftaki herhangi bir uyarandan duruma uygunsuz bir sekilde etkilendi ve dikkati dagildi mi?	☐ Hayır	☐ Değerlendirilemedi	☐ Evet	→			
18. Soru degerlendirmesi esnasinda, hastanin bilinc duzeyi degisken gozuktu mu? (Mesela, soruya cevap vermeye baslayip, sonuna dogru uykuya daldi mi?)	☐ Hayır	☐ Değerlendirilemedi	☐ Evet				
19. Soru degerlendirmesi esnasinda hastanin dikkati degisken gozuktumu? (Örneğin, hastanın odaklanma ve dikkatini verme yeteneği görüşmenin farklı bölümleri arasında değişti mi?	☐ Hayır	☐ Değerlendirilemedi	☐ Evet				
20. Soru degerlendirmesi esnasinda hastanin konusma veya dusunmesinde dalgalanmalar gozlendi mi? (Mesela, cok yavas konusup sonra hizlanmasi gibi)	☐ Hayır	☐ Değerlendirilemedi	☐ Evet				
OPSIYONEL SORULAR (Sayfanin sag alt kosesindeki Delirium kriter 1-4 olarak numaralandirilmis kutulara bakin. Eger Delirium 1. kriter kutusu bos ise ve de 2. kriter pozitif olup 3 veya 4. kriter kutusu da pozitif ise, bu sorulari sorabilirsiniz. (Yani delirium kriterlerinden 2+3 positif veya 2+4 positif ise bu ek sorulari sorabilirsiniz)							
21. Hastanin bir aile bireyine, hastanin yakin bir arkadasina veya hastayi bilen bir saglik calisanina ulasabilir ve hastanin dusunme sinsilesinde (hafiza ve dusunmesinde) herhangi bir akut degisiklik gozlediniz mi diye sorunuz.	☐ Hayır	☐ Değerlendirilemedi	☐ Evet				
22. Hastanin hastanedeki 2.gunu veya sonrasi donemdeyseniz, hastanin daha onceki 3D-Cam degerlendirmelerine bakarak, eldeki "yeni pozitif" semptomlar isiginda akut bir degisiklik olup olmadigina karar veriniz.	☐ Hayır	☐ Değerlendirilemedi	☐ Evet				
CAM Ozeti: Eger sutunun yukarindaki kutularda isaret var ise, 1-4 kutusuna isaret koyunuz.				1	2	3	4
Delirium tanisi icin pozitif kriter 1, pozitif kriter 2, ve ek olarak 3 veya 4 kriterlerinden birisinin pozitif olmasi gerekmektedir. ----------var----------yok							

Figure 1. Turkish Version of 3D-CAM.

The MMSE was performed. Patients with an MMSE score above 20 were included in the study. Patients excluded for any reason, including technical issues or contraindications, were recorded.

Delirium Assessment

3D-CAM Delirium Assessment

Before the study period, researchers from all centers participated in web-based instruction on the 3D-CAM. The assessment of delirium was conducted by two different clinicians utilizing the 3D-CAM tool each evening from 18:00 to 20:00 for a period of three days postoperatively. If the patient was transferred from the ICU to the ward, the assessment was conducted in the ward.

DSM-5 Delirium Assessment

An impartial psychiatrist researcher, who was blind to the 3D-CAM assessment results, assessed the patients based on DSM-5 criteria within a 3-minute timeframe following the 3D-CAM evaluation.

Statistical Analysis

Sample Calculation

A prior study found the incidence of delirium to be approximately 13%, with a sensitivity of 85% and specificity of 97%. We set the confidence interval (CI) width at 0.2 and determined that 377 assessments were needed.[1]

Outcome Analysis

Mean and standard deviation were provided for numerical variables, and frequency and percentage statistics were provided for categorical variables. Cohen's kappa statistic was used to calculate inter-rater agreement, with a 95% CI provided (Additionally, McNemar test results were included). Analyses were performed using R 4.3.2 (R Core Team, 2024). A *P* value of <0.05 was considered significant.

Results

Between October 2021 and December 2024, 135 patients from this group who met the inclusion criteria and provided written informed consent were included in the study; 2 of these patients did not complete the study, and the analysis was completed with 133 patients (Figure 2). The mean age of the enrolled patients was 60.63±15.55 years, and the MMSE score was 27.8±2.60. Socio-demographic and perioperative data are presented in Table 1.

A total of 399 paired assessments were conducted over a period of three consecutive days for each patient. Based on the psychiatrist's evaluation using the DSM-5, 19.55% (26 out of 133) of the patients encountered at least one episode of delirium.

When compared to the reference standard DSM-5 psychiatrist evaluation, the sensitivity and specificity of the 3D-CAM-TR assessment were 95% and 97% for rater 1, and 93% and 99% for rater 2, respectively (Table 2). The inter-rater reliability, expressed as the Kappa coefficient, was found to be 0.898 with a CI of 0.84 to 0.96.

A total of 274 paired assessments were conducted in the ICU, while 125 assessments were conducted in the ward, encompassing all enrolled patients. The sensitivity of the 3D-CAM-TR in the ICU was 92% for rater 1 and 94% for rater 2; the specificity was 96% for rater 1 and 99% for rater 2 (Table 3).

The sensitivity of the 3D-CAM-TR in the ward was 100% for both rater 1 and rater 2; the specificity was 98% for rater 1 and 100% for rater 2 (Table 4).

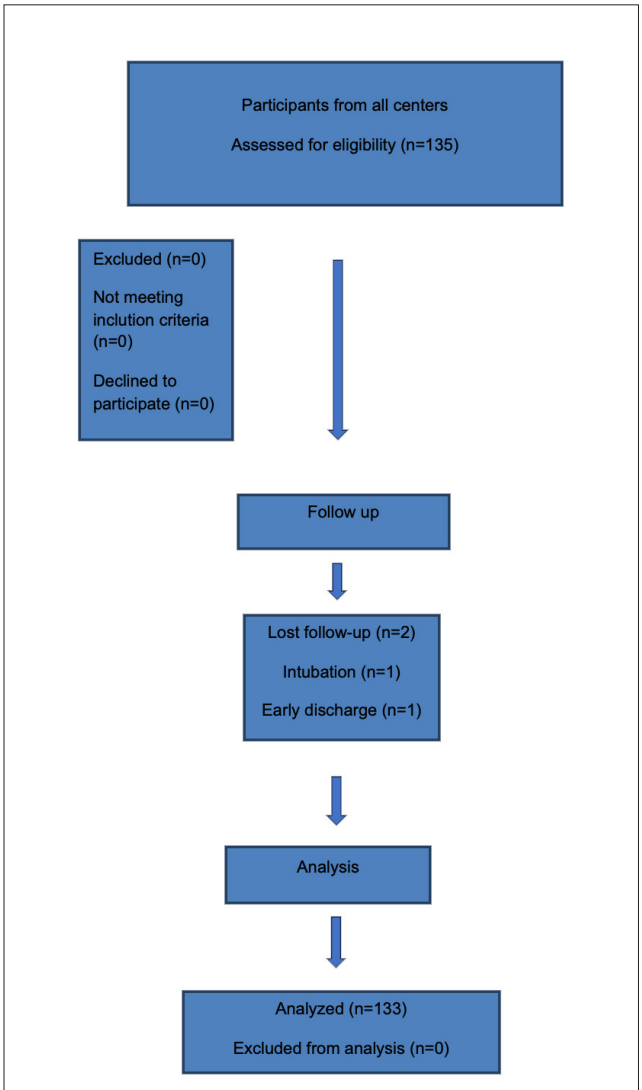


Figure 2. Flow chart.

Table 1. Socio-demographic and Perioperative Data	
Variable	**n = 1331**
Age, years	60.63±15.55
Gender	
Female	44.00 (33.08%)
Male	89.00 (66.92%)
Height, cm	168.92±9.10
Body weight, kg	68.49±13.37
Education level	
Secondary	87.00 (65.41%)
High school	32.00 (24.06%)
University	9.00 (6.77%)
Postgraduate	5.00 (3.76%)
Marital status	
Married	111.00 (83.46%)
Never married	10.00 (7.52%)
Divorced	3.00 (2.26%)
Widowed	9.00 (6.77%)
Illnesses	
Stroke	3 (1.4%)
Hypertension	57 (27.3%)
CAD	32 (15.3%)
Arrhythmia	7 (3.3%)
COPD	15 (7.2%)
DM	28 (13.4%)
Hyperlipidemia	5 (2.4%)
CRD	10 (4.8%)
Hyperthyroidism	1 (0.5%)
Hypothyroidism	1 (0.5%)
None	50 (23.9%)
ASA	
1	15.00 (11.28%)
2	75.00 (56.39%)
3	43.00 (32.33%)
MMSE, score	27.80±2.60

Data was presented as mean (standard deviation) or number (percentage)
CAD, coroner artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; CRD, chronic renal disease; ASA, American Society of Anesthesiologists; MMSE, mini-mental state examination

Discussion

This study provides evidence that the Turkish version of 3D-CAM is a dependable instrument for evaluating delirium in patients, with an MMSE score of 20 and above, who are receiving intensive care after surgery. When compared to the reference standard DSM-5 psychiatrist evaluation, the sensitivity and specificity of the 3D-CAM-TR assessment were 95% and 97% for rater 1, and 93% and 99% for rater 2, respectively. 3D-CAM-TR also yielded positive results when evaluated separately for patients in the ICU and the ward. A total of 274 paired assessments were conducted in the ICU, while 125 assessments were conducted in the ward, encompassing all enrolled patients. The sensitivity of the 3D-CAM-TR in the ICU was 92% for rater 1 and 94% for rater 2; the specificity was 96% for rater 1 and 99% for rater 2.

Delirium is frequently overlooked in clinical settings, and more than 28 diagnostic techniques have been created and implemented to aid in its screening.[7,8] These tools have greatly enhanced the efficiency and precision of diagnosing delirium. Among these tools, CAM has been proposed as the most effective.[7,8] Nevertheless, one disadvantage of CAM is that, despite extensive training, there may still be inconsistencies in the assessment criteria used by different assessors.[7] Hence, the proficiency of the evaluator's interrogative abilities might greatly influence the outcomes of the evaluation. The 3D-CAM, a derivative of CAM, offers a concise and organized assessment technique to expedite and streamline the diagnostic procedure.[5] The 3D-CAM's capacity to conduct evaluations within just three minutes is a notable benefit for clinical practice.

This study confirmed the efficacy and dependability of the 3D-CAM-TR in both the ICU (without the use of endotracheal intubation) and ward settings for surgical patients. Several diagnostic methods, such as CAM-ICU and the critical Care Delirium Screening Checklist, have been utilized to diagnose delirium in patients in ICUs.[9] Nevertheless, the comparison between these tools and the 3D-CAM has only been conducted in a limited number of studies. A study was conducted with 101 elderly patients (aged 75 years or older) who were not in the ICU. The study found that the 3D-CAM method was more effective than the CAM-ICU method in identifying delirium.[10]

In a study similar to our study validating the 3D-CAM-CN, it was reported to be a reliable tool for diagnosing delirium in postoperative patients.[1] They highlighted the strengths of the study, including comprehensive pre-study preparation and strict criteria provided by a panel of psychiatrists. In our study, we planned to demonstrate the 3D-CAM application through online training. Subsequently, evaluators applied the 3D-CAM-TR without supervision. We believe that extended training periods reduce the efficiency of test administration, which is one of the test's advantages. We suggest that future research could explore evaluations after different levels of training and determine the optimal training duration.

Table 2. Raters' Concordance with the Reference Standard

	Reference Standard by DSM-5			
	Positive, n = 61[1]	**Negative, n = 338[1]**	**Kappa**	**p[2]**
Rater 1			0.871	0.061
Positive	58 (95.1%)	11 (3.3%)		
Negative	3 (4.9%)	327 (96.7%)		
Rater 2			0.932	>0.9
Positive	57 (93.4%)	3 (0.9%)		
Negative	4 (6.6%)	335 (99.1%)		

[1]n (%)
[2]McNemar's chi-squared test with continuity correction

Table 3. Raters' Concordance with the Reference Standard in the Intensive Care Unit

	Reference Standard by DSM-5 in ICU			
	Positive, n = 50[1]	**Negative, n = 224[1]**	**Kappa**	**p[2]**
Rater 1			0.860 (0.78, 0.94)	0.15
Positive	47 (94.0%)	9 (4.0%)		
Negative	3 (6.0%)	215 (96.0%)		
Rater 2			0.914 (0.85, 0.98)	>0.9
Positive	46 (92.0%)	3 (1.3%)		
Negative	4 (8.0%)	221 (98.7%)		

[1]n (%)
[2]McNemar's chi-squared test with continuity correction
ICU, intensive care unit.

Table 4. Raters' Concordance with the Reference Standard in the Ward

	Reference Standard by DSM-5 in ward			
	Positive, n = 11[1]	**Negative, n = 114[1]**	**Kappa**	**p[2]**
Rater 1			0.908 (0.78, 1)	0.5
Positive	11 (100.0%)	2 (1.8%)		
Negative	0 (0.0%)	112 (98.2%)		
Rater 2			1.00 (1.1)	
Positive	11 (100.0%)	0 (0.0%)		
Negative	0 (0.0%)	114 (100.0%)		

[1]n (%)
[2]McNemar's chi-squared test with continuity correction.

Study Limitations

Our study's strengths include a culturally appropriate translation and a sufficient sample size. However, there are also limitations. Types of delirium identified in the study were not recorded, so the reliability of the test among hypoactive, hyperactive, and mixed types could not be evaluated. The reliability of the test in patients with major cognitive impairment has been previously established. However, since we included only patients with an MMSE score above 20 and no diagnosis of cognitive impairment, the reliability in the group with major cognitive impairment could not be assessed.

Conclusion

This study successfully linguistically validated the 3D-CAM for use in the Turkish population, enabling its application for assessing delirium in Turkish-speaking patients. The Turkish version of the questionnaire is now ready for use in post-

surgical patients who are not intubated and who do not have cognitive impairment.

Ethics

Ethics Committee Approval: The research protocol received approval from the Aydın Adnan Menderes University Faculty of Medicine, Non-Interventional Clinical Research Ethics Committee (date: 28.01.2021, approval no.: 2021/28).

Informed Consent: All enrolled patients or their proxies provided written informed consent.

Footnotes

Author Contributions: Surgical and Medical Practices - S.S., P.D., T.E., S.Ş., M.D.Ş., B.D., P.Ö., H.Ö., A.D., F.T., D.K., M.K., İ.İ.; Concept - S.S., P.D., T.E., İ.İ., A.T.; Design - S.S., P.D., T.E., O.T., İ.İ., A.T.; Data Collection and/or/Processing - S.S., P.D., T.E., S.Ş., M.D.Ş., B.D., P.Ö., H.Ö., A.D., F.T., D.K., M.K.; Analysis and/or/Interpretation - S.S., P.D., T.E., M.S.İ.; Literature Review - S.S., P.D., T.E., S.Ş., M.D.Ş., B.D., P.Ö., H.Ö., A.D., M.S.İ., O.T., F.T., D.K., M.K., İ.İ., A.T.; Writing - S.S., P.D., T.E., S.Ş., M.D.Ş., B.D., P.Ö., H.Ö., A.D., M.S.İ., O.T., F.T., D.K., M.K., İ.İ., A.T.

Declaration of Interests: The authors declare no conflicts of interest.

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Endotracheal Tube Size Estimation in Paediatric Patients: A Head-to-head Comparison of Accuracy Between Ultrasonography and Age-based Formula

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Abstract

Objective: In the paediatric population, the selection of an appropriately sized endotracheal tube (ETT) is extremely important not only to ensure adequate ventilation but also to avoid post-extubation stridor and stenosis. Conventionally, formulas based on age, height, or weight are used to determine the most appropriate size. In this study, we compared ultrasonography (USG) and age-based formula for predicting the best microcuff ETT size in paediatric patients aged 1-5 years.

Methods: One hundred eighteen patients, aged 1 to 5 years, with American Society of Anesthesiologists, classifications of I or II, were included. After standard general anaesthesia protocols, the subglottic diameter was assessed by USG. Intubation was performed using ETT size according to age-based formula. The best clinical fit was determined after the leak test. The internal and external diameters of the ETTs were predicted by both methods and correlated with the best-fit ETT sizes used during the procedures using Pearson's correlation. Cohen's kappa was used for statistical agreement between two methods.

Results: USG had a significantly higher correlation with the best-fit model as compared to the age-based formula, with 99.2% and 77.1% agreement rates. The best-fit ETT showed a better correlation with the USG-guided estimate ($r = 0.994$, $P < 0.001$). The Cohen's Kappa value of 0.986 showed a statistically significantly higher agreement between USG-guided estimate and best-fit ETT.

Conclusion: USG-guided estimation of subglottic diameter is a better predictor for optimally sized microcuff ETT than the age-based formula in the paediatric age group of 1-5 years. 22% of tube changes could have been prevented with ultrasound-guidance as a primary approach for estimating ETT size.

Keywords: Airway management, cricoid cartilage, intubation, paediatric anaesthesia, ultrasonography

Main Points

- Our study aims to compare the effectiveness of ultrasonography (USG)-based estimation with age-based formula estimation for determining the appropriate endotracheal tube (ETT) size in children aged 1 to 5 years.
- The uniqueness of our study is a larger sample size, younger age group with a mean of 2.79±1.14 years, the use of USG measurement done after the paralytic agent and cessation of ventilation, and the use of a microcuff tube.
- 22% of ETT changes could have been prevented with ultrasound-guidance as a primary approach for estimating ETT size.

Introduction

General anaesthesia is the cornerstone of anaesthetic care for paediatric patients. Prior to performing tracheal intubation, it is essential to possess a thorough understanding of airway anatomy. Paediatric airway anatomy differs significantly from that of adults.[1] In paediatric anaesthesia, the use of precise endotracheal tube (ETT) size is extremely

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crucial for irst attempt success at intubation. Failure in selecting the appropriate ETT size can result in inadequate ventilation and the nability to maintain general inhalational anaesthesia.[2]

Recent evidence further suggests that, even though the microcuff tubes are marketed as safe, their cuff design may be associated with cuff-induced injury to the vocal cords.[3] If the ETT size is bigger, it can significantly cause friction and compression on the tracheal mucosa, leading to mucosal ischemia and airway edema. This insult can subsequently result in post-extubation complications, which can be subglottic stenosis or stridor.[4] Conversely, using an ETT that is too small can increase the flow resistance, leading to inadequate ventilation and to higher chances of aspiration.[5] Additionally, a leak from an undersized ETT can result in the release of anaesthetic gases into the environment.

To overcome these issues at both ends, various formulas were derived and studied to choose the perfect size of ETT based on age, weight, and height.[6-8] Age-based formulas derived by Cole[9] and Motoyama[10], which have been in clinical use for over half a century, calculate the internal diameter (ID) of the uncuffed tube.

However, it's important to note that the ETT dimensions vary over a wide range among the manufacturers. The ETT with the same ID can have different outer diameters (OD) depending on manufactures, potentially resulting in misleading calculations. None of these calculations demonstrate optimal effectiveness, and moreover, they may not be applicable to all ethnic populations worldwide.

The modernization of the healthcare system has led to the increasing popularity of ultrasonography (USG) in perioperative airway management. USG serves various purposes in airway management, such as identifying structures, ensuring proper positioning, and selecting the correct ETT size.[11,12]

Although previous studies have explored the feasibility of USG for assessing subglottic diameter as a predictor of ETT size, there are very few studies estimating the size of the microcuff tubes, which are now a standard of care in paediatric anaesthesia.[13] Therefore, we designed our study with the aim to compare USG-guided and age-based formula estimation of ETT size for paediatric patients and to assess if the USG method provides a better estimation. We have further studied the frequency of reintubations and the time taken by both methods.

Methods

After approval from the Bharati Vidyapeeth (Deemed to be University) Medical College, Institutional Research Ethics Committee (approval no.: BVDUMC/IEC/80, date: 12.08.2022), the Clinical Trials Registry-India (CTRI) registration (CTRI/2023/06/054327), and written informed consent from guardians, a prospective observational study was conducted in a tertiary care hospital. The inclusion criteria were 118 patients, posted for elective surgeries needing general anaesthesia, aged 1 to 5 years, with American Society of Anesthesiologists classifications of I or II.

Patients with pre-existing laryngeal or pharyngeal pathology, airway deformity, presence of a scar on the neck, ulcer or mass, upper respiratory tract infection were excluded.

The sample size was calculated with reference to Gehlaut et al.[14]

$$\text{Sample size (n)} = \frac{2z^2(1-\alpha/2)\times(S)^2}{d^2}$$

z (1-α/2) = 1.96 (standard normal value at 5% level of significance).

S = 0.781 pooled standard deviation (SD) value from previous reference study.

d = 0.2 allowable error (absolute precision).

As per standard protocols, all patients were nil per oral on the day of surgery. The standard anaesthesia workstation check protocol was followed before each anaesthetic to ensure safety and proper functioning of equipment.

The patient was then escorted to the operation theatre, where standard monitoring was initiated. This includes continuous monitoring of heart rate by electrocardiography, saturation level of oxygen by pulse oximetry, blood pressure by non-invasive blood pressure monitoring, temperature monitoring, as well as the end-tidal CO_2.

Standard general anaesthesia protocols were followed in all patients as follows:

- Premedication: Intravenous (IV) Inj. glycopyrrolate 4 μg kg^{-1} and midazolam 0.05 mg kg^{-1}
- Preinduction: Inj. fentanyl 2 μg kg^{-1} IV,

Patients were pre-oxygenated with 100% oxygen for a span of 3 minutes.

- Induction: Inj. propofol 2-2.5 mg kg^{-1} IV, titrated to effect.
- A loading dose of the neuromuscular blocking agent: Inj. atracurium 0.5 mg kg^{-1} intravenously was given for facilitating intubation. Ventilation was continued for another 4 minutes.

After giving muscle relaxant and before intubation, in sniffing position with continued mask ventilation, an ultrasound scan was done using a linear probe (6-13 Hz

frequency) to identify the level of cricoid cartilage. The ventilation was momentarily ceased, and the timer was started simultaneously until we obtained an optimal view at the level of cricoid (subglottic tracheal diameter). The screen was then frozen and ventilation resumed. The distance (air column width) was calculated on the "frozen" USG screen using the caliper function of the ultrasound machine. This diameter was used as a surrogate of the OD of the microcuff ETT. Figure 1, dotted line shows the OD. Now, the corresponding ID was determined from the diameters marked on the surface of the different microcuff tubes. With the OD by USG noted as 4.3, 5.0, 5.6, 6.3, 6.77 millimetres (mm) the corresponding ID as 3.0, 3.5, 4.0, 4.5, 5.0 was respectively noted.

In all patients, endotracheal intubations were performed with the micro-cuffed ETT of size, calculated by the age-based formula.

ID (mm) = 0.25×(age in years)+3.5

The time required for the calculation of the age-based formula was measured by starting the timer once the calculator was turned on and stopping it upon the completion of the calculation. The timer stopped following the last answer regarding the tube size.

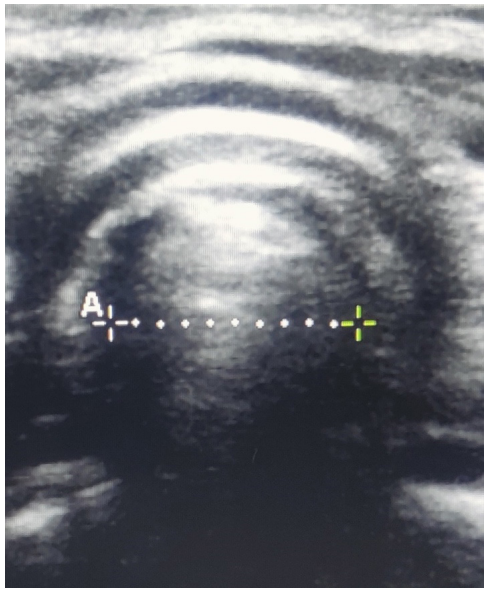

Figure 1. USG view of cricoid arch and air-column. Cricoid cartilage is a round hypoechoic structure with hyperechoic edges. The air column (dotted line) appeared hyperechoic and created a posterior acoustic shadow. The mucosa-air interface, a hypoechoic edge, was easily recognized. The dotted line represents the measured air-column width.

USG, ultrasonography.

The microcuff tubes used were from the same manufacturer (Halyard). Endotracheal intubations were then performed with the size determined by age-based formula; and after performing the leak test, the actual ETT used clinically was labeled as "best-fit" and noted.

The leak test technique was applied to determine the optimal size. This method uses leak pressure (LP) to determine the ideal ETT size for paediatric patients. LP, which is the pressure at which air escapes around the tube, was measured by placing a stethoscope over the suprasternal notch while monitoring the manometer on the ventilator to detect the pressure at which the leak was audible. The ETT size was considered optimal when the tracheal leak occurred at an inflation pressure between 10 and 25 cmH_2O. If no air leak was detected at airway pressures of 25 cmH_2O, tube was replaced with one that was 0.5 mm smaller. Conversely, if the leak was detected at a pressure lower than 10 cmH_2O, a 0.5 mm larger tube was selected.[15-17] Due to the use of a cuffed ETT, the LP measurement was evaluated prior to cuff inflation.

Statistical Analysis

The data for normally distributed continuous variables were presented as mean±SD, while categorical variables were expressed as frequencies n (% of cases). A paired t-test was applied to compare the means of the continuous variables (i.e., ETT sizes and time taken to calculate ETT size). Pearson's correlation was used for correlation analysis. The normality assumption was assessed before applying the t-test and Pearson's correlation analysis to the study variables. Cohen's Kappa is used for statistical agreement between two methods. To visualize the statistically significant difference more clearly, these results were shown in both tabular and graphical formats.

The complete study data were statistically analysed using the Statistical Package for Social Sciences (SPSS version 24.0, IBM Corp., Armonk, NY, USA) for Microsoft Windows. The p values <0.05 were considered to be statistically significant for the entire study.

Results

The total number of patients assessed for eligibility was 119; 1 patient was excluded because of an unanticipated difficult airway, and finally the study involved 118 paediatric patients aged 1-5 years and undergoing surgery under general anaesthesia, as demonstrated in Strobe's chart (Figure 2). The mean age of patients included was 2.74±1.37 years. 46.6% of patients were between the age of 1-2 years (55 patients) and 53.4% of patients were between age of 3-5 years (63 patients). They comprised 88 male and 30 female patients. Minimum weight of 8 kg and maximum of 22 kg with mean 12.15±2.94 kg. The mean weight for the age group of 1-2 years and 3-5 years was 10±1.5 kg and 13.98±2.63 kg, respectively.

The mean±SD of ETT size by best-fit and USG-guided method was 4.28±0.41 mm and 4.29±0.42 mm, respectively. For the age group of 1-2 years, the ETT size by best-fit and USG-guided method was 4.06±0.30 mm and 4.07±0.32 mm, respectively. On the other hand, for patients aged 3-5 years, the ETT size by both the best-fit and USG-guided method was 4.47±0.40 mm.

On a paired t-test, the mean best-fit ETT size did not differ significantly from the mean ETT by USG-guided method, ($p > 0.05$). The mean±SD of ETT size by best-fit and age-based estimation was 4.28±0.41 mm and 4.22±0.38 mm, respectively. In a paired t-test, the mean best-fit ETT size is significantly higher than the mean ETT size based on age estimation ($p < 0.05$). The mean percentage change or absolute deviation in ETT size by age-based estimation with reference to the best-fit ETT size was 2.88%. The mean percentage change or absolute deviation in ETT size by the USG-guided method compared to the best-fit ETT size was 0.094%. Table 1 shows the paired comparison of ETT size (ID) by different methods.

Out of 118 cases, 117 (99.2%) had a perfectly matched size, 1 (0.8%) had an overestimated size, and none underestimated the ETT size by the USG-guided method against the best-fit ETT size. Out of 118 cases, 91 (77.1%) had perfectly matched size, 8 (6.8%) had the overestimated size, and 19 (16.1%) had the underestimated ETT size by age-based estimation against the best-fit ETT size.

For 1-2 years, out of 55 cases, 54 (98.2%) had a perfectly matched size, 1 (0.8%) had an overestimated size, and none had underestimated the ETT size by the USG-guided method against the best-fit ETT size. On the other hand, 42 patients (80.7%) had a perfectly matched best-fit size, 4 (7.27%) had an overestimated size, and 9 (16.36%) had an underestimated ETT size by age-based estimation against the best-fit ETT size. Out of 63 patients aged 3-5 years, the ETT size determined by USG correlated 100%. While on other hand for age based estimation method only 54 patients (85%) had a perfect matched size with best-fit, 3 (4.7%) had an overestimated size and 6 (9.37%) had an underestimated the ETT size (Figure 3).

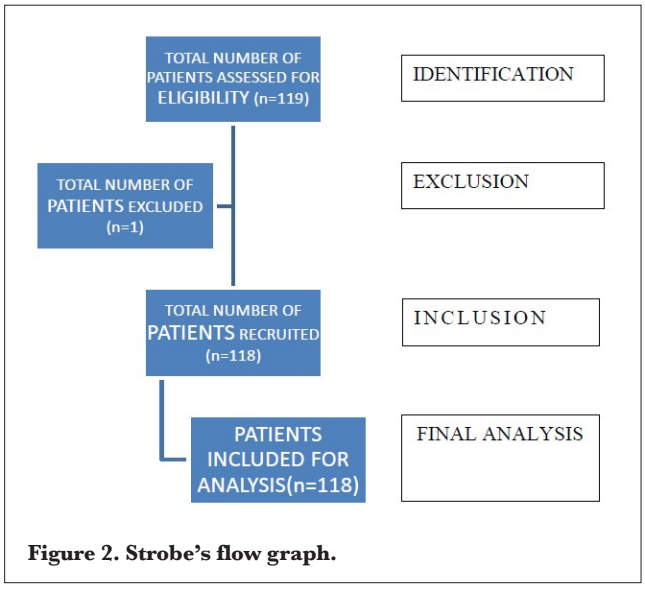

Figure 2. Strobe's flow graph.

Table 1. Paired Comparison of ETT Size (Inner Diameter) by Different Methods

	ETT size (mm)	
Method	Mean±SD	Median (Min.-Max.)
Best-fit	4.28±0.41	4.00 (3.5-5.0)
Age-based	4.22±0.38	4.00 (3.5-5.0)
USG-guided	4.29±0.42	4.00 (3.5-5.0)
Age based vs best-fit (% deviation)	2.88%	
USG guided vs best-fit (% deviation)	0.094%	
P value (Paired comparisons)		
Best-fit vs Age-based	0.019*	
Best-fit vs USG-based	0.319NS	

P value by paired t-test; $P < 0.05$ is considered to be statistically significant; *$P < 0.05$.

NS, statistically non-significant; USG, ultrasonography; ETT, endotracheal tube; SD, standard deviation; Min.-Max., minimum-maximum.

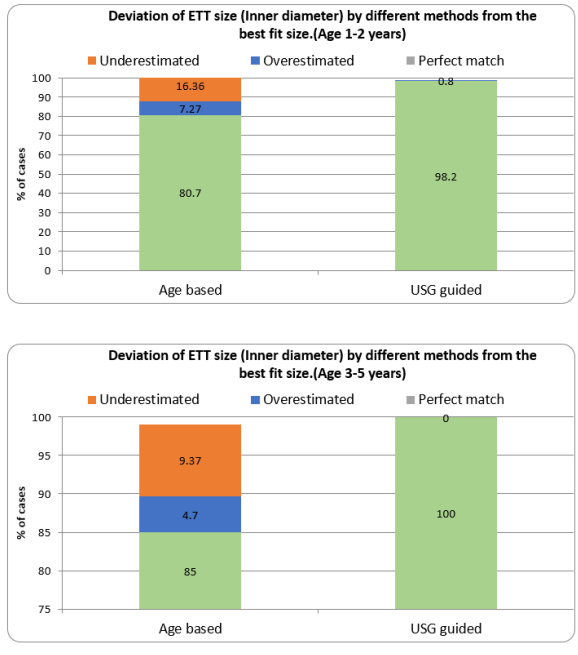

Figure 3. Deviation of ETT size by different methods from the best-fit size.

USG, ultrasonography; ETT, endotracheal tube.

The distribution of ETT size by USG-guided method is significantly associated with the best-fit ETT size ($p < 0.05$) with a Cohen's Kappa value of 0.986. There is a proven statistically significant and higher-to-perfect agreement with regard to USG-guided ETT size and the best-fit ETT size in our study group (Table 2). The distribution of ETT size by age-based and best-fit ETT shows statistically moderate agreement, indicated by a Cohen's Kappa value of 0.601 (Table 3).

As per Pearson's correlation analysis, ETT size by the USG-guided method showed a statistically strong positive correlation with the best-fit ETT size with correlation coefficient r = 0.994, ($p < 0.001$). On the contrary, ETT size by age-based estimation showed a statistically moderate correlation with the best-fit ETT size, with a correlation coefficient r = 0.772 ($p < 0.001$) (Figure 4a, b).

The mean±SD time taken to calculate ETT size by age-based estimation and USG-guided estimation was 6.63±0.98 seconds and 13.00±1.33 seconds, respectively. On a paired t-test, the mean time taken to calculate ETT size by the USG-guided method is significantly longer than the mean time taken to calculate ETT size by age-based estimation ($P < 0.05$). Out of 118 patients, 26 needed their ETT replaced, which accounts for 22% of the total participants.

Table 2. The Statistical Agreement Between ETT Size by USG Guided Method and Best-fit ETT Size

	ETT Size in mm (Best-fit)									
	3.5		4.0		4.5		5.0		Total	
ETT size in mm (USG guided)	n	%	n	%	n	%	n	%	n	%
3.5	5	100.0	0	0.0	0	0.0	0	0.0	5	4.2
4.0	0	0.0	62	100.0	0	0.0	0	0.0	62	52.5
4.5	0	0.0	0	0.0	29	96.7	0	0.0	29	24.6
5.0	0	0.0	0	0.0	1	3.3	21	100.0	22	18.6
Total	5	100.0	62	100.0	30	100.0	21	100.0	118	100.0
Cohen's Kappa value = 0.986, *P*=0.001***										

P value by chi-square test. Cohen's Kappa for statistical agreement between two methods. $P < 0.05$ is considered to be statistically significant. ***$P < 0.001$.
ETT, endotracheal tube; USG, ultrasonography.

Table 3. The Statistical Agreement Between ETT Size by Age-Based Estimation and Best-fit ETT Size

	ETT size in mm (Best-fit)									
	3.5		4.0		4.5		5.0		Total	
ETT size in mm (Age based)	n	%	n	%	n	%	n	%	n	%
3.5	1	20.0	0	0.0	0	0.0	0	0.0	1	0.8
4.0	4	80.0	60	96.8	14	46.7	3	14.3	81	68.6
4.5	0	0.0	2	3.2	14	46.7	2	9.5	18	15.3
5.0	0	0.0	0	0.0	2	6.6	16	76.2	18	15.3
Total	5	100.0	62	100.0	30	100.0	21	100.0	118	100.0
Cohen's Kappa value = 0.601, *P*=0.001***										

P value by chi-square test; Cohen's Kappa for statistical agreement between two methods. $P < 0.05$ is considered as statistically significant; ***$P < 0.001$.
ETT, endotracheal tube.

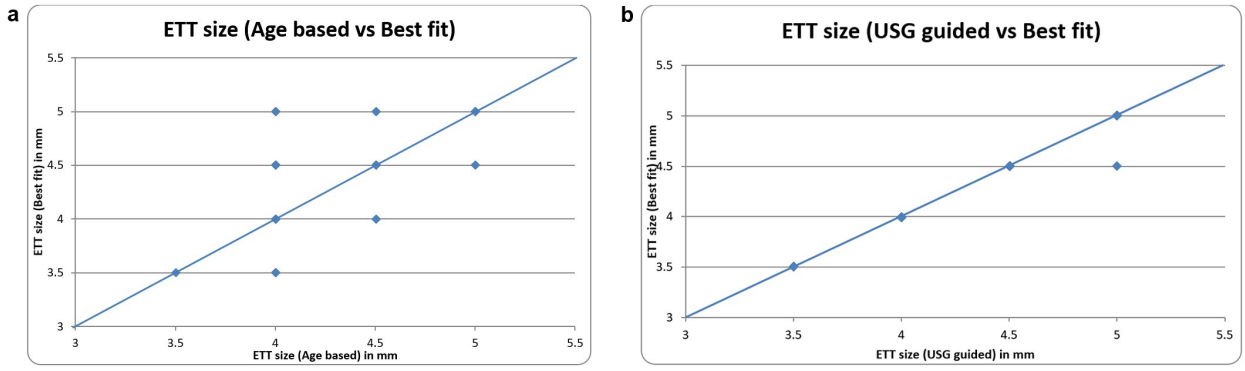

Figure 4. a) Scatter diagram showing correlation between ETT size (Inner diameter) by age-based estimation and best-fit ETT size. b) Scatter diagram showing correlation between ETT size (Inner diameter) by USG guided method and best-fit ETT size.

USG, ultrasonography; ETT, endotracheal tube.

Discussion

Securing the paediatric airway with an appropriately sized ETT is both extremely important and daunting. If the tube is oversized or the cuff overinflated, it may damage the tracheal mucosa, leading to airway oedema, post-extubation stridor, subglottic stenosis, or cartilaginous ischemia. On the other hand, if the tube is too small, it will increase the risk of aspiration, occlusion, increase the resistance to airflow, resulting in insufficient ventilation and make the monitoring of end tidal gases unreliable.[5] Moreover, the correlation between age, height, weight, body surface area, and tracheal shape or size is poor, and hence the formulae may not accurately estimate the tube size.[18]

The tube exchanges and repeated airway instrumentation result in subsequent oedema or trauma leading to complications and long-term sequelae in children, more clinically significant than in adults, which makes it even more pertinent to intubate them with the appropriately sized tube at the first attempt. A reliable way to estimate the variable is important. Ultrasound has proven to be a safe, reliable, non-invasive, and point-of-care method to assess the airway diameter. These attributes make it a feasible tool in the paediatric cohort.[12]

Similar to our study, Gupta et al.[5] in their study on 112 patients, in the age group of 3-18 years, have shown a higher correlation between clinically used ETTs and predetermined ETTs by USG than the predicted ETT by age and height-based formulas. They have further validated the reliability of an ultrasound for measuring the subglottic diameter and hence avoiding intubation-related complications.

Hatfield and Bodenham[19], in their report on the feasibility of USG in assessing the subglottic diameter, have shown a positive correlation between USG and magnetic resonance image measurements of the transverse subglottic diameter. Lakhal et al.[12] have also concluded that USG is a reliable, non-invasive, bedside tool in assessing the smallest transverse diameter of the cricoid lumen.

Laksono et al.[20], in their study on Indonesian paediatric patients, compared the accuracy of uncuffed ETT size estimation using USG, the body length formula, and the left-hand 5th fingernail width method, and observed that USG had the highest accuracy at 92%, while the body length formula had the lowest at 64% in estimating uncuffed ETT size. USG is seven times more likely to estimate the precise uncuffed ETT size than the body length formula and five times more likely than the left-hand 5th fingernail width.

Bae et al.[21] also concluded that ultrasound was a better means for estimating ETT size in paediatric patients than the age-based formula. Both these studies, however, estimated the accuracy in estimating the size of uncuffed ETT, whereas we have used microcuffed tubes in our study.

Umbarkar and Vaishnav[22] concluded that the rate of differences between ultrasonographically determined ETT size and correctly sized ETT with a maximum allowed deviation of ≤0.3 mm was 89.18% for uncuffed tubes and 86.95% for cuffed tubes. They further concluded that, as compared to physical indices-based formulae, the USG predicted the appropriate ETT size ($p < 0.05$) better for both cuffed and uncuffed tubes.

Similar to our study, Pillai et al.[23] in their study, observed that age-based formula showed poor correlation (27.5%) compared to ultrasound (87.8%) in predicting the best-fit ETT. They concluded that paediatric patients with congenital heart disease required a larger ETT as compared to that predicted by age-based formula, and ultrasound is

a safe and accurate method for estimating the best-fit ETT size in the paediatric cardiac population.

Similarly, Singh et al.[24] used Pearson's correlation and concluded that there was only a moderate correlation of the best-fit ETT with the estimated ETT size by age-based formula (r = 0.743), body length-based formula (r = 0.683), right little finger-based formula (r = 0.587), left little finger-based formula (r = 0.587) and multivariate formula (r = 0.741). However, the correlation of best-fit ETT with USG estimated ETT size was strong (r = 0.943). Similar to our study, all the radiological measurements in this study were performed by an experienced and trained anaesthesiologist.

In addition, we have also used other ways to prove the significance; 0.986 as the Cohen's Kappa value showed a statistically significant near perfect agreement between USG-guided ETT size and best-fit ETT size in the study group.

Recent studies by Gunjan et al.[25], Putra et al.[26], Ekor et al.[27], Gooty et al.[28], and Zengh et al.[29] have all concluded that USG, in addition to being safe and non-invasive, also offers greater accuracy in estimating the best-fit ETT as compared to the conventional methods.

The findings of Bae et al.[21] partly concur with those of our study. They assessed the usefulness of USG in determining uncuffed tracheal tube sizes for paediatric patients. They concluded that USG could provide a valuable alternative to the conventional age-based formula for selecting an appropriate ETT size in paediatric patients. However, despite the use of USG in their study, only 60% of cases achieved the correct tube size. The reason for this, according to the authors, could be the variations in the external diameter of tracheal tubes according to the manufacturer. In our study, we found that USG-guided ETT size has 99.2% agreement with the best-fit ETT. This difference could be attributable to the fact that in our study we exclusively used microcuffed tubes by the same manufacturer.[21]

In our study, we have further compared the time required for calculation of ETT size by age-based formula as well as by ultrasound. The time taken to calculate ETT by age-based formula was around 7 seconds, whereas with ultrasound it was around 14 seconds.

Though the time was less with the age-based formula, out of 118 patients, 26 patients needed the tube change after the first intubation. These 22% ETT changes would have been avoided if we had used USG guided method as our primary tool for ETT size estimation. This high incidence of tube exchange negates any advantage of faster calculation with the age-based formula. This finding is consistent with the results of Schramm et al.[30], who found that the initial choice of ETT was incorrect in 23 out of 50 patients (46%), requiring the insertion of an alternative tube. They concluded that USG aids in selecting the correct ETT size in paediatric patients and may help decrease the need for reintubations.[23,30]

Study Limitations

Our study has a few limitations. We included patients only from a single center, and larger, multicentric studies are recommended.

The cessation of ventilation is required for accurate calculation of ETT size in paediatric patients. However, the saturation was maintained in all patients and patients were ventilated soon after freezing the screen for further calculation. The avoidance of tube exchanges with ultrasonographic assessment is a definite advantage. Also, in our study, we have not included postoperative bronchoscopy to visualize if any anatomical injuries are caused due to a "non-fitting" ETT.

However, our study is unique in various aspects. We studied a larger sample size, and a younger age group of patients with a mean 2.79±1.14 years, using microcuff tube instead of uncuffed or regular cuffed tubes. Also, for avoiding miscalculation, USG measurement is done after paralytic agent and momentary cessation of ventilation. All the USG measurements and intubations were performed by an experienced anaesthesiologist trained in paediatric anaesthesia and ultrasonography. We have gone further ahead and compared the time required for calculating the best-fit ETT with an age-based formula and ultrasound which has important clinical implications in a paediatric patients. All these factors make our study stand out as compared to the previous studies.

Conclusion

To conclude, USG-guided subglottic diameter is a better predictor of the optimal size of the microcuff ETT than the age-based formula. USG has proved to be a non-invasive, safe, and reliable tool. We recommend the use of USG on a regular basis as a primary tool for ETT size determination in paediatric patients to avoid multiple laryngoscopies attempts and change of ETT.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Bharati Vidyapeeth (Deemed to be University) Medical College, Institutional Research Ethics Committee (approval no.: BVDUMC/IEC/80, date: 12.08.2022).

Informed Consent: Written informed consent was obtained from guardians.

Footnotes

Author Contributions: Surgical and Medical Practices - A.B., S.S., K.P.; Concept - A.B., S.S., K.P.; Design - A.B., S.S., K.P.; Data Collection or Processing - A.B., S.S., K.P.; Analysis or Interpretation - A.B., S.S., K.P.; Literature Search - A.B., S.S., K.P.; Writing - A.B., S.S., K.P.

Declaration of Interests: The authors declare no conflicts of interest.

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Case Report
Airway Management

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A Hybrid Technique Using Video Laryngoscope-assisted Flexible Bronchoscopy to Facilitate Endotracheal Intubation in Children with Anticipated Difficult Airway: A Case Series

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Abstract

We present a case series using a hybrid technique of video laryngoscope-assisted flexible bronchoscopy to facilitate endotracheal intubation in children with anticipated difficult airway. This series describes the management of difficult airways in four paediatric cases using the hybrid technique: two cases of Apert syndrome scheduled for cranial remodelling with orbito-facial advancement, one case of an incomplete cleft palate and retrognathia scheduled for palatoplasty, and another case of Parry Romberg syndrome scheduled for a reconstructive procedure. This case series aims to highlight the value of the hybrid technique as a safe and effective intubation modality in paediatric difficult airways.

Keywords: Difficult airway, intubation, video laryngoscope, flexible bronchoscope

Main Points

- The hybrid technique of intubation is an approach combining the advantages of a video laryngoscope and a flexible bronchoscope.
- The intubation is conducted by two anaesthesiologists: one inserts the video laryngoscope into the oral cavity, improving the visual field of the airway, and the other manipulates the endotracheal tube, loaded flexible bronchoscope through the vocal cords.
- It improves the success of tracheal intubation in children with difficult airways.

Introduction

A difficult airway can result in multiple intubation attempts, leading to airway trauma and hypoxia.[1] Apart from direct laryngoscopy, laryngoscope blades of alternative design and size, adjuncts, video laryngoscopes (VLS), flexible intubation scopes, supraglottic airway (SGA), optical stylets, or rigid bronchoscopes could be used.[2,3] Flexible bronchoscope-guided intubation is considered the gold standard for paediatric difficult airway, although manipulating the device may be difficult due to a smaller airway.[4]

We report a case series of four successful endotracheal intubations in children with difficult airways using VLS as a supplement for flexible bronchoscope navigation. This manuscript adheres to the Enhancing the Quality Transparency of Health Research guidelines. Written consent was obtained from the parents or legal guardians of all patients to publish their case details.

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Case Presentations

Case 1

An 8-month-old female infant, weighing 8 kg, with Apert syndrome was scheduled for cranial remodelling with orbitofrontal advancement. She had a cleft palate, flat occiput, midfacial hypoplasia, and orbital proptosis. Her airway examination using the Colorado Paediatric Airway Score was 12 (Table 1).[5] Computed tomography (CT) of the neck showed an anteriorly placed larynx, near the C1 vertebra, and a small mandibular space.

Table 1. Colorado Paediatric Airway Score (COPUR)

COPUR		Points
C: Chin		
From the side view, is the chin:		
• Normal size?		1
• Small, moderately hypoplastic?		2
• Markedly recessive?		3
• Extremely hypoplastic?		4
O: Opening		
Interdental distance between the front teeth:		
• 40 mm		1
• 20-40 mm		2
• 10-20 mm		3
• <10 mm		4
P: Previous intubations, obstructive sleep apnoea (OSA)		
• Previous intubations without difficulty		1
• No past intubations, no evidence of OSA		2
• Previous difficult intubations, or symptoms of OSA		3
• Difficult intubation-extreme or unsuccessful; emergency tracheotomy; unable to sleep supine		4
U: Uvula Mouth open, tongue out, observe palate		
• Tip of uvula visible		1
• Uvula partially visible		2
• Uvula concealed, soft palate visible		3
• Soft palate not visible at all		4
R: Range		
Observe line from ear to orbit, estimate range of movement, looking up and down		
• >120°		1
• 60°-120°		2
• 30°-60°		3
• <30°		4
Modifiers: add point for		
• Prominent front "buck" teeth		1
• Very large tongue, macroglossia		1
• Extreme obesity		1
• Mucopolysaccharidoses		2
Prediction points	**Intubation difficulty**	**Glottic view**
5-7	Easy, normal intubations	1
8-10	More difficult, laryngeal pressure may help	2
12	Difficult intubation, fibreoptic less traumatic	3
14	Difficult intubation, requires fibreoptic or other advanced methods	3
16	Dangerous airway, consider awake intubation, advanced methods, potential tracheotomy (Patients with hypercarbia	4
16+ scores	> 16 are usually incompatible with life without an artificial airway	

Intravenous (IV) dexmedetomidine infusion at 1 µg kg^{-1} hr^{-1}, glycopyrrolate at 10 µg kg^{-1}, and dexamethasone at 0.1 mg kg^{-1} were given, with intermittent IV ketamine at 0.5 mg kg^{-1} boluses. Nebulization along with superior laryngeal nerve and transtracheal blocks with 2% lignocaine was administered.

Oral intubation with the H-SteriScope, a paediatric flexible video bronchoscope (FOB) manufactured by Vathin Medical Instrument Co. Ltd, Hunan, China, with an outer diameter of 2.2 mm, was attempted alongside oxygen supplementation through nasal prongs to prevent desaturation. Owing to the narrow oral cavity, the FOB had little room, and intubation was unsuccessful. A second attempt was made with the McGrath MAC VLS (Aircraft Medical Ltd., Edinburgh, UK) with a size 1 blade. Due to the anterior larynx and inadequate angulation of the stylet or bougie, advancing the endotracheal tube (ETT) or bougie into the trachea was unsuccessful, despite a percentage of glottic opening score of 25% (Figure 1). The patient experienced a drop in saturation, and the attempt was abandoned, and the patient was ventilated.

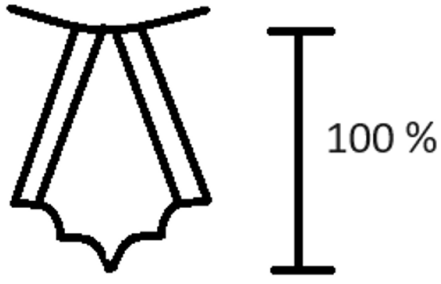

Figure 1. The percentage of glottic opening (POGO) score for laryngeal grading. The POGO score represents the linear span from the anterior commissure to the interartytenoid notch.

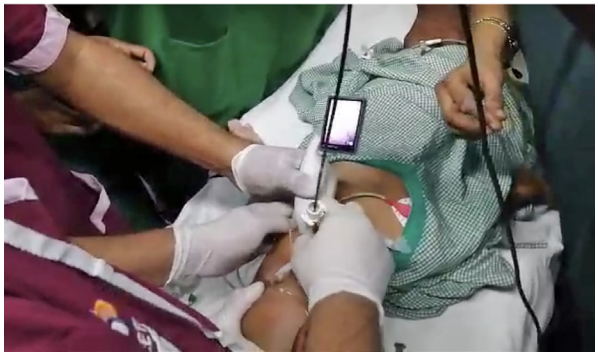

Figure 2. In first case with Apert syndrome a video laryngoscope is introduced into the oral cavity by one anaesthesiologist to improve visualisation of the airway and the second anaesthesiologist simultaneously manipulates the fibreoptic bronchoscope loaded with an endotracheal tube into the vocal cords.

Finally, FOB and VLS were used simultaneously by anaesthesiologists experienced in this technique. Intubation was conducted by two anaesthesiologists: one inserted the VLS into the oral cavity to improve the visual field of the airway, and the other manipulated the FOB (Figure 2). The tip of the bronchoscope, as visualised on the VLS, could be manoeuvred and passed through the vocal cords; followed by smooth insertion of the 3.5 mm ETT. After confirming adequate ventilation with capnography, the ETT was fixed.

IV fentanyl 2 µg kg^{-1} and atracurium 0.5 mg kg^{-1} were given. Anaesthesia was maintained with dexmedetomidine at 0.5 µg kg^{-1} hr^{-1}, and with isoflurane at 0.8-1.0 minimum alveolar concentration (MAC). After the procedure, the patient was shifted to the paediatric intensive care unit (PICU) and extubated the next day.

Case 2

A 9-year-old child, weighing 19 kg, with Parry Romberg syndrome comprising right progressive hemifacial atrophy with en coup de sabre deformity, was scheduled for free anterolateral thigh adipofascial flap. Difficult intubation was anticipated again as the COPUR score was 13. CT showed hypoplasia of the right mandible. After securing IV access, IV fentanyl 2 µg kg^{-1}, and propofol 2 mg kg^{-1} were administered. After confirming adequate mask ventilation, atracurium 0.5 mg kg^{-1} was administered. A C-MAC VLS (Karl Storz GmbH, Tuttlingen, Germany) with a Macintosh blade 2 was inserted. Following this H-SteriScope, a flexible

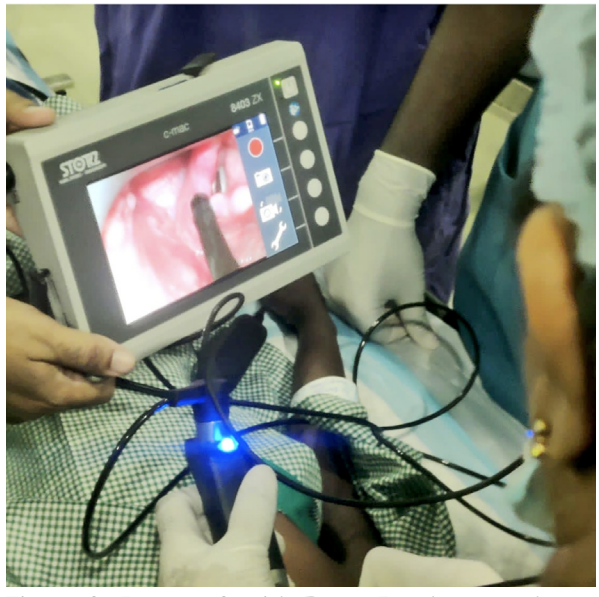

Figure 3. In case 2 with Parry Romberg syndrome the fibreoptic bronchoscope is manipulated into the vocal cords after visualization under the C-MAC video laryngoscope.

video bronchoscope, with an outer diameter of 3.2 mm, loaded with 5 mm cuffed armoured ETT, was passed under VLS guidance through the vocal cords and intubation was accomplished successfully in the first attempt (Figure 3). Upon completion of the surgery, the patient was shifted to the PICU and extubated the next day.

Case 3

A 1-year-old child, weighing 9 kg, with an incomplete cleft palate and retrognathia, was scheduled for palatoplasty. The patient had a history of difficult intubation. The COPUR score was 14. IV access was secured after inhalation induction with oxygen and sevoflurane. IV fentanyl, 2 µg kg^{-1}, and atracurium 0.5 mg kg^{-1} were administered after adequate mask ventilation. A McGrath MAC VLS with a size 1 blade was inserted, and the arytenoids were visualised. An H-SteriScope, a flexible bronchoscope with an outer diameter of 2.2 mm and loaded with a 3.5 mm cuffed armoured ETT, was passed, and the child was intubated without any complications. The child was extubated at the end of surgery.

Case 4

A 1-year-old child with Apert syndrome and craniosynostosis, weighing 7 kg, was scheduled for bilateral fronto-orbital advancement. The child had a cleft palate. The COPUR score was 13. CT neck showed an anteriorly placed larynx and a small mandibular space. After premedication with oral midazolam 0.5 mg kg^{-1}, inhalation induction was performed with oxygen and sevoflurane. Following IV cannulation, fentanyl 2 µg kg^{-1} and atracurium 0.5 mg kg^{-1} were administered after adequate mask ventilation. Following visualisation of the arytenoids using a McGrath MAC VLS with a size 1 blade, an H-SteriScope, a paediatric flexible bronchoscope with an outer diameter of 2.2 mm, loaded with a 3.5 mm cuffed armoured ETT, was passed. Anaesthesia was maintained with oxygen, air, and isoflurane, (MAC 0.8-1). The child was extubated on the table.

Discussion

Ours is a tertiary centre catering to all specialities, and our paediatric cases comprise primarily cleft repair or neurosurgical and abdominal cases. In a child with a difficult airway, alternative techniques are imperative to ensure successful intubation.[6] We ensured the availability of various sizes of Mackintosh and Miller laryngoscope blades, adjuncts like bougies and stylets, VLS with different sized blades, flexible bronchoscopes and invasive access. SGAs were available in all cases as a backup plan except the first case, where there was a leak in the size 1.5 ProSeal on the day of the procedure.

SGAs allow effective oxygenation and ventilation by relieving upper airway obstruction as they displace the tongue and the soft tissue of the posterior pharynx. SGAs can be used as the primary device in recognized difficult airways.[7] However, considering limited access in head and neck procedures or the duration of the case, we decided to intubate our patients.

Intubation through a SGA can be a suitable option in difficult airways by acting as a conduit for the FOB loaded with an ETT to pass through. While it restores the oxygenation and ventilation, it is important to avoid inadvertent extubation when removing the SGA, as the ETT may extend only a short distance beyond the distal tip of the SGA.[7]

VLS is associated with better glottic visualisation, higher success rate (92%), and a faster learning curve.[8] However, despite a good glottic view, it does not always aid in the easy passage of an ETT, as was the case in our first instance, due to the misalignment of the axes between the optical visualisation of the vocal cords and ETT introduction.[8] The failure rate of VLS is 2% as a primary technique and 8% as a rescue technique.[9]

Flexible bronchoscopy is the gold standard for elective difficult intubation.[10] It is associated with a higher success rate of intubation compared to VLS in patients with difficult airways.[11] On the downside, manipulating the device could be difficult due to the smaller airway in children, resulting in poor visualization.[4] H-SteriScope is a new single-use flexible video-bronchoscope (Vathin Medical Instrument Co. Ltd, Hunan, China), designed with outer diameters of 2.2-6.2 mm. Except for the 2.2 mm bronchoscope, the other bronchoscopes have a working channel with diameters ranging from 1.2-3.2 mm.[12]

We have described a hybrid technique using a VLS to assist in flexible bronchoscopy for endotracheal intubation. The VLS is inserted by one anaesthesiologist, who improves visualisation of the glottis, while the flexible bronchoscope with a mounted ETT is inserted orally and manipulated through the vocal cords by a second anaesthesiologist. In a simulated study, it was shown that a single anaesthesiologist can introduce the laryngoscope, which can be held in place by a second person without airway training.[13]

The hybrid technique showed a greater first-attempt intubation success rate in adult patients compared to either individual technique.[13,14] The hybrid technique would facilitate easier and quicker intubation, thereby minimizing episodes of desaturation. In our case series, we did not observe any significant oxygen desaturation or bradycardia events. By choosing this technique, we were able to intubate the children safely in a much shorter time, average 60 seconds. Proper communication between team members is of prime importance for this technique to be effective.

Since ventilation with face mask was adequate, we paralysed a few of our cases before attempting intubation. Due to unavailability of sugammadex in this part of the world at the time of conducting the cases and in order to avoid possible bradycardia with succinylcholine, we used atracurium. When available, rocuronium and sugammadex are better alternatives to succinylcholine and atracurium in patients with difficult airways.[15]

Conclusion

The hybrid technique of VLS-assisted flexible bronchoscopy facilitates safe and successful tracheal intubation in children with difficult airways, and can be used electively or as a rescue measure.

Ethics

Informed Consent: Written consent was obtained from the parents or legal guardians of all patients to publish their case details.

Footnotes

Author Contributions: Surgical and Medical Practices - K.G., R.J., P.K., V.S.G.Y.; Concept - K.G., P.K., V.S.G.Y.; Design - K.G., P.K., V.S.G.Y.; Data Collection and/or Processing - K.G., R.J.; Analysis and/or/ Interpretation - R.J.; Literature Review - R.J.; Writing - K.G., R.J., P.K., V.S.G.Y.

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Case Report
Perioperative Care

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Challenging Perioperative Management of a MEN2A Syndrome Patient Complicated by Eisenmenger Syndrome

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Abstract

Multiple endocrine neoplasia type 2A (MEN2A), is associated with pheochromocytoma and medullary carcinoma of the thyroid. A surgical procedure in these patients can be complicated if they have any congenital heart disease (CHD). Nowadays, CHD patients are increasingly presenting at advanced age for non-cardiac surgeries, posing unique challenges to anesthesiologists. We hereby present a 44-year-old male with Eisenmenger syndrome (ES) and MEN2A, scheduled for bilateral adrenal excision and thyroidectomy. Patients with ES require meticulous and goal-directed management during non-cardiac surgery, depending upon pulmonary hypertension, cyanosis, and right ventricular dysfunction.

Keywords: Cardiovascular and thoracic anaesthesia, Eisenmmenger syndrome, intensive care, MEN2A, perioperative care, pheochromacytoma

Main Points

- Optimal perioperative medical management is essential for hemodynamics and shunt management in Eisenmenger syndrome (ES) patients for non-cardiac surgery.
- Anemia correction in the postoperative period is essential in patients with ES as they require a relatively higher hemoglobin concentration than healthy adults to compensate for chronic hypoxemia.
- Point-of-care ultrasound, intermittent non-invasive ventilation, and awake proning are crucial in managing refractory hypoxemia in Eisenmenger patients for non-cardiac surgery.
- We aimed to share our perioperative experience of adult ES patients posted for two major non-cardiac surgeries in one sitting, together.

Introduction

Congenital heart disease (CHD) patients may develop Eisenmenger syndrome (ES) as age advances, which leads to an increase in perioperative complications when non-cardiac surgery is performed. The risks of surgery in patients with ES vary according to the nature, complexity, and urgency of the procedure (emergency cardiac surgery versus routine abdominal surgery versus dental procedures).[1] Ammash et al.[2] described 24 patients with ES who underwent 28 non-cardiac surgeries. They found that the perioperative mortality rate was 7%. Bennet et al.[1] examined a cohort of 33 patients with ES and reported systemic hypotension in 26%, oxygen desaturation in 17%, and 30-day mortality of 3.8%. We hereby present a clinical case of a patient with ES undergoing

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two major non-cardiac surgeries. The complete procedure was explained to the patient, and informed consent was obtained.

Case Report

A 44-year-old male with a body weight of 45 kg was posted for bilateral adrenal mass excision and total thyroidectomy. The patient had been diagnosed with CHD and pulmonary hypertension for 11 years. The echocardiogram revealed a large peri membranous ventricular septal defect (16 mm), with bidirectional shunting, dilated main pulmonary artery, and right pulmonary artery (RPA) thrombus with pulmonary artery hypertension (right ventricular systolic pressure of 136 mmHg). The high-resolution computed tomography (CT)-thorax of the patient showed a heterogeneous right pulmonary hilar mass and bilateral adrenal lesion (Figure 1a). The CT angio revealed a thrombus (large, eccentric) Figure 1b.

The patient was informed of his comorbid condition and associated high risk. The patient's metabolic equivalents (METs) were six, and the patient was kept on tab rivaroxaban 20 mg, tab tadalafil 20 mg tab ambrisentan 5 mg OD, tab prazosin 2.5 mg OD, and tab furosemide/amiloride (5/40). The anaesthetic plan included an epidural catheter at the T10-11 region and 0.5 mg of morphine in the epidural space. The patient underwent general anaesthesia with muscle relaxation. The patient had hemodynamic fluctuations during surgical manipulations of adrenal tumours, and they were managed by titration of infusion of injection (inj.) nitroglycerine [5-20 µg minimum (min)] initially followed by inj. nitroprusside (0.5-10 µg kg^{-1} min^{-1}), in the final stages of tumour excision. Following adrenalectomy of bilateral adrenal tumours, the patient had hypotension and a fall in oxygen saturation down to 80%. Noradrenaline infusion (0.01-0.3 µg kg^{-1} min^{-1}) was titrated to maintain hemodynamics, and an intravenous (IV) inj. of sildenafil 10 mg was given for oxygenation. Inj. hydrocortisone (200 mg 24 h) infusion was initiated after persistent hypotension following bilateral adrenalectomy, suspecting acute adrenocortical insufficiency as a cause and the fluid status was optimized. During thyroidectomy, the patient again had a fall in saturation. IV inj. sildenafil 10 mg was administered slowly, and saturation improved to 88-90%. After thyroidectomy surgery, the patient was transferred to the post-anaesthesia care unit.

The patient was extubated the day after surgery. Initially, the patient-maintained oxygen saturation (SpO_2) of around 88-90% on a face mask with slightly higher pCO_2, and normal lactates. Gradually, the patient showed progressive hypoxemia, and Intermittent non-invasive ventilation (NIV) was started. On POD-3, hypoxemia persisted with SpO_2 of 68-70% along with tachypnoea. The patient's hemoglobin was 7.5 g dL^{-1}, and a packed red blood cell (PRBC) transfusion was planned. The patient was kept on: tab tadalafil 20 mg, tab ambrisentan 5 mg OD, inj. unfractionated heparin (UFH) IV 5000 units TDS, and tab furosemide/amiloride (5/40).

A total of 4 PRBCs were transfused in 4 days. However, the patient's hypoxemia persisted, and intermittent NIV was continued. The NT pro-BNP levels were >10,000 pg mL^{-1}. Chest X-ray revealed basal atelectasis and blunting of costophrenic angles, Figure 1c. Point-of-care ultrasound (POCUS) revealed moderate pleural effusion on the right side with moderate ascites: Figure 1d. Inj. furosemide 40 mg BD was started for negative fluid balance, UFH was replaced with tab rivaroxaban 20 mg, and inj. albumin infusion of 40 g in 24 hours was initiated. For persistent hypoxemia, prone positioning and incentive spirometry were initiated (Figure 2a, 2b). The patient SpO_2 (80-85%) improved with the prone positioning. The patient's tachypnoea gradually settled and SpO_2 on nasal prongs returned to 88-90% at POD-15. POCUS revealed minimal right-sided pleural effusion. There were decreasing trends of NT pro-BNP levels (10,000 pg mL^{-1}, 5,500 pg mL^{-1}, 2,200 pg mL^{-1}, and 1,305 pg mL^{-1}). Gradually, the patient was weaned off oxygen support and transferred to the ward on room air.

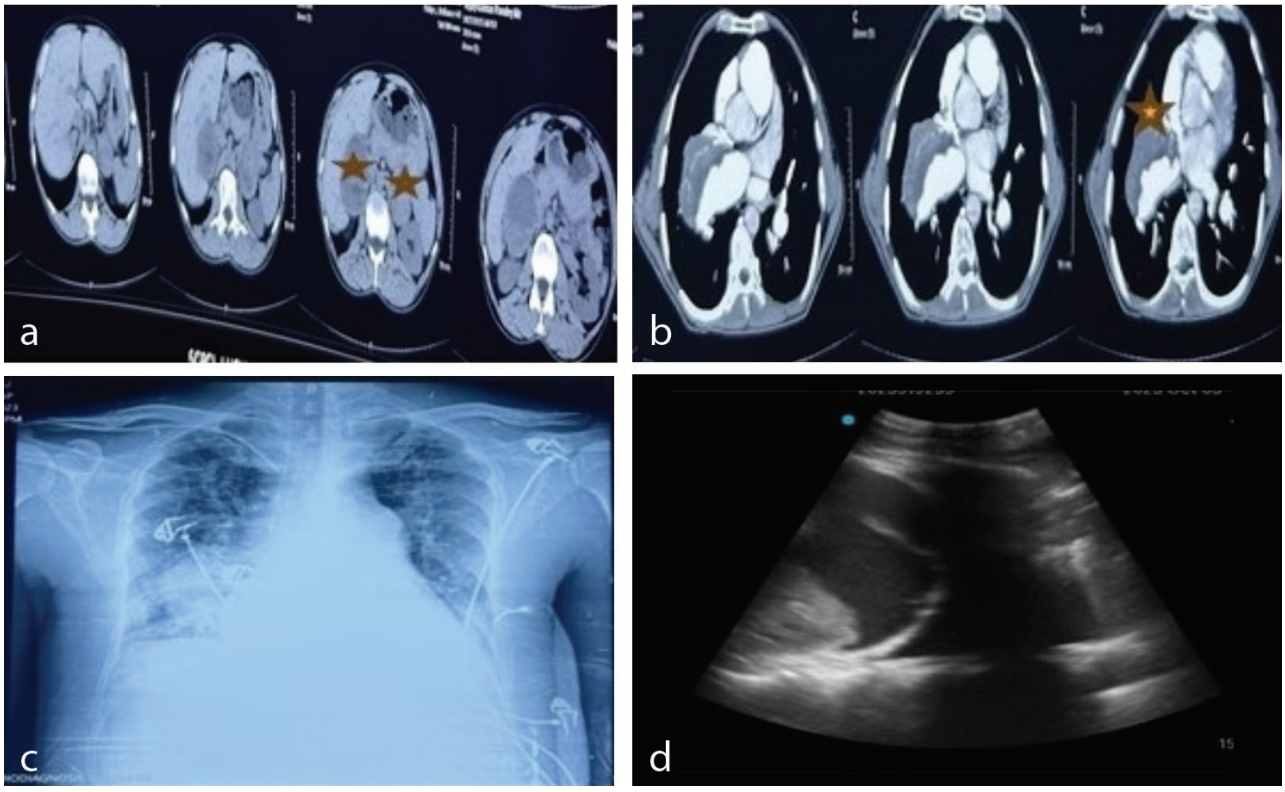

Figure 1. (a) Preoperative CT scan of the abdomen showing bilateral adrenal tumors (see star). (b) Preoperative CT Pulmonary Angio showing thrombus in the right pulmonary artery (see star). (c) Postoperative chest skiagram showing basal atelectasis and blunting of costophrenic angles. (d) POCUS lung showing pleural effusion.

CT, computed tomography; POCUS, point-of-care ultrasound.

Figure 2. (a) Patient undergoing prone ventilation. (b) Patient undergoing incentive spirometry while in prone position.

Discussion

Mortality with cyanotic heart disease or pulmonary arterial hypertension following non-cardiac surgery is around 7% to 10%.[2,3] In patients with ES, multiple organs are affected due to chronic cyanosis, collaterals, platelet dysfunction, and alterations in coagulation.[4] When METs are less than 4, it equates to an inability to climb two flights of stairs and is associated with a greater incidence of postoperative cardiac events.[5] The average peak VO_2 of a patient with ES is 11.5 mL kg^{-1} min^{-1}, which equates to less than 4 METs and indicates a higher risk.[6] Our patient has >6 METs; however, MET information is challenging to interpret in PAH-CHD patients who underplay their symptoms.

Maintenance of oxygenation with increased systemic vascular resistance via IV noradrenaline infusion was essential. Pulmonary vascular resistance is usually fixed in patients with shunt reversal; however, IV phosphodiesterase-5 (PDE-5) inhibitors have given us leverage, during the surgery to maintain acceptable saturation. PDE-5 inhibitors like tadalafil in patients with ES are well tolerated and significantly improve exercise capacity, functional class, systemic oxygen saturation, and pulmonary hemodynamics.[7] The endothelin receptor antagonist, ambrisentan, showed promising results in patients with Eisenmenger's in terms of 6-minute walking distance and a reduction in the pulmonary vascular resistance index and mean pulmonary artery pressure.[8]

Patients with ES have structural and functional changes in the pulmonary vessels attributed to the thrombotic phenomenon. These characteristic structural changes of pulmonary hypertension occur in the neo-muscularized small arteries and larger vessels, whereby they may dilate and become aneurysmal.[9]

The universal transfusion trigger is 8 g dL^{-1}; however, cyanotic patients have relative anemia. A total of 4 PRBCs were transfused to achieve hemoglobin of 12 g dL^{-1}, close to the pre-operative level of 14 g dL^{-1}. Patients with ES require a higher hemoglobin concentration than healthy adults to compensate for the chronic hypoxemia (secondary erythrocytosis).[6] However, when we searched the literature regarding transfusion trigger blood in ES, we found a paucity of descriptions of transfusion triggers in ES. The POCUS, indicated the pleural effusion and ascites, which are indicative of right-sided heart failure, so aggressive IV diuretic therapy, along with inj. albumin infusion (40 g in 24 hours) and inj. milrinone infusion (0.375-0.75 µg kg^{-1} min^{-1}) were initiated. NT pro-BNP levels are a sensitive indicator of RV dysfunction. Our diuretic therapy, PDE-5 inhibitors, and endothelin receptor antagonist therapy showed reduced trends in NT pro-BNP levels.[10] During the entire perioperative course, lactate and carbon dioxide pressure was within the normal range, which could be attributed to our vigilant monitoring and guided clinical actions. Our patient's refractory hypoxemia was the biggest hurdle to recovery. In such circumstances, ventilation in the prone position induces alveolar recruitment and reduces the right ventricle afterload.[11]

Conclusion

The adult ES patient can be successfully managed with meticulous planning, optimal perioperative management of shunt function, correction of relative anemia, and planned ventilatory strategies.

Ethics

Informed Consent: The complete procedure was explained to the patient, and informed consent was obtained.

Footnotes

Author Contributions: Surgical and Medical Practices - A.R., G.A., A.K., P.D., S.S.; Concept - A.R., G.A., A.K., P.D., S.S.; Design - A.R., P.D.; Data Collection and/or Processing - A.R., P.D.; Analysis and/or/ Interpretation - A.R., G.A, P.D.; Literature Review - A.R., G.A, P.D.; Writing - A.R., G.A.

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