www.myja.pub

Volume 3 . Issue 1 . 2024

MALAYSIAN JOURNAL OF ANAESTHESIOLOGY

THE OFFICIAL JOURNAL OF

Malaysian Society of Anaesthesiologists

College of Anaesthesiologists, AMM

New guideline

on the **Peri-operative management** of **neuromuscular blockade (NMB)**

Images are for illustrative purposes only.

SCAN to VIEW the ESAIC 2022 Guidelines Paper

The **European Society of Anaesthesiology and Intensive Care** (ESAIC) published their 1st guideline on the perioperative management of neuromuscular blockade, on November 16th 2022.[1]

Recent data indicated a high incidence of inappropriate management of neuromuscular block (NMB), with a high rate of residual paralysis and relaxant-associated postoperative complications. Therefore, the ESAIC presented an evidence-based set of practice guidelines for the perioperative management of NMB.[1]

To facilitate its implementation in current clinical practice, the guidance focuses on

3 clinically relevant core issues[1]:

01 significance of neuromuscular blocking agents for tracheal intubation.

02 contribution of neuromuscular blocking agents to improve surgical conditions.

03 significance of neuromuscular monitoring (NMM) and pharmacological reversal to reduce residual paralysis and postoperative pulmonary complications (POPCs).

8 recommendations from **ESAIC[1]:**

R1	Recommends using a muscle relaxant to facilitate tracheal intubation (1A).
R2	Recommends the use of muscle relaxants to reduce pharyngeal and/or laryngeal injury following endotracheal intubation (1C).
R3	Recommends the use of a fast-acting muscle relaxant for rapid sequence induction intubation (RSII) such as succinylcholine 1mg kg^{-1} or rocuronium 0.9 to 1.2mg kg^{-1} (1B).
R4	Recommends deepening neuromuscular blockade if surgical conditions need to be improved (1B).
R5	There is insufficient evidence to recommend deep neuromuscular blockade in general to reduce postoperative pain or decrease the incidence of peri-operative complications (2C).
R6	Recommends the use of ulnar nerve stimulation and quantitative neuromuscular monitoring at the adductor pollicis muscle to exclude residual paralysis (1B).
R7	Recommends using sugammadex to antagonise deep and moderate neuromuscular blockade induced by aminosteroidal agents (rocuronium, vecuronium) (1A).*
R8	Recommends advanced spontaneous recovery (i.e. TOF ratio >0.2) before starting neostigmine-based reversal and to continue quantitative monitoring of neuromuscular blockade until a TOF ratio of more than 0.9 has been attained (1C).

*disclaimer-part of recommendations are modified to remove the off-label content.

GRADE definitions

1A: Strong recommendation, high-quality evidence; 1B: Strong recommendation, moderate-quality evidence; 1C: Strong recommendation, low-quality evidence; 2C: Weak recommendation, low-quality evidence; TOF: Train of Four

Guidelines Conclusion

- There is documented evidence that residual paralysis and relaxation-associated pulmonary complications are less common after sugammadex-based pharmacological reversal than after neostigmine.[1]
- Reliable quantitative neuromuscular monitoring is the principal prerequisite of any appropriate strategy for peri-operative neuromuscular management, whether that is spontaneous recovery, sugammadex-based recovery or neostigmine-based recovery.[1]

Selected Safety Information for BRIDION® (Sugammadex Sodium)
INDICATIONS Reversal of neuromuscular blockade induced by rocuronium or vecuronium. For the pediatric population: sugammadex is only recommended for routine reversal of rocuronium induced blockade in children and adolescents. **DOSAGE AND METHOD OF USE** Sugammadex should only be administered by, or under the supervision of an anesthetist. Sugammadex should be administered intravenously as a single bolus injection. The bolus injection should be given rapidly, within 10 seconds, into an existing intravenous line. The recommended dose of sugammadex depends on the level of neuromuscular blockade to be reversed. **Adults** Routine reversal A dose of 4 mg/kg sugammadex is recommended if recovery has reached at least 1-2 post tetanic counts (PTC) following rocuronium or vecuronium induced blockade. Median time to recovery of the T_4/T_1 ratio to 0.9 is around 3 minutes. A dose of 2 mg/kg sugammadex is recommended, if spontaneous recovery has occurred up to at least the reappearance of T_2 following rocuronium or vecuronium induced blockade. Median time to recovery of the T_4/T_1 ratio to 0.9 is around 2 minutes. Immediate reversal of rocuronium-induced blockade A dose of 16 mg/kg sugammadex is recommended. Re-administration of sugammadex A repeat dose of 4 mg/kg sugammadex is recommended. **Renal impairment** For mild and moderate renal impairment (creatinine clearance ≥30 and <80 ml/min), the dose recommendations are the same as for adults without renal impairment. For patients with severe renal impairment (including patients requiring dialysis (CrCl <30 ml/min)), the use of sugammadex is not recommended. Elderly patients Same dose recommendation as for adults should be followed. Obese patients In obese patients, including morbidly obese patients, the dose of sugammadex should be based on actual body weight. The same dose recommendations as for adults should be followed. **Hepatic impairment** For mild to moderate hepatic impairment, no dose adjustments are required. **Pediatric populations (Children and adolescents)** Bridion 100 mg/ml may be diluted to 10 mg/ml to increase the accuracy of dosing in the pediatric population. Routine reversal A dose of 2 mg/kg is recommended for reversal of rocuronium induced blockade at reappearance of T_2 in children and adolescents (2-17 years). Immediate reversal Immediate reversal in children and adolescents has not been investigated. **CONTRAINDICATIONS** Hypersensitivity to the active substance or to any of the excipients. **WARNINGS AND PRECAUTIONS** Should neuromuscular blockade reoccur following extubation, adequate ventilation should be provided. Bleeding risk has not been studied systematically at higher doses than sugammadex 4 mg/kg, thus, coagulation parameters should be carefully monitored in patients with known coagulopathies and those using anticoagulants who receive a dose of 16 mg/kg sugammadex. The use of lower than recommended doses may lead to an increased risk of recurrence of neuromuscular blockade after initial reversal and is not recommended. When rocuronium 1.2 mg/kg is administered within 30 minutes after reversal with sugammadex, the onset of neuromuscular blockade may be delayed up to approximately 4 minutes and the duration of neuromuscular blockade may be shortened up to approximately 15 minutes. Recommended waiting time in patients with mild or moderate renal impairment for re-use of 0.6 mg/kg rocuronium or 0.1 mg/kg vecuronium after routine reversal with sugammadex should be 24 hours. A nonsteroidal neuromuscular blocking agent should be used for patients requiring neuromuscular blockade prior to passing the recommended waiting time. Sugammadex is not recommended for use in patients with severe renal impairment, including those requiring dialysis. Due to the administration of sugammadex, certain medicinal products could become less effective due to a lowering of the (free) plasma concentrations. Due to the administration of certain medicinal products after sugammadex, theoretically rocuronium or vecuronium could be displaced from sugammadex. Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade. Patients with severe hepatic impairment should be treated with great caution. Sugammadex should not be used to reverse block induced by nonsteroidal neuromuscular blocking agents and steroidal neuromuscular blocking agents other than rocuronium or vecuronium. Clinicians should be prepared for the possibility of drug hypersensitivity reactions (including anaphylactic reactions) and take the necessary precautions. If more than 2.4 ml solution needs to be administered, this should be taken into consideration by patients on a controlled sodium diet. **PREGNANCY AND LACTATION** Pregnancy Caution should be exercised when administering sugammadex to pregnant women. Lactation Caution should be exercised when administering sugammadex to a breast-feeding woman. **ADVERSE EVENTS** In the subset of Pooled Placebo-controlled trials where subjects received anesthesia and/or neuromuscular blocking agents, the following adverse events occurred in ≥ 2% of subjects treated with sugammadex and at least twice as often compared to placebo including airway complication of anesthesia, anesthetic complication, procedural hypotension, procedural complication and cough. In post-marketing, isolated cases of marked bradycardia and bradycardia with cardiac arrest have been observed within minutes after administration of sugammadex. A limited database suggests that the safety profile of sugammadex (up to 4 mg/kg) in pediatric patients was similar to that in adults.

Reference: 1. Fuchs-Buder T, Romero CS, Lewald H, et al. Perioperative management of neuromuscular blockade: A guideline from the European Society of Anaesthesiology and Intensive Care. EurJ Anaesthesiol. 2022 Nov 16. doi: 10.1097/EJA.0000000000001769. Epub ahead of print.

Before administering Bridion®, please read the full prescribing information

SCAN TO DOWNLOAD THE FULL PRESCRIBING INFORMATION at https://quest3plus.bpfk.gov.my/pmo2/index.php

Merck Sharp & Dohme (Malaysia) Sdn. Bhd.
B-22-1 & B-22-2, The Ascent Paradigm, No. 1, Jalan SS 7/26A, Kelana Jaya, 47301, Petaling Jaya, Selangor Darul Ehsan.
Tel: +603 7499 1600 Fax: +603 7499 1700 www.msd-malaysia.com
Copyright © 2024 Merck & Co., Inc., Rahway, NJ, USA and its affiliates.
All rights reserved. MY-XBR-00442 Jun/2024

MSD

Malaysian Journal of Anaesthesiology

Focus and Scope

Malaysian Journal of Anaesthesiology (MyJA) is an official journal of the Malaysian Society of Anaesthesiologists and College of Anaesthesiologists, Academy of Medicine Malaysia. MyJA is an English-language, peer-reviewed journal that publishes articles in the fields of anaesthesiology, critical care, and pain medicine.

MyJA aims to provide a platform for anaesthesiologists, clinicians, researchers, and trainees in Malaysia to publish high-quality clinical and scientific materials on all aspects of anaesthesiology, critical care, and pain medicine. It also welcomes submissions from researchers all over the world. In addition to publishing original articles (clinical trials, experimental research, meta-analysis, and systematic reviews), MyJA also features reviews, case reports and case series, and letters to the editor. The primary considerations for publication are clarity, uniqueness, scientific rigor, and advancement in design, performance, and knowledge.

I: www.myja.pub
E: myja@myja.pub

International ISSN
Online: 2949-7789
Print: 2772-9524

Malaysian ISSN
Online: 2948-4480

Publisher
Kugler Publications
P.O. Box 20538
1001 NM Amsterdam
The Netherlands
info@kuglerpublications.com
www.kuglerpublications.com
Published for Malaysian Society of Anaesthesiologists and College of Anaesthesiologists.

Manuscript submissions
Author guidelines are available *www.myja.pub*, through which all manuscripts should be submitted. For inquiries, please contact us via *myja@myja.pub*.

Publication frequency
MyJA is primarily an online journal that publishes two digital issues per year; print editions may be published, but not periodically.

Advertising inquiries
MyJA offers online and in print sponsorship and advertising opportunities. Please contact Kugler Publications for inquiries.

Cover image
Dr. Haslan Ghazali

Publication Frequency
MyJA is primarily an online journal that publishes two digital issues per year; print editions may be published, but not periodically.

Open Access Policy
In the interest of disseminating scientific research, MyJA is a fully open-access journal that does not require registration to access articles. However, registration is encouraged for readers to receive notifications about journal content. There is currently no charge for submitting, processing, and publishing articles.

Copyright
Authors who publish in MyJA agree to the following terms:
a. Authors retain copyright and grant the journal MyJA right of first publication, with the work twelve (12) months after publication simultaneously licensed under a Creative Commons Attribution License that allows others to share the work with an acknowledgement of the work's authorship and initial publication in MyJA.
b. After 12 months from the date of publication, authors are able to enter into separate, additional contractual arrangements for the non-exclusive distribution of MyJA's published version of the work, with an acknowledgement of its initial publication in MyJA.

Article Referencing
As a member of Crossref, MyJA references articles by DOIs included in the first page header of each article, *i.e.*, https://doi.org/10.35119/myja.v1i1.1. Please use DOIs when referencing MyJA articles.

Disclaimer
All published articles, including editorials and letters, represent the opinions of the authors and do not reflect the official policy of MyJA, its sponsors, the publisher, or the institution with which the author is affiliated, unless this is clearly specified. Although every effort has been made to ensure the technical accuracy of the contents of MyJA, no responsibility for errors or omissions is accepted. MyJA and the publisher do not endorse or guarantee, directly or indirectly, the quality or efficacy of any product or service described in advertisements or other material that is commercial in nature in any issue. All advertising is expected to conform to ethical and medical standards. No responsibility is assumed by MyJA or the publisher for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein. Because of rapid advances in the medical sciences, independent verification of diagnoses and drug dosages should be made.

Editorial Board

Chief Editor
Prof. Dr. Ina Ismiarti Shariffuddin

Deputy Chief Editors
Prof. Dr. Azrina Md Ralib
Dr. Shahridan Mohd Fathil

Section Editors

Airway
Assoc. Prof. Dr. Muhammad Maaya
Assoc. Prof Dr. Rhendra Hardy Mohd Zaini

Critical Care
Dr. Wan Fadzlina Wan Muhd Shukeri
Prof. Dr. Rafidah Atan

Cardiothoracic Anaesthesia
Assoc. Prof. Dr. Noorjahan Haneem Md Hashim
Dato' Dr. Yong Chow Yen

General Anaesthesia
Assoc Prof. Dr. Azarinah Izaham
Assoc. Prof. Dato' Dr. Wan Rahiza Wan Mat
Assoc. Prof. Dr. Loh Pui San

Neuroanaesthesia
Dr. Jeyaganesh Veerakumaran
Assoc. Prof. Dr. Wan Mohd Nazaruddin Wan Hassan

Obstetric Anaesthesia
Dr Carolyn Yim Chue Wai
Dr. Lee Meng-Li

Paediatric Anaesthesia
Assoc. Prof. Dr. Chaw Sook Hui
Assoc. Prof. Dr. Rufinah Teo

Pain Medicine
Prof. Dr. Marzida Mansor
Dr. Ahmad Afifi Mohd Arshad

Regional Anaesthesia
Dr. Beh Zhi Yuen
Dr. Lim Siu Min

Statistical Editors

Dr. Abqariyah Yahya
Dr. Edre Mohamad Aidid

Journal Manager

Dr. Ngoi Soo Tein

Technical Reviewer

Miss Foong Yi Xian

Advisory Board

Anaesthesia
Prof. Dr. Chan Yoo Kuen

Critical Care
Prof. Dato' Dr. Mohd Basri Mat Nor

Pain Medicine
Dr. Mary Suma Cardosa

International Editorial Board

Prof. Dr. Michael G. Irwin
Prof. Dr. Manoj Karmakar
Prof. Dr. Pankaj Kundra
Prof. Dr. Nuala Lucas
Assoc. Prof. Dr. Rob McDougall
Prof. Dr. John Pickering
Prof. Deepak Sharma
Prof. Dr. Kim Tae-Yop
Prof. Dr. André van Zundert

Sponsors

Malaysian Society of Anaesthesiologists

Malaysian Society
of Anaesthesiologists

College of Anaesthesiologists

College of
Anaesthesiologists, AMM

Table of contents

Editorial

Original articles

Review articles

Case series

Case reports

© Malaysian Journal of Anaesthesiology 2024; 3:7-10
Editorial
https://doi.org/10.35119/myja.v3i1.72

Our choices in the face of genocide: resistance or collaboration†

Shahridan **Mohd Fathil**[1]*, Ina Ismiarti **Shariffuddin**[2]

[1]Gleneagles Hospital Medini Johor, Johor, Malaysia; [2]Department of Anaesthesiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

> "Medicine is a social science, and politics is nothing more than medicine *on a grand scale."*
> *Rudolph Virchow*

On October 7, 2023, Hamas fighters broke out of Gaza and launched an attack into Israel. The final death toll stood at 1,139, including 695 civilians.[1] Shortly after, the United Nations (UN) Secretary-General, António Guterres, in his address to the Security Council stated, "It is important to also recognize the attacks by Hamas did not happen in a vacuum. The Palestinian people have been subjected to 56 years of suffocating occupation".[2] Israel claiming the right to self-defence has waged a brutal war on Gaza. As of May 17, 2024, the Israel-Hamas war has claimed the lives of 34,844 Palestinians, of which 52% were women and children.[3]

†The views and opinions expressed in editorials are solely those of the authors and do not necessarily reflect the official policy or position of the Editorial Board, sponsoring societies, sponsors/advertisers, or publisher.

*Dr Shahridan has recently volunteered in Gaza with Mercy Malaysia under the World Health Organization Emergency Medical Team initiative.

Correspondence: Ina Ismiarti Shariffuddin, Consultant Anaesthesiologist, Department of Anaesthesiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.
E-mail: ismiarti@ummc.edu.my

On January 26, 2024, the International Court of Justice (ICJ), the principal judicial body of the UN has ruled that Israel was committing plausible genocide in Gaza.[4] This was followed by an ICJ order on May 24, 2024 for Israel to halt its ground invasion in Rafah, the most southern part of the strip, which was designated before as a "safe zone" by the Israelis.[5] The top prosecutor of the International Criminal Court (ICC) on May 20, 2024 sought arrest warrants for the Israeli Prime Minister and Defence Minister, and 3 top Hamas leaders for war crimes and crimes against humanity. [6] The ICC is a body independent of the UN, with jurisdiction over crimes of genocide, crimes against humanity, war crimes and crimes of aggression.

The healthcare system in Gaza has been systematically dismantled by the conflict.[7] Only 10 out of 36 hospitals remain somewhat functional.[8] Hospitals, health units, and ambulances have been severely damaged and destroyed by heavy bombardment, resulting in the deaths of numerous healthcare professionals. The right of patients to receive safe treatment has been denied. Many civilians, especially children and women, have suffered, undergoing surgery without anaesthesia or analgesia due to a lack of medication and equipment. Medication supplies into Gaza were restricted by the Israelis.[9] Since the start of the war, 493 healthcare workers have been killed, and another 214 detained.[10] This has worsened the availability of treatment due to a shortage of doctors and nurses.

Editors of leading medical journals have demanded an immediate resolution and an end of the violence in Palestine.[11,12] The editors of the Journal of the American Medical Association (JAMA) emphasised in their reply to a call for content moderation in response to 2 JAMA Viewpoint articles on the Gazan conflict that they will continue to publish on the health consequences of war.[13]

There is no doubt that this is a humanitarian disaster and the world must declare that enough is enough, and this must end. As doctors, we have made a solemn commitment to restore health and preserve the sanctity of life, particularly at its most vulnerable stages. In the face of the humanitarian catastrophe in Gaza, we as healers, drawing on our conscience, must choose on how to respond. The options are resistance or collaboration. Collaboration with oppression manifests in many ways, from indifference to subtle or obvious support. The only ethical stand for doctors is to advocate for a permanent ceasefire, an immediate cessation of ethnic cleansing in Palestine, and the end of the Zionist colonialism that perpetuates a continuous and intermittent cycle of violence. The editors of MyJA contend that, as a professional fraternity, we have a duty to exert our influence on the issue of attacks on hospitals and healthcare workers, and the obstruction of safe anaesthesia care in conflict zones.

Medicine on a grand scale is politics.

References

1. Agence France Press. Israel social security data reveals true picture of Oct 7 deaths. 2023. [Available from: https://www.france24.com/en/live-news/20231215-israel-social-security-data-reveals-true-picture-of-oct-7-deaths
2. António Guterres. Secretary-General's remarks to the Security Council - on the Middle East 2023. [Available from: https://www.un.org/sg/en/content/sg/speeches/2023-10-24/secretary-generals-remarks-the-security-council-the-middle-east%C2%A0#:~:text=I%20respectfully%20note%20the%20presence,56%20years%20of%20suffocating%20occupation
3. Overton I. Gaza War: UN revises death toll for women and children. 2024. [Available from: https://aoav.org.uk/2024/gaza-war-un-revises-death-toll-for-women-and-children/
4. International Court of Justice. Application of the Convention on the Prevention and Punishment of the Crime of Genocide in the Gaza Strip (South Africa v. Israel). 2024. [Available from: https://www.icj-cij.org/sites/default/files/case-related/192/192-20240126-ord-01-00-en.pdf
5. International Court of Justice. Application of the Convention on the Prevention and Punishment of the Crime of Genocide in the Gaza Strip (South Africa v. Israel): The Court reaffirms its previous provisional measures and indicates new measures (No. 2024/47). 2024. [Available from: https://www.icj-cij.org/sites/default/files/case-related/192/192-20240524-pre-01-00-en.pdf
6. International Criminal Court. Statement of ICC Prosecutor Karim A.A. Khan KC: Applications for arrest warrants in the situation in the State of Palestine. 2024. [Available from: https://www.icc-cpi.int/news/statement-icc-prosecutor-karim-aa-khan-kc-applications-arrest-warrants-situation-state
7. United Nations. Gaza: 'Systematic dismantling of healthcare must end' says WHO. 2024. [Available from: https://news.un.org/en/story/2024/04/1148316
8. World Health Organization. Six months of war leave Al-Shifa hospital in ruins, WHO mission reports. 2024. [Available from: https://www.who.int/news/item/06-04-2024-six-months-of-war-leave-al-shifa-hospital-in-ruins--who-mission-reports
9. Beaumont P. Medical crisis in Gaza hospitals at 'unimaginable' level, aid agencies say. 2024. [Available from: https://www.theguardian.com/world/2024/mar/25/gaza-medical-crisis-hospitals-aid-agencies
10. United Nations. UN expert horrified by death of Gazan orthopedic surgeon in Israeli detention. 2024. [Available from: https://www.ohchr.org/en/press-releases/2024/05/un-expert-horrified-death-gazan-orthopedic-surgeon-israeli-detention
11. Smith J, Kwong EJL, Hanbali L, Hafez S, Neilson A, Khoury R. Violence in Palestine demands immediate resolution of its settler colonial root causes. BMJ Global Health. 2023;8(10):e014269. https://doi.org/10.1136/bmjgh-2023-014269

12. Buss P, Alcázar S, Souza LE. End the violence and help the victims in Gaza. Lancet. 2023;402(10413):1622-1623. https://doi.org/10.1016/s0140-6736(23)02362-0
13. Curfman G, Bibbins-Domingo K. Reporting on Health and War in Medical Journals. JAMA. 2024;331(16):1368. https://doi.org/10.1001/jama.2024.5476

© Malaysian Journal of Anaesthesiology 2024; 3:11
Editorial

Reviewer Acknowledgement June 2024

The Editorial Board of Malaysian Journal of Anaesthesiology gratefully acknowledges the following individuals for reviewing the papers submitted for publication:

1. Dato Professor Dr Wang Chew Yin
2. Professor Dr Abdul Hadi Mohamed
3. Professor Dr Grace Herbosa
4. Associate Professor Dr Farida Ithnin
5. Associate Professor Dr Mohd Zulfakar Mazlan
6. Dr Aliza Mohamad Yusof
7. Dr Hasmizy Muhammad
8. Dr Iskandar Khalid
9. Dr Mohd Afiq Syahmi bin Ramli
10. Dr Muhamad Rasydan Abd Ghani
11. Dr Sanah Mohtar

© Malaysian Journal of Anaesthesiology 2024; 3:12-24
Original article
https://doi.org/10.35119/myja.v3i1.58

Comparative study on efficacy of ultrasound-guided supraclavicular versus costoclavicular brachial plexus block in patients for arteriovenous fistula surgery

Rhendra Hardy **Mohamad Zaini**[1,2], Nurul Izzati **Mohd Noor**[1,2], Sanihah **Che Omar**[1,2], Praveena **Seevaunnamtum**[1,2], Nurul 'Aifaa **Mohd Azmi**[1,2]

[1]Department of Anesthesiology and Intensive Care, School of Medical Sciences, Health Campus, University Sains Malaysia, Kubang Kerian, Kelantan, Malaysia; [2]Hospital Universiti Sains Malaysia, Health Campus, University Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Abstract

Background: Patients with end-stage renal failure (ESRF) who require arteriovenous fistula (AVF) creation often have multiple comorbidities, making the brachial plexus block a suitable choice for anaesthesia. The objective of this study is to compare the efficacy of ultrasound-guided supraclavicular and costoclavicular brachial plexus blocks for AVF creation.

Methods: A total of 70 patients scheduled for the creation of AVF in the distal upper extremity were randomly assigned to 2 groups: supraclavicular block (SCB), Group A: *n* = 35, and costoclavicular block (CCB), Group B: *n* = 35. Both groups received 20 ml of 0.5% ropivacaine and 10 ml of 1% lidocaine. The measured parameters included the speed of onset of motor and sensory blockade, the quality of blockade, procedural-related pain score, patient satisfaction, and regional perfusion.

Correspondence: Dr Sanihah Binti Che Omar MD (UNIMAS) MMED (USM), Department of Anesthesiology and Intensive Care, School of Medical Sciences, University Sains Malaysia, Jalan Raja Perempuan Zainab II, Kubang Kerian, 16150 Kota Bharu, Kelantan, Malaysia.
E-mail: sanihah_che@usm.my

Results: The costoclavicular block demonstrated a significantly faster onset to achieve complete paralysis ($p = 0.01$) in all sensory and motor nerves compared to the supraclavicular block. Additionally, there was a significant difference in regional perfusion, with higher perfusion observed in the supraclavicular block ($p = 0.013$). However, there were no significant differences in the quality of block ($p = 0.573$), and procedural-related pain score ($p = 0.117$) between the 2 groups.

Conclusion: The costoclavicular block offers a faster onset of sensory and motor blockade compared to the supraclavicular block. However, they are comparable in terms of the quality of the block and procedural-related pain. This new technique can be considered as an alternative for providing anaesthesia in patients with ESRF undergoing AVF creation.

Keywords: arteriovenous fistula, brachial plexus, ultrasound-guided supraclavicular block, ultrasound-guided costoclavicular block

Introduction

The global incidence of end-stage renal failure (ESRF) is increasing. The preferred procedure for patients with ESRF undergoing maintenance haemodialysis (HD) is the placement of an arteriovenous fistula (AVF). Patients with ESRF might encounter severe complications that represent a great challenge to the anaesthesiologists, such as congestive heart failure, systemic hypertension, electrolyte imbalances, metabolic acidosis, coagulopathy, and unpredictable intravascular fluid volume status. These issues require anaesthesiologists to steer clear of general anaesthesia and explore alternative methods.[1,2]

In patients with ESRF, brachial plexus block (BPB) is frequently employed to administer anaesthesia for the establishment or modification of AVF. This technique offers pain relief, sympathetic blockade, ideal surgical conditions, and a sufficient duration of postoperative block, preventing arterial spasms and graft thrombosis.[2] Several methods are available for BPB, including axillary, supraclavicular, and infraclavicular approaches. These procedures have historically been performed using blind techniques or neurostimulation. However, these methods are associated with a high failure rate and serious complications.

The utilization of ultrasonography has become increasingly popular and more convenient. Its application in these blocks enhances the success rate and reduces

complications significantly.[3] Ultrasound-guided BPB improves the visualization of nerve bundles, enables real-time assessment of needle placement, helps in avoiding crucial structures such as blood vessels and pleura, and promotes the even spread of local anaesthetic along the targeted nerves. Incorporating this non-invasive technology for nerve blocks has substantially increased the success rate of the procedure and enhanced its safety. Additionally, the precise localisation and direct visualisation of nerves using ultrasound have led to a reduction in the total volume of drugs required.

Supraclavicular and costoclavicular BPB offer anaesthesia and pain relief to the upper extremities below the shoulder. These techniques are particularly suitable for surgeries involving the elbow and hand. Supraclavicular BPB is often referred to as the spinal anaesthesia of the upper extremities due to its rapid onset of blockade. However, it carries a higher incidence of complications. Common risks and complications associated with this technique include phrenic nerve block leading to diaphragmatic paralysis and sympathetic nerve block resulting in Horner's syndrome. Fortunately, these complications are usually self-limiting. More serious complications, such as intravascular injection causing systemic local anaesthetic toxicity, haematoma formation, and pneumothorax, can also occur. The use of ultrasound guidance can help reduce the risk of these complications.[3,4]

Costoclavicular BPB is a recently developed technique for infraclavicular BPB, introduced by Karmakar *et al.*[5] With the ultrasound-guided costoclavicular approach, all 3 cords of the brachial plexus are clearly visible in a single plane. These cords are relatively superficial and are clustered together lateral to the axillary artery within the costoclavicular space, forming a triangular arrangement.[6,7] In this space, the cords are positioned more superficially compared to the classical approach in the lateral infraclavicular fossa. They are clustered together yet maintain a consistent anatomical relationship with each other.[8] This results in a rapid onset of BPB similar to the supraclavicular approach, but with superior surgical effectiveness and fewer adverse events.

Methods

This study was a prospective, double-blinded, randomised-controlled trial conducted in the operation theatre, Hospital Universiti Sains Malaysia from November 2020 to October 2021. After receiving approval from the Human Research Ethics Committee at Universiti Sains Malaysia (USM/JEPeM/20120629) and written informed consent from the patients, 70 elective patients scheduled for creation of AVF in the distal upper extremity were recruited. The inclusion criteria were

American Society of Anesthesiologists (ASA) classification I–III and patient age ranging between 18 and 60 years old. The exclusion criteria included allergies to local anaesthetic drugs, pregnancy, prior history of brachial plexus injury, underlying coagulopathy, local infection at the block area, and neuropathy in the involved arm.

Patients were randomly assigned to 2 groups (Group A, $n = 35$, ultrasound-guided supraclavicular block; Group B, $n = 35$, ultrasound-guided costoclavicular block) using computer-generated numbers. The randomisation sequence was kept confidential in an opaque envelope until it was opened on the morning of the surgery by the anaesthesiology officer in charge.

A pre-anaesthetic evaluation was conducted before the scheduled surgery, and all patients fasted for at least 6 hours prior to the procedure. No premedication was administered to the patients. All patients in the study were undergoing chronic haemodialysis, with a session completed 1 day before the block procedure. Their routine preoperative laboratory investigations showed within acceptable values, particularly with urea levels less than 25 mg/dl. Both the patients and the assessor were unaware of the type of block being performed. The primary researcher served as the sole operator for the block, and the sealed envelope containing the group allocation was opened by an anaesthesiology officer responsible for the operating theatre (OT). The operator, a registrar in anaesthesiology training, had received hands-on workshops in peripheral nerve block and was trained and supervised in performing ultrasound-guided supraclavicular BPB on 15 patients before the research study. All nerve blocks were performed in the regional block bay within the OT.

Upon arriving at the regional block bay, an intravenous (IV) catheter was inserted using a 20-G or 18-G needle in the upper limb opposite to the surgical site. Haemodynamic parameters, such as non-invasive blood pressure, heart rate, oxygen saturation, and electrocardiography, were recorded for all patients. All patients were administered supplemental oxygen at a rate of 3 L/min through a nasal prong. Conscious sedation was adjusted with intermittent boluses of IV fentanyl (25 µg) and IV midazolam (1 mg) as necessary. The block was performed with the patient in the supine position, and the head was turned contralaterally away from the side where the block was administered. The supraclavicular and costoclavicular areas were prepared using an aseptic technique and draped. The skin was infiltrated with 2% lignocaine using a 22-G needle before introduction of the needle for the block.

Both ultrasound-guided approaches utilized a portable ultrasound machine, specifically the Wisonic Clover ultrasound (Clover, Wisonic, Shenzhen, China). A 22-gauge, 50–80 mm nerve stimulator needle model (B. Braun Medical Inc.,

Germany) was used for all participants. A depth of 3–4 cm and a frequency of 10–12 Hz were employed. In both groups, the local anaesthetic (LA) solution comprised 20 ml of 0.5% ropivacaine and 10 ml of 1% lidocaine, resulting in a total injected volume of 30 ml. The solution, a mixture of ropivacaine and lidocaine, was similar to that described by Oh *et al.*[1] and was administered incrementally with repeated aspiration in between, and its characteristic distribution around the nerves was observed.

In the supraclavicular group, the ultrasound probe was positioned in the supraclavicular fossa, directed caudal, and moved laterally and medially to locate the subclavian artery. The hyperechoic first rib was identified beneath the artery, and the pleura was visualised, observing its sliding movement during respiration. The brachial plexus was consistently identified with a characteristic "honeycomb" appearance, located laterally and superficially to the subclavian artery and superior to the first rib. After strict aseptic precautions and skin infiltration, the nerve block needle was inserted through the skin from lateral to medial, in line with the transducer, while maintaining constant visualization, and directed toward the deep border of the nerve group. Two separate injections were administered at various sites within the bundle, typically starting deep in the "corner pocket" near the artery and moving more superficially.

In the costoclavicular group, the patient's arm was abducted to 90° with flexion of the elbow, bringing the artery and plexus closer to the skin. The anatomical points were then identified and marked on the skin: clavicle, midpoint of the clavicle, and the tip of the coracoid process.[5] The coracoid process was identified by palpating the bony prominence just medial to the shoulder while the arm was elevated and lowered. Scanning began with the transducer positioned directly over the clavicle midsection in the transverse orientation. The transducer was gently moved caudally until it sliped off the inferior border of clavicle, revealing the visualisation of the axillary artery (first part) and vein.[6] While keeping the transducer in the same position, it was gently tilted cephalad to aim the ultrasound beam towards the costoclavicular space, which denotes the area between the posterior surface of the clavicle and the second rib.[6] The ultrasound image was optimised until all 3 cords of the brachial plexus were clearly visualized lateral to the axillary artery. After strict aseptic precautions and skin infiltration, the nerve block needle was inserted in-plane and from a lateral-to-medial direction. Our goal was to position the needle tip precisely at the centre of the nerve cluster by advancing the needle through the space between the lateral and posterior cord and advancing it toward the medial cord. A total volume of 20 mL of 0.5% ropivacaine and 10 ml of 1% lidocaine was injected in small aliquots and at a single site over 2 to 3 minutes.

The primary outcome measure for assessing the speed of onset was the

proportion of patients experiencing complete sensory and motor blockade at 30 minutes after the local anaesthetic (LA) injection. Sensory blockade of the 4 nerves was assessed every 5 minutes until 30 minutes post-injection by double-blinded observers using a 3-point scale (0 = no block, 1 = partial anaesthesia, 2 = complete anaesthesia). Similarly, motor block was evaluated and graded on a 3-point scale (0 = no block, 1 = paresis, 2 = paralysis). Overall sensory and motor scores were calculated for each patient at predefined intervals. To standardize the assessment, complete sensory or motor blockade was defined as a score equal to or greater than 7 points. The onset times were defined as the intervals measured when complete sensory or motor blockade was achieved.

Sensory blockade was assessed in the cutaneous distribution of each nerve using a cold test at specific locations: the lateral forearm for the musculocutaneous nerve (MCN), the palmar aspect of the second finger for the median nerve (MN), the dorsum of the hand between the thumb and second finger for the radial nerve (RN), and the ventral side of the fifth finger for the ulnar nerve (UN). Motor blockade of each nerve was evaluated by specific movements: elbow flexion for MCN, wrist flexion and opposition of the second and third fingers and the thumb for MN, wrist extension for RN, and flexion and opposition of the fifth finger toward the thumb for UN.

The quality of the block was determined based on the successful achievement of blockade within 30 minutes after needle withdrawal. Surgical anaesthesia, characterised by painless surgery without the need for block supplementation, and patient satisfaction were assessed using a procedural-related pain score. Pain scores were evaluated using a numerical rating scale ranging from 0 to 10 and documented. To assess regional perfusion and sympatholytic effects, the diameter of the basilic vein was measured using colour Doppler Wisonic Clover ultrasound before and 30 minutes after the administration of the local anaesthetic for the regional block.[9] Any changes in the vein diameter were recorded. The examination site was designated 1 cm proximal to the radial-ulnar styloid process to maintain consistency across all measurements. Vessels were imaged using a colour duplex Doppler ultrasound equipped with a 6–12 MHz linear array probe. To ensure reliability, multiple ultrasonography examinations were performed. Three images were obtained once the cross-sectional area of blood flow was confirmed. Subsequently, the results from the 3 measurements were compared. The incidence of pneumothorax, Horner syndrome, and hemidiaphragmatic paralysis were also documented. After the block procedure, patients were transported to the OT for surgery. Surgery began only if the block was deemed adequate. Block failure was defined as the need for an additional block, sedation, or general anaesthesia. After completion of the surgery, patients were transferred to the post-anaesthesia care unit (PACU) for observation.

Table 1. Patient demographic and clinical characteristics

Variable	Supraclavicular	Costoclavicular	p[a]
Age*	52.55 ± 13.11	49.35 ± 13.76	0.335
Weight*	63.70 ± 10.20)	67.06 ± 10.23	0.183[c]
Height*	159.70 ± 6.70	158.38 ± 5.94	0.408[c]
BMI*	24.96 ± (3.91)	26.74 ± (4.34)	0.082[c]
ASA[†]			
I –II	31 (93.9%)	29 (85.3%)	0.427[b]
III	2 (6.1%)	5 (14.7%)	
Gender[†]			
Male	16 (48.5%)	18 (52.9%)	0.715
Female	17 (51.5%)	16 (47.1%)	
Comorbidities[†]			
Diabetes mellitus			
Yes	26 (78.8%)	22 (64.7%)	0.201
No	7 (21.2%)	12 (35.3%)	
Hypertension			
Yes	27 (81.8)	28 (82.4)	0.954
No	6 (18.2)	6 (17.6)	
Hyperlipidaemia			
Yes	2 (6.1%)	7 (20.6%)	0.081
No	31 (93.9%)	27 (79.4%)	
Vital signs*			
SBP	155.30 ± 23.19	148.41 ± 20.75	0.204[c]
DBP	84.0 ± 13.11	79.26 ± 10.67	0.111[c]
HR	77.00 ± 16.35	81.26 ± 9.50	0.195[c]
SpO2	99.12 ± 1.36	99.3 ± 0.83	0.603[c]
Type of AVF[†]			
Radiocephalic	21 (48.8%)	22 (51.2%)	
Brachiocephalic	12 (50%)	12 (50%)	

*Reported as mean ± SD; [†]Reported as *n* (%); [a]Chi-square test; [b]Fisher exact test; [c]Independent t-test

Table 2. Onset of sensory blockade

Nerve	Costoclavicular		Supraclavicular		*p**
	Median	IQR (min)	Median	IQR (min)	
Musculocutaneous	10	5	15	10	< 0.001
Median	10	10	15	6	< 0.001
Radial	10	5	15	6	< 0.001
Ulnar	10	10	20	5	< 0.001
Sensory nerve set	10	5	15	5	< 0.001

*Mann-Whitney U test

Table 3. Onset of motor blockade

Nerve	Costoclavicular		Supraclavicular		*p**
	Median	IQR (min)	Median	IQR (min)	
Musculocutaneous	10	5	15	10	< 0.001
Median	10	10	15	10	< 0.001
Radial	10	5	15	10	0.01
Ulnar	10	5	15	5	0.012
Sensory nerve set	10	5	15	10	0.01

IQR: interquartile range
*Mann-Whitney U test

Table 4. Quality of blockade

Variable	Block	Supraclavicular		Costoclavicular		*p**
		n	%	n	%	
Quality of block	Complete	32	97.0%	32	94.1%	0.573
	Partial	1	3.0%	2	5.9%	

*Fisher exact test

Table 5. Procedural related pain score

Variable	Supraclavicular		Costoclavicular		*p*
	Mean/Median	(SD/IQR)	Mean/Median	(SD/IQR)	
Pain score	1.0	0.00	1.00	1.00	0.177

The sample size was calculated using G* power version 3.1 based on a previous study by Shyam Meena *et al.*[10] that indicated the percentage of visibility in the controls (P0) of 0.4, the percentage of visibility in the experimental group (P1) of 0.8, the power of 0.8, and the type I error of 0.05. The sample size was 32 patients in each group, and, after we considered 10% drop-out, the total sample for both groups was 70 patients. In this analysis, all categorical data are presented in frequency and percentage, while the numerical data are presented in mean and standard deviation or median and interquartile range based on their normality. The normality was tested using Kolmogorov-Smirnova test. We applied Chi-square, Fisher's exact test, independent T-test and Mann-Whitney U-test accordingly in the analysis. A p level of less than 0.05 was considered statistically significant. Statistical analysis was performed using version 26 of the SPSS software (IBM, Armonk, NY, USA).

Results

A total of 70 patients were initially enrolled in this study, with 35 patients assigned to each group. However, there were failed blocks observed in 2 patients in Group A (supraclavicular) and 1 patient in Group B (costoclavicular). Consequently, these 3 patients were excluded from the study. The final analysis included 67 patients, with 33 in Group A and 34 in Group B.

In terms of patient demographic data, no significant associations or mean differences were found between the supraclavicular and costoclavicular block groups regarding variables such as age, gender, ASA classification, weight, and height (Table 1). However, for the speed of onset of sensory blockade, it was observed that all sensory nerves of the costoclavicular block achieved complete anaesthesia significantly faster than those in the supraclavicular block group (10 ± 5 vs 15 ± 10; $p < 0.001$; Table 2). Similarly, for the speed of onset of motor blockade, it was found that all motor nerves of the costoclavicular block achieved complete paralysis significantly faster than those in the supraclavicular block group (10 ± 5 vs 15 ± 10; $p = 0.01$; Table 3).

The study revealed no significant association between the quality of block (complete anaesthesia without supplementation) in both types of anaesthesia blocks, with a rate of 97% in the supraclavicular block group compared to 94% in the costoclavicular block group ($p = 0.573$; Table 4). Patient satisfaction was assessed by procedural related pain score; there was no significant difference in the procedure-related pain scores between the 2 groups (1 ± 0 vs 1 ± 1; $p = 0.117$; Table 5). In this study, no incidence of pneumothorax, Horner syndrome, or hemidiaphragmatic paralysis was documented in either group.

Discussion

Our study found that ultrasound-guided costoclavicular block is superior to the conventional supraclavicular block in terms of the speed of motor and sensory onset. Additionally, both costoclavicular and supraclavicular approaches to the brachial plexus were found to be comparable in providing excellent blockade quality, procedure-related pain scores, and patient satisfaction. To the best of our knowledge, there has been no previous comparison between these 2 types of BPB (supraclavicular vs costoclavicular) for AVF creation. Nevertheless, we have compared our results with previous studies on both these nerve blocks.

The costoclavicular space was clearly visualized as a distinct intermuscular area situated deep to the midpoint of the clavicle posteriorly. The cords of the brachial plexus were observed as hypoechoic clusters, displaying a consistent anatomical arrangement in relation to each other and to the axillary artery. These findings are in line with the study conducted by Demondion *et al.*[10] This consistent anatomical arrangement of the brachial plexus could account for the high success rate of this approach.

In a study conducted by Li *et al.*[7], the ultrasound-guided costoclavicular BPB was successfully performed on 30 patients using 20 ml of 0.5% ropivacaine injection. This technique resulted in a rapid onset of sensory-motor blockade, with a median time to readiness for surgery of 10 minutes (ranging from 5 to 20 minutes). It proved to be effective as surgical anaesthesia in 97% of the patients. A more recent study by Koscielniak-Nielsen *et al.*[12] compared ultrasound-guided supraclavicular and infraclavicular blocks for upper extremity surgery in 120 patients. Their findings indicated that the infraclavicular block had a faster onset, better motor block, and higher surgical effectiveness, attributed to improved analgesia of the median and UN. After 30 minutes, 93% of patients in the infraclavicular group were ready for surgery compared to 78% in the supraclavicular group. The authors speculated that the lesser efficacy of the supraclavicular block in their patients might be due to parts of the plexus not being visualized and thus not surrounded by the local anaesthetic. In our study, we observed that the onset of sensory and motor blockade was significantly faster in the costoclavicular group compared to the supraclavicular group. Specifically, all sensory nerves (MCN, MN, RN, and UN) of the costoclavicular block achieved complete anaesthesia significantly faster (10 ± 5 vs 15 ± 10; $p < 0.001$), and all motor nerves of the costoclavicular block achieved complete paralysis significantly faster as well (10 ± 5 vs 15 ± 10; $p = 0.01$).

Royse *et al.* reported that they might have missed anatomical variations of the inferior trunk in up to 15% of the volunteers.[13] This could explain the poorer analgesia of the UN and MN, which originate from this cord, in supraclavicular group

patients. Similar to our findings, UN sparing was noted in the supraclavicular BPB, leading to a slower onset of blockade.

A more recent study by Yang *et al.*[14] compared infraclavicular and supraclavicular approaches to the brachial plexus using neurostimulation in 100 patients. They found no significant differences in the level of patient satisfaction between the 2 groups. The authors concluded that both the supraclavicular and infraclavicular approaches to the brachial plexus had similar clinical efficacy. Consistent with our study, we also found no significant association between the quality of the block and different types of anaesthesia block, with a success rate of 97% in the supraclavicular group and 94% in the costoclavicular group ($p = 0.573$).

Concerning block-related pain, the infraclavicular block has historically faced challenges due to uncertain surface landmarks and the perception that it is a more painful procedure,[7] which has been mitigated by the current use of ultrasound guidance. The reliability of ultrasonic landmarks has contributed to minimizing patient discomfort. In our study, the procedure-related pain scores for the supraclavicular block did not significantly differ from those for the costoclavicular block (1 ± 0 vs 1 ± 1; $p = 0.117$). This finding aligns with the results reported by Arcand *et al.*,[15] where the pain scores were (2.0 ± 2) and (2.0 ± 2) for the infraclavicular group and the supraclavicular group, respectively.

Sahin *et al.*[16] reported an increase in brachial artery diameter, blood flow, and AVF blood flow after BPB compared with controls. In our study, both the supraclavicular block and costoclavicular block exhibited a sympatholytic-like effect and an increase in regional perfusion. However, the supraclavicular block demonstrated higher perfusion (0.48 ± 0.19 vs 0.47 ± 0.13; $p = 0.013$).

Conclusion

Based on our study findings, it is clear that both the costoclavicular and supraclavicular approaches to the brachial plexus have demonstrated comparable efficacy in providing excellent blockade quality, procedure-related pain scores, and patient satisfaction. Therefore, we confidently conclude that the costoclavicular BPB can serve as a viable alternative technique to the supraclavicular approach for providing surgical anaesthesia in patients with chronic renal failure undergoing the creation of AVF in the distal upper extremity.

Declarations

Ethics approval and consent to participate

The clinical trial on which this study is based has been registered with the Human Research Ethics Committee of the Universiti Sains Malaysia (approval code: USM/JEPeM/20120629).Written formal consent for the study was obtained from all participants in accordance with the Declaration of Helsinki.

Competing interests

Dr. Rhendra Hardy Mohamad Zaini serves as Section Editor in Malaysian Journal of Anaesthesiology. He has not been involved in any part of the publication process prior to manuscript acceptance; peer review for this journal is double blind. The remaining authors have no competing interests to declare.

Funding

None to declare.

Acknowledgements

None to declare.

References

1. Oh C, Noh C, Eom H, et al. Costoclavicular brachial plexus block reduces hemidiaphragmatic paralysis more than supraclavicular brachial plexus block: retrospective, propensity score matched cohort study. Korean J Pain. 2020 Apr 4;33(2):144. https://doi.org/10.3344/kjp.2020.33.2.144
2. Yang CW, Kwon HU, Cho CK, et al. A comparison of infraclavicular and supraclavicular approaches to the brachial plexus using neurostimulation. Korean J Anesthesiol. 2010 Mar;58(3):260. https://doi.org/10.4097/kjae.2010.58.3.260
3. Albrecht E, Mermoud J, Fournier N, Kern C, Kirkham KR. A systematic review of ultrasound-guided methods for brachial plexus blockade. Anaesthesia. 2016 Feb;71(2):213-27. https://doi.org/10.1111/anae.13347
4. Luo Q, Yao W, Shu H, Zhong M. Double-injection technique assisted by a nerve stimulator for ultrasound-guided supraclavicular brachial plexus block results in better distal sensory–motor block: A randomised controlled trial. Eur J Anaesthesiol. 2017 Mar 1;34(3):127-34. https://doi.org/10.1097/EJA.0000000000000542

5. Karmakar MK, Sala-Blanch X, Songthamwat B, Tsui BC. Benefits of the costoclavicular space for ultrasound-guided infraclavicular brachial plexus block: description of a costoclavicular approach. Reg Anesth Pain Med. 2015 May 1;40(3):287-8. https://doi.org/10.1097/AAP.0000000000000822
6. Sala-Blanch X, Reina MA, Pangthipampai P, Karmakar MK. Anatomic basis for brachial plexus block at the costoclavicular space: a cadaver anatomic study. Reg Anesth Pain Med. 2016 May 1;41(3):387-91. https://doi.org/10.1097/AAP.0000000000000393
7. Li JW, Songthamwat B, Samy W, Sala-Blanch X, Karmakar MK. Ultrasound-guided costoclavicular brachial plexus block: sonoanatomy, technique, and block dynamics. Reg Anesth Pain Med. 2017 Mar 1;42(2):233-40. https://doi.org/10.1097/AAP.0000000000000566
8. Fredrickson MJ, Patel A, Young S, Chinchanwala S. Speed of onset of 'corner pocket supraclavicular and infraclavicular ultrasound guided brachial plexus block: a randomised observer-blinded comparison. Anaesthesia. 2009 Jul;64(7):738-44. https://doi.org/10.1111/j.1365-2044.2009.05918.x
9. Shemesh D, Olsha O, Orkin D, et al. Sympathectomy-like effects of brachial plexus block in arteriovenous access surgery. Ultrasound Med Biol. 2006 Jun 1;32(6):817-22. https://doi.org/10.1016/j.ultrasmedbio.2006.02.1420
10. Meena S, Arya V, Sen I, Minz M, Prakash M. Ultrasound-guided supraclavicular brachial plexus anaesthesia improves arteriovenous fistula flow characteristics in end-stage renal disease patients. South Afr J Anaesth Analg. 2015 Sep 3;21(5):131-4. https://doi.org/10.1080/22201181.2015.1075764
11. Demondion X, Herbinet P, Boutry N, Fontaine C, Cotton A. Sonographic mapping of a normal brachial plexus. AJNR Am J Neuroradiol. 2003.
12. Koscielniak-Nielsen ZJ, Frederiksen BS, Rasmussen H, Hesselbjerg L. A comparison of ultrasound-guided supraclavicular and infraclavicular blocks for upper extremity surgery. Acta Anaesthesiol Scand. 2009 May;53(5):620-6. https://doi.org/10.1111/j.1399-6576.2009.01909.x
13. Royse CF, Sha S, Soeding PF, Royse AG. Anatomical study of the brachial plexus using surface ultrasound. Anaesth Intensive Care. 2006 Apr;34(2):203-10. https://doi.org/10.1177/0310057X0603400212
14. Yang CW, Kwon HU, Cho CK, et al. A comparison of infraclavicular and supraclavicular approaches to the brachial plexus using neurostimulation. Korean J Anesthesiol. 2010 Mar;58(3):260. https://doi.org/10.4097/kjae.2010.58.3.260
15. Arcand G, Williams SR, Chouinard P, et al. Ultrasound-guided infraclavicular versus supraclavicular block. Anesth Analg. 2005 Sep 1;101(3):886-90. https://doi.org/10.1213/01.ANE.0000159168.69934.CC
16. Sahin L, Gul R, Mizrak A, et al. Ultrasound-guided infraclavicular brachial plexus block enhances postoperative blood flow in arteriovenous fistulas. J Vasc Surg. 2011 Sep 1;54(3):749-53. https://doi.org/10.1016/j.jvs.2010.12.045

© Malaysian Journal of Anaesthesiology 2024; 3:25-40
Original article
https://doi.org/10.35119/myja.v3i1.67

Development of a nomogram for predicting perioperative blood transfusions in major hepatobiliary and colorectal surgeries: a retrospective study

Mohamad Zahir **Anverdeen**[1], Syarifah Noor Nazihah **Sayed Masri**[2], Mohd Faizal **Ramli**[3], **Tan** Tse Siang[2], Siti Nidzwani **Mohamad Mahdi**[2], Nadia **Md Nor**[2]

[1]Department of Anaesthesiology and Intensive Care, National Heart Institute, Kuala Lumpur, Malaysia; [2]Department of Anaesthesiology and Intensive Care, Hospital Canselor Tuanku Muhriz, Kuala Lumpur, Malaysia; [3]Clinical Research Department, National Heart Institute, Kuala Lumpur, Malaysia

Abstract

Background: Major hepatobiliary and colorectal surgeries are associated with a risk of blood transfusions. However, risk assessment tools for predicting blood transfusions have not been studied extensively among patients undergoing these types of surgeries. We aimed to evaluate the risk factors for perioperative blood transfusions in our patients who underwent major hepatobiliary and colorectal surgeries and subsequently to create a nomogram.

Methods: Medical records for patients who underwent elective major hepatobiliary and colorectal surgeries in a single tertiary university hospital in Malaysia from 2015 to 2020 were retrospectively reviewed. A nomogram to predict transfusions risk was developed, and its discriminatory ability was tested using the area under the receiver operating characteristic (ROC) curve.

Correspondence: Syarifah Noor Nazihah Sayed Masri, Department of Anaesthesiology and Intensive Care, Hospital Canselor Tuanku Muhriz, Jalan Yaacob Latif, Kuala Lumpur, Malaysia.
E-mail: syarifahnazihah@yahoo.com.my

Results: Data from 293 patients (61.1% male) with an average age of 59.7 years old (± SD 14.51) were analysed. The prevalence of anaemia was 61.1%. A total of 127 patients (43.3%) received at least 1 unit of packed red cells transfusions. On multivariable analysis, gender (odds ratio [OR 1.646), preoperative haemoglobin of 8.0 g/dl or less (OR 0.777), Charlson Comorbidity Index score (OR 1.14) and procedure type (versus colonic surgery, major hepatectomy, OR 6.094; other pancreatomy, OR 1.487; Whipple's procedure, OR 9.667; and anterior resection, OR 3.569) were associated with a significantly higher risk of transfusions. All 4 of these factors were included in the nomogram. The nomogram's discrimination and calibration results showed good prediction abilities (AUROC curve 0.754).

Conclusion: The nomogram, which consists of gender, preoperative haemoglobin, Charlson Comorbidity Index, and procedure type effectively predicted the need for blood transfusions in major colorectal and hepatobiliary surgeries in our patients.

Keywords: blood transfusions, hepatobiliary and colorectal surgery, nomogram, risk prediction tool

Introduction

Colorectal and hepatopancreatic biliary surgeries are commonly performed for malignant and benign diseases and are associated with intraoperative and postoperative blood transfusions.[1] Blood transfusions are potentially lifesaving but also come with several adverse effects, such as immune suppression, increased infection rates, and increased mortality rates.[2-4] Identifying which patients are likely to need transfusions is a significant step towards better blood management. Scoring systems, regression models, nomograms, and artificial intelligence have been previously used to predict blood transfusions.[5-7]

A nomogram is a tool used to calculate charts graphically using scales that contain the values of 3 or more mathematical variables. Nomograms are primarily used in the fields of medicine, industry, engineering, and the physical and biological sciences to make predictions regarding the targeted aspect.[8] Several nomograms have been developed to predict blood transfusion in different types of surgery, such as total knee replacement, hip surgery, and pheochromocytoma surgeries.[5,6,9]

Kim *et al.* developed a nomogram to predict blood transfusions for hepatopancreatic biliary and colorectal surgeries.[10] Important predictive factors were age greater than 65 years, white and Asian race, preoperative haemoglobin levels, Charlson Comorbidity Index (CCI), preoperative international normalized ratio (INR),

and type of surgery. The nomogram was created by assigning a weighted score to each independent prognostic factor; higher total score was associated with higher likelihood of blood transfusions. However, the nomogram developed by Kim and colleagues has not been validated in an external population. To our knowledge, the only local study in this field has been conducted by Yusof *et al.*, which found that preoperative platelet count was the most important factor associated with risk of blood transfusions in liver transplant surgeries.[11]

In this study, we aimed to evaluate the risk factors for perioperative blood transfusions in patients who underwent major hepatobiliary and colorectal surgeries in a single tertiary university hospital in Malaysia. Specifically, we aimed to create a nomogram from these risk factors that can be used to predict the need for blood transfusions in patients undergoing these types of surgeries.

Materials and methods

This retrospective observational study was approved by the Research Committee of the Department of Anaesthesiology and Intensive Care, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, and the institution's Medical Research and Ethics Committee (Project Approval Code: HTM-2021-028). All adult patients who underwent elective major hepatobiliary and colorectal surgeries from January 2015 to December 2020 were included in the study. Patients with missing data or medical records and those who underwent open and closed surgeries whereby the intended surgery did not proceed due to disease progression were excluded from the study.

The medical records of the included patients were retrieved, reviewed, and analysed retrospectively. Data were collected on demographic details (*i.e.*, age, gender, race, weight, height, body mass index [BMI], and American Society of Anaesthesiologists [ASA] fitness grade), underlying medical illness (*i.e.*, pulmonary disease, congestive heart failure, peripheral arterial disease, diabetes, renal conditions, and hypertension), along with anaemia, relevant preoperative haematological profile (*i.e.*, haemoglobin concentration, INR, platelet level, and CCI), operative profile type of surgery (*i.e.*, anterior resection, hemi-hepatectomy, pancreatectomy, duedenopancreactectomy, Whipple's procedure, open colectomy, or minor hepatectomy), estimated blood loss, surgery duration, and units of transfused packed red blood cells.

The sample size for this study was based on the work of Peduzzi *et al.*[12] The minimum number of samples to include was $N = 10k/p$, where k is the number of independent variables, and p is the proportion of cases. A proportion of 30% of

blood transfusion cases was considered in the study population, with 7 independent variables included in the multiple logistic regression analysis and a total of 20% of dropout cases. The minimum sample size required was therefore 280 cases.

Data were cleaned, explored, and analysed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and STATA version 16.0 (STATACorp, College Station, TX, USA). The distribution of the continuous data was explored using skewness, kurtosis, and histograms. Continuous data were presented as mean and standard deviation if the data were normally distributed, otherwise median (25^{th} percentile, 75^{th} percentile) was used. Categorical variables were presented as frequency and percentage. Descriptive statistics were used to present the characteristics and perioperative details of the patients, and the differences in outcomes between those who did not receive and those who received perioperative blood transfusion were compared using the independent sample T test, Mann-Whitney U test, Pearson chi-squared test, and Fisher exact test, whichever was appropriate.

The factors affecting the requirement for blood transfusions after surgeries were analysed using logistic regression models that were employed in the nomogram's development. When conducting the univariable analysis using simple logistic regression to identify the factors associated with perioperative blood transfusions, variables with $p < 0.200$ were noted. The forward logistic regression approach was used to incorporate results from the univariable analysis into the multivariable model's variable selection procedure. Nomograms indicating the need for intraoperative blood transfusions were generated using regression coefficients from multivariable logistic regression models. Multicollinearity and interaction terms were checked, and model fit was assessed using the Hosmer-Lemeshow goodness of fit test and classification table.

Model discrimination (the capacity of a proposed model to identify patients with different outcomes) and calibration (the distance between forecasts and results) were also used to evaluate model performance. The area under the receiver operating characteristics (ROC) curve was used to determine the discriminatory ability of the nomogram (AUC). AUC values can range from 0.5, demonstrating poor discrimination, to 1.0, showing perfect discrimination. Model calibration was assessed using a calibration plot, in which the predicted probabilities were plotted against the observed outcome frequencies. Predictions from a properly calibrated model should lie along the 45° diagonal line. All tests were conducted as 2-tailed, and $p < 0.05$ was taken to denote statistical significance. Finally, a comparison was conducted between the AUC of the nomogram established by Kim *et al.* and our newly generated nomogram. This comparison aimed to assess the discriminatory power of both nomograms in predicting the need for blood transfusions.

Results

During the data collection process, a total of 305 patients were taken into consideration; however, 12 patients were excluded since they did not meet the inclusion criteria. The 293 individuals who were involved in the study were separated into 2 groups: those who required a transfusion (43.3%) and those who did not require a transfusion (56.7%) (Fig. 1).

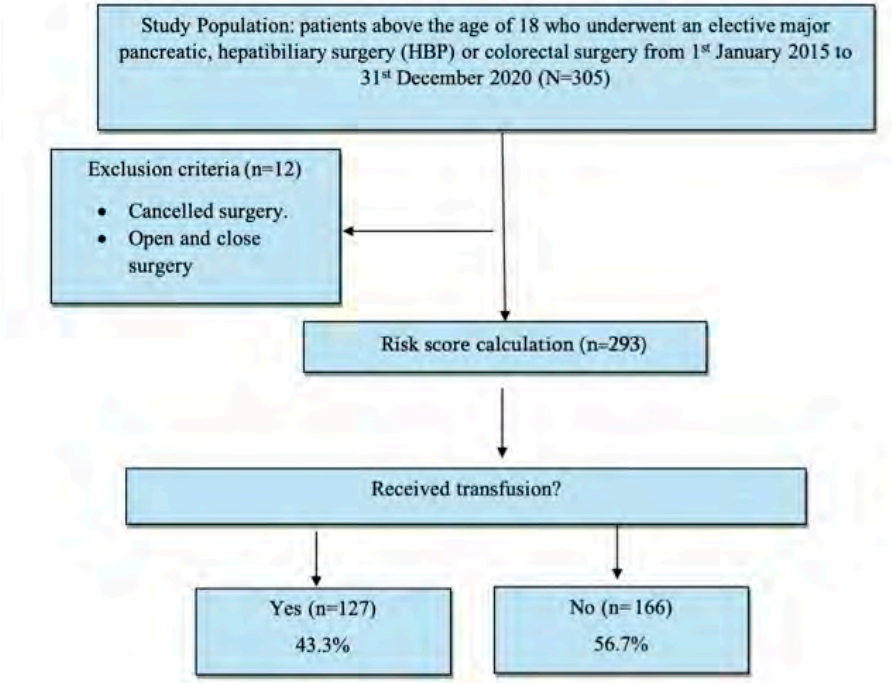


Fig. 1. Flow diagram of study.

Demographic and clinical data

The baseline characteristics of the included patients are shown in Table 1. The mean age was 59.69 years old (SD: 14.51). The majority were male (61.1%) and Malay (60.4%) with a median BMI of 23.31 kg/m^2 (IQR: 21.16, 26.39). Almost all patients were non-smokers (95.9%), with an ASA grade of I–II (93.2%). The reported mean perioperative haemoglobin was 11.84 g/dL (SD: 1.88), while the median perioperative INR and platelet were 1.01 (IQR: 0.98, 1.08) and 278.0 (IQR: 215.0, 364.0) x 10^9/L,

Table 1. Characteristics of the patients

Characteristics	Overall	Perioperative blood transfusion	
		No	Yes
Age in years, mean ± SD	59.69 ± 14.51	59.78 ± 14.79	59.56 ± 14.30
Gender, *n* (%) Female Male	 114 (38.9) 179 (61.1)	 73 (44.0) 93 (56.0)	 41 (32.3) 86 (67.7)
Race, *n* (%) Malay Chinese Indian Others	 177 (60.4) 98 (33.4) 16 (5.5) 2 (0.7)	 97 (58.4) 57 (34.3) 11 (6.6) 1 (0.6)	 80 (63.0) 41 (32.3) 5 (3.9) 1 (0.8)
BMI in kg/m^2, median (IQR)	23.31 (21.16, 26.39)	23.66 (21.43, 27.07)	22.97 (20.90, 26.12)
ASA grade, *n* (%) I–II III–IV	 273 (93.2) 20 (6.8)	 158 (95.2) 8 (4.8)	 115 (90.6) 12 (9.4)
Perioperative Hb, mean ± SD	11.84 ± 1.88	12.20 ± 1.79	11.35 ± 1.89
Perioperative INR, median (IQR)	1.01 (0.98, 1.08)	1.01 (0.99, 1.07)	1.02 (0.98, 1.10)
Perioperative platelet, median (IQR)	278.0 (215.0, 364.0)	276 (217.5, 434.8)	285.0 (211.0, 491.8)
Smoking status, *n* (%) Non-smoker Smoker	 281 (95.9) 12 (4.1)	 160 (96.4) 6 (3.6)	 121 (95.3) 6 (4.7)
Charlson Comorbidity Index, *n* (%) 0–3 ≥ 4	 59 (20.1) 234 (79.9)	 39 (23.5) 127 (76.5)	 20 (20.1) 107 (84.3)
Coexisting medical condition, *n* (%)			
Diabetes	105 (35.8)	51 (30.7)	54 (42.5)
Hypertension	153 (52.2)	80 (48.2)	73 (57.5)
Ischaemic heart disease	14 (4.8)	7 (4.2)	7 (5.5)
Anaemia	9 (3.1)	3 (1.8)	6 (4.7)
Chronic kidney disease	10 (3.4)	4 (2.4)	6 (4.7)
Dyslipidaemia	33 (11.3)	20 (12.0)	13 (10.2)

respectively. The CCI of 4 or higher was reported among 234 (79.9%) of the patients. Reported coexisting medical conditions included diabetes (35.8%), hypertension (52.2%), ischaemic heart disease (4.8%), chronic kidney disease (3.4%), and dyslipidaemia (11.3%).

Factors associated with perioperative blood transfusions

The results of univariable and multivariable logistic regression analysis of factors associated with perioperative blood transfusion are shown in Table 2. On univariable analysis, factors that were significantly associated with perioperative blood loss were gender, perioperative haemoglobin, CCI, diabetes mellitus, and type of procedure.

The final multivariable model revealed that factors significantly associated with the perioperative blood transfusion included gender, perioperative haemoglobin, and type of procedure ($p < 0.05$). Males were observed to have 2.031 times higher odds for perioperative blood transfusion compared to females ($p = 0.012$). Every unit increase in perioperative haemoglobin will decrease the odds for blood transfusion by 25.5% ($p < 0.001$). A unit increase in CCI score was observed to increase the odds for perioperative blood transfusion by 9% ($p = 0.050$). The type of procedure also played an important role. Hemihepatectomy (or more), duodenopancreatectomy/Whipple's procedure, and anterior resection were observed to have 6.213 times ($p = 0.001$), 8.260 times ($p < 0.001$), and 3.550 times ($p = 0.011$) higher odds for perioperative blood transfusion compared to open colectomy, respectively.

Nomogram generation

Based on the results of multiple logistic regression, a nomogram was generated to predict perioperative blood transfusions (Fig. 2). The nomogram was created by assigning a weighted score to each of the independent prognostic factors. The total score was calculated from the sum of the assigned number of points for each risk factors in the nomogram. For example, a male (1.4 points) who underwent duodenopancreatectomy/Whipple's procedure (4.4 points) with a perioperative haemoglobin concentration of 9.95 g/dl (8.3 points) and CCI score of 0 (0.0 points) would score a total of 14.1 points, and therefore have a 94.9% predicted risk for blood transfusions.

The resulting model's ability to discriminate between patients requiring and not requiring perioperative blood transfusions was measured by its AUC (Fig. 3). The probability that a patient receiving a blood transfusion had a higher score than a patient who did not was 75.4%, indicating good discriminatory power of the prediction model.

Table 2. Univariable and multivariable logistic regression analysis of factors associated with perioperative blood transfusions

Factors	Univariable			Multivariable			Points contributed
	OR	95% CI	*P-value	Adjusted OR	95% CI	‡P-value	
Age	0.999	0.983, 1.015	0.896				
Gender							
Female	Ref			Ref			0
Male	1.646	1.017, 2.666	**0.043***	2.031	1.170, 3.526	**0.012***	1.4
Race							
Malay	Ref						
Chinese	0.872	0.530, 1.436	0.591				
Indian	0.551	0.184, 1.652	0.287				
Others	1.213	0.075, 19.693	0.892				
BMI in kg/m^2	0.982	0.933, 1.033	0.479				
ASA grade							
I–II	Ref						
III–IV	2.061	0.816, 5.204	0.126				
Perioperative haemoglobin	0.777	0.681, 0.887	**< 0.001***	0.745	0.640, 0.868	**< 0.001***	4.3–10.0
Perioperative INR	8.012	0.946, 67.838	0.056				
Perioperative platelets	1.001	0.999, 1.003	0.267				
Smoking status							
Non-smoker	Ref						
Smoker	1.322	0.416, 4.201	0.636				
Charlson Comorbidity Index	1.14	1.05, 1.22	**0.001***	1.090	1.000–1.188	**0.049***	0.0–3.3
Diabetes mellitus							
No	Ref						
Yes	1.668	1.030, 2.701	**0.038***				
Hypertension							
No	Ref						
Yes	1.453	0.913, 2.314	0.115				
Ischaemic heart disease							
No	Ref						
Yes	1.325	0.453, 3.879	0.608				
Anaemia							
No	Rf						
Yes	2.694	0.661, 10.988	0.167				
Chronic kidney disease							
No	Ref						
Yes	2.008	0.555, 7.273	0.288				
Dyslipidaemia							
No	Ref						
Yes	0.832	0.397, 1.745	0.627				
Type of procedure							
Open colectomy	Ref			Ref			0
Minor hepatectomy	1.074	0.266, 4.335	0.920	1.148	0.274, 4.820	0.849	0.3
Hemihepatectomy or more	6.094	2.164, 17.164	**0.001***	6.213	2.125, 18.166	**0.001***	3.8
Duodenopancreatectomy	9.667	3.398, 27.497	**< 0.001***	8.260	2.857, 23.879	**< 0.001***	4.4
Anterior resection	3.569	1.374, 9.274	**0.009***	3.550	1.333, 9.459	**0.011***	2.6
Other pancreatectomy	1.487	0.358, 6.179	0.585	2.015	0.445, 9.125	0.363	1.5

Ref: Reference value; OR: Odd ratio; CI; Confidence interval; BMI: body mass index; ASA: American Society of Anesthesiologists
*P value in univariable analysis, ‡P value in multivariable analysis
Multicollinearity and interaction terms were checked and not found; Negelkerke $R^2 = 0.242$
Hosmer Lemenshow goodness of fit test ($p = 0.276$); Classification table (overall correctly classified percentage: 70.3%); Area under ROC curve = 75.4%

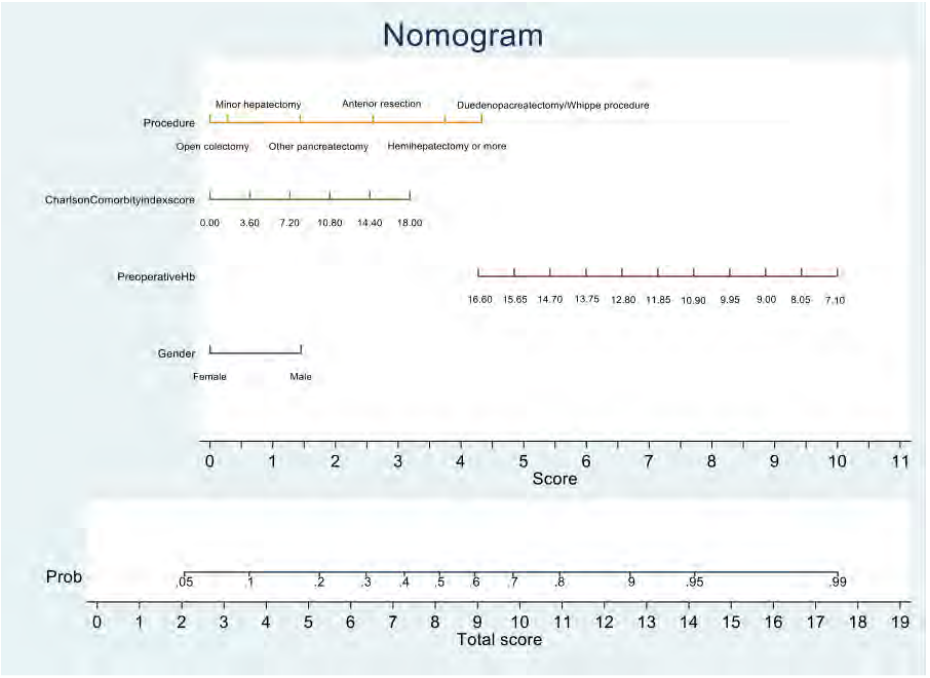


Fig. 2. Nomogram for predicting perioperative blood transfusion. Negative coefficient in variable perioperative haemoglobin was forced positive to facilitate the calculation so that the nomogram can be used by adding scores up only, instead of adding and subtracting scores.

The model fit was further assessed using a calibration plot (Fig. 4). The calibration plot revealed a satisfactory fit of the model predicting perioperative blood transfusion as the predictions fell along the 45° diagonal line.

The discriminative ability of the nomogram by Kim *et al.*[10] and our model were compared using AUC in Figure 5. It was observed that our model (AUC: 0.754) has better discriminative ability compared to the model by Kim *et al.* (AUC: 0.650). The sensitivity and specificity for the nomogram by Kim *et al.* was 43.41% and 76.83%, respectively; for ours, it was 62.02% and 76.83%, respectively. Our score has better sensitivity than the score by Kim *et al.*, with comparable specificity.

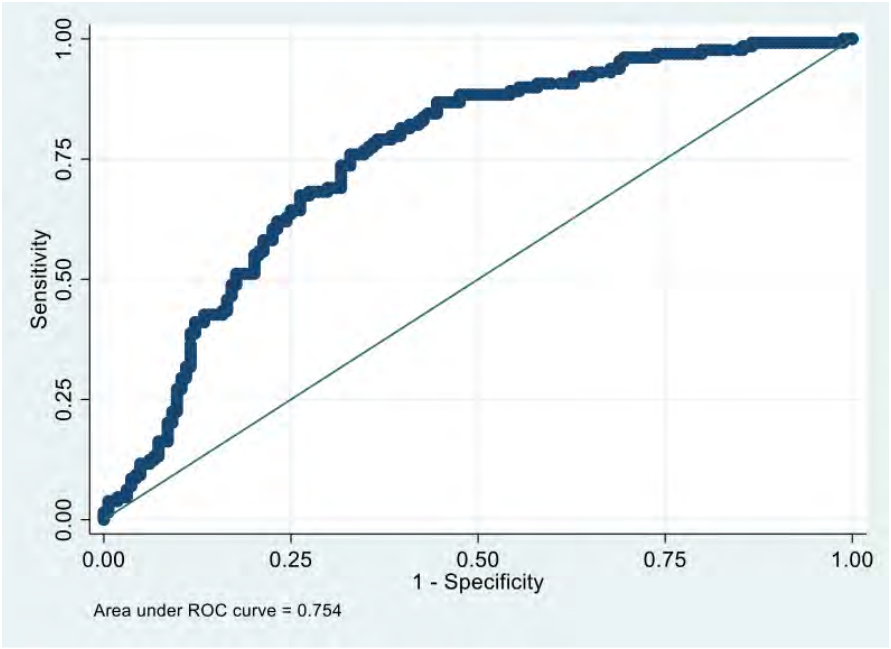


Fig. 3. Receiver operating characteristics (ROC) curve for the nomogram model.

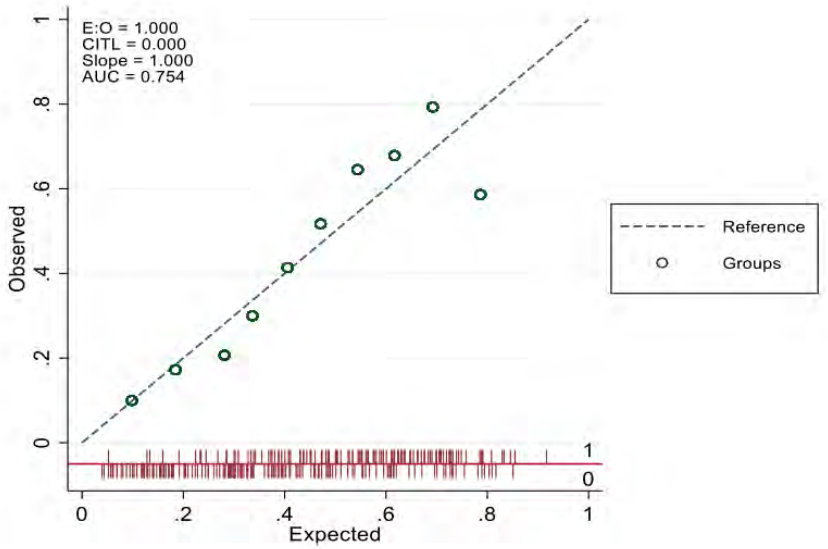


Fig. 4. Calibration plot for the nomogram model.

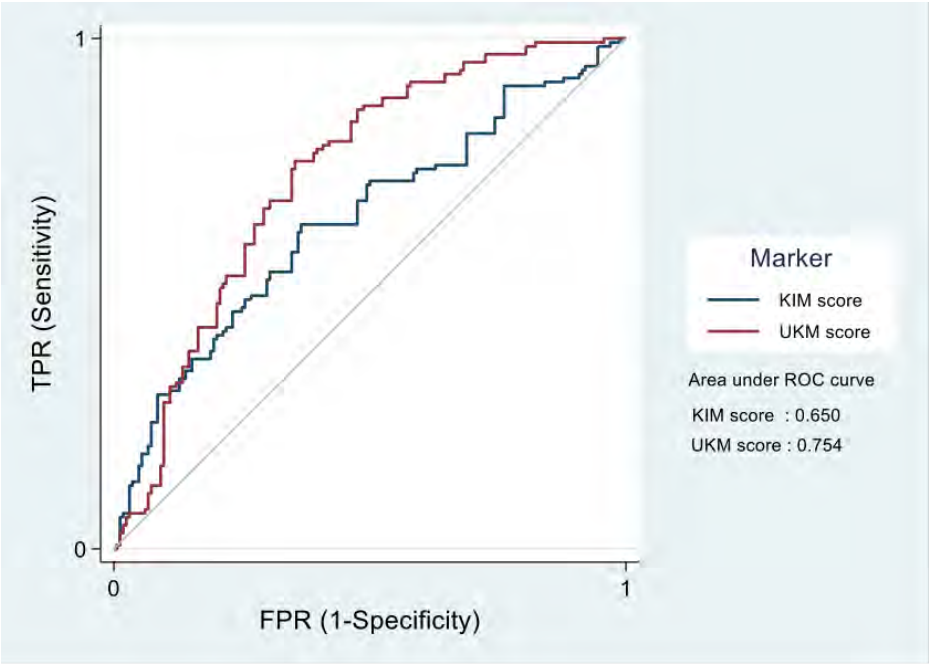


Fig. 5. Comparison of receiver operating characteristics (ROC) curves for the Kim *et al.* nomogram and our newly generated nomogram.

Discussion

Preoperative anaemia as an independent risk factor for adverse outcomes in major hepatobiliary and colorectal surgeries is well documented in the literature.[12,13] Even though transfusion of packed red blood cells can be vital in patients with severe anaemia, it also carries risk of complications and morbidity.[2] These include reduced immune function and transfusion-related events, such as infection and lung injury.[14] Therefore, to facilitate effective management of blood transfusions and reduce morbidity, early identification of patients who would require transfusions is useful.[15] The present study found no association between BMI, age, preoperative platelet count, and receipt of blood transfusions, as in the study by Pulitano *et al.*[16] Other sociodemographic variables were, however, predictive of increased odds of transfusions, such as gender, type of procedure, and CCI. Roubinian *et al.* found that preoperative variables such as age, comorbidities, type of surgery, and preoperative serum haemoglobin levels were enough to develop a model with high accuracy and performance in both medical and surgical cohorts of patients.[17]

Preoperative haemoglobin (OR 0.777, $p < 0.001$) emerged as the strongest factor in predicting whether a patient would require a transfusion in our study, as it carries the highest weightage in terms of points in the nomogram. As expected, similar results have been found by other groups.[18,19] A recent study found that serum haemoglobin greater than 13 g/dl reduces the risk of transfusions. Rather than just focusing solely on the level of haemoglobin, the inclusion of preoperative patient characteristics may help in deciding whether to transfuse or not and lead to much more effective blood management.[17]

CCI is another factor that is significant in this study (OR 1.14, $p = 0.049$). In 1987, Mary Charlson and coworkers devised the CCI, a numerical score that indicates how likely a patient is to die within a year of being hospitalised based on the presence of certain comorbid conditions.[20] The index covered a total of 19 medical issues. Every condition was assigned a score between 1 and 6 in order to calculate the hazard ratio for dying within a year using the Cox proportional hazards model. A total of these values was used to calculate the CCI score. Although CCI dates back more than 30 years, it still has a place in current practise. In 2017, Lakomkin *et al.* found that a higher CCI score was associated with an increased incidence of complications, transfusions events, and length of stay following revision hip arthroplasty.[21] Lee *et al.* showed that CCI score is one of the main predictors of mortality and blood transfusion among COVID-19 patients as recently as 2022.[7]

We noted that our patient cohort had a higher prevalence of anaemia (61.1 %) compared to the global prevalence dataset (23.2%) and among the dataset from Zwiep *et al.*, who studied the prevalence of anaemia in hepatopancreatic biliary patients (44.1%).[22,23] This variation in anaemia prevalence may have resulted in the limited utility of the Kim *et al.* nomogram outside the control cohort and may need to be recalibrated to retain generalizability.[24] The mean number of packed red blood cells transfused in this study was 2 (IQR 1–3), which is the same as the study by Kim *et al.*[10] In a large multicentre study, Kooby et al. reported that 43% of liver resection patients who needed a transfusion received only 1 to 2 units of packed red blood cells.[25]

To improve clinical utility and ease of use, a nomogram grading system was developed from commonly gathered preoperative data. The nomogram has good discrimination and calibration, and its performance has been internally verified. Most commonly, serum haemoglobin levels with wide variation in practice is used to decide on transfusion.[26] While many risk scoring tools have been developed to identify those at risk of requiring perioperative blood transfusions in other surgical fields, especially cardiothoracic surgery, this has not been the case in the hepatobiliary and colorectal field. Recently, Kim *et al.* developed a nomogram to predict the likelihood of blood transfusion in major hepatobiliary and colorectal surgery

consisting of 7 factors with an area under ROC curve of 0.756 on internal validation. However, our validation of Kim's nomogram with dataset from our population resulted in an area under ROC curve of only 0.650. The lack of agreement between the predicted and observed probability of transfusion may be attributed to variations in perioperative haematological profiles, as well as differences in the demographic composition and racial diversity of the sample group.[27]

A particular strength of this study was that it advocates a patient profile adjusted to the Malaysian population. To provide safer therapy and better coordination of the blood management system, it is crucial to identify individuals at greater risk. Questions regarding the most effective way to care for a patient at increased risk arise as blood systems are increasingly focused on safe and responsible use of healthcare resources. As a result, this research provides a risk classification tool to guide decision making to boost cost-effectiveness and patient outcomes. Transfusion decisions are determined by the surgeon or anaesthesiologist in charge, who will take into account the patient's medical history and other circumstances unique to the case. However, each individual's clinical experience is bound by a unique set of constraints, making it challenging to standardise. Using the obtained retrospective data, we devised a simple and accurate scoring system to predict the risk of blood transfusion for patients having major colorectal and hepatobiliary surgery.

As a retrospective database analysis, our research is subject to the usual caveats, such as biases and erroneous data collection, as well as unaccounted-for confounders. This single-centre design meant that the sample size was limited, which could compromise the generalizability of results, as well as underpowered to detect other risks that could have significant impact on transfusions in major hepatobiliary and colorectal surgery. Potential unaccounted-for determinants of blood transfusion include surgeon expertise and other provider-level characteristics. Finally, further evaluation of this nomogram as a blood transfusion risk prediction tool, ideally using a prospective cohort study design with a larger sample size in a main hepatobiliary and colorectal centre is needed to ascertain its utility.

Conclusion

In summary, a nomogram using predictor variables of gender, type of surgery, preoperative haemoglobin level, and CCI score predicted the risk of perioperative blood transfusions with a good performance in our cohort of patients who underwent major hepatobiliary and colorectal surgeries. Further prospective studies are warranted to externally validate the performance of this nomogram

and to evaluate whether this nomogram can provide better guidance for clinicians to intervene perioperatively.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Research and Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre (HTM-2021-028). Informed consent was not required as the data employed were retrospective.

Competing interests

None to declare.

Funding

None to declare.

Acknowledgements

None to declare.

References

1. Bennett S, Baker L, Shorr R, Martel G, Fergusson D. The impact of perioperative red blood cell transfusions in patients undergoing liver resection: a systematic review protocol. Syst Rev. 2016;5:38. https://doi.org/10.1186/s13643-016-0217-5
2. Fong IW. Blood Transfusion-Associated Infections in the Twenty-First Century: New Challenges. Current Trends and Concerns in Infectious Diseases. 2020:191-215.
3. Stramer SL, Dodd RY. Transfusion-transmitted emerging infectious diseases: 30 years of challenges and progress. Transfusion. 2013;53(10 Pt 2):2375-2383. https://doi.org/10.1111/trf.1237
4. Webster NR. Stranger danger-mortality after transfusions. Br J Anaesth. 2017;118(3):280-282. https://doi.org/10.1093/bja/aew405
5. Bian FC, Cheng XK, An YS. Preoperative risk factors for postoperative blood transfusion after hip fracture surgery: establishment of a nomogram. Journal

of Orthopaedic Surgery and Research. 2021;16(1):406. https://doi.org/10.1186/s13018-021-02557-5
6. Guo Y, You L, Hu H, et al. A Predictive Nomogram for Red Blood Cell Transfusion in Pheochromocytoma Surgery: A Study on Improving the Preoperative Management of Pheochromocytoma. Front Endocrinol (Lausanne). 2021;12:647610. https://doi.org/10.3389/fendo.2021.647610
7. Lee B-H, Lee K-S, Kim H-I, et al. Blood Transfusion, All-Cause Mortality and Hospitalization Period in COVID-19 Patients: Machine Learning Analysis of National Health Insurance Claims Data. Diagnostics. 2022;12(12):2970. https://www.mdpi.com/2075-4418/12/12/2970
8. Balachandran VP, Gonen M, Smith JJ, DeMatteo RP. Nomograms in oncology: more than meets the eye. Lancet Oncol. 2015;16(4):e173-180. https://doi.org/10.1016/s1470-2045(14)71116-7
9. Hu C, Wang Y-h, Shen R, et al. Development and validation of a nomogram to predict perioperative blood transfusion in patients undergoing total knee arthroplasty. BMC Musculoskeletal Disorders. 2020;21(1):315. https://doi.org/10.1186/s12891-020-03328-9
10. Kim Y, Bagante F, Gani F, et al. Nomogram to predict perioperative blood transfusion for hepatopancreaticobiliary and colorectal surgery. Br J Surg. 2016;103(9):1173-1183. https://doi.org/10.1002/bjs.10164
11. Yusop Mohd Faeiz Mtn, Syed Azim Sharifah Mai Sarah, Kamaruzaman Ameera Ashyila, Kugaan Arvend, Osman Mohd Fairuz, Hatta Nur Raihan, Tengku Yazid Tengku Norita, Mokhtar Suryati, Omar Haniza, Amir Ahmad Suhaimi. Intraoperative Blood Loss and Blood Transfusion Requirement Among Liver Transplant Recipients. A National Single Center Experience 2020. Asian Journal of Transfusion Science. 2021. https://doi.org/https://doi.org/10.5281/zenodo.5457866
12. Tohme S, Varley PR, Landsittel DP, Chidi AP, Tsung A. Preoperative anemia and postoperative outcomes after hepatectomy. HPB (Oxford). 2016;18(3):255-261. https://doi.org/10.1016/j.hpb.2015.09.002
13. Bansal SS, Hodson J, Khalil K, et al. Distinct risk factors for early and late blood transfusion following pancreaticoduodenectomy. Hepatobiliary Pancreat Dis Int. 2018;17(4):349-357. https://doi.org/10.1016/j.hbpd.2018.07.001
14. Guo K, Ma S. The Immune System in Transfusion-Related Acute Lung Injury Prevention and Therapy: Update and Perspective. Front Mol Biosci. 2021;8:639976. https://doi.org/10.3389/fmolb.2021.639976
15. Klein AA, Collier T, Yeates J, et al. The ACTA PORT-score for predicting perioperative risk of blood transfusion for adult cardiac surgery. Br J Anaesth. 2017;119(3):394-401. https://doi.org/10.1093/bja/aex205
16. Pulitanò C, Arru M, Bellio L, Rossini S, Ferla G, Aldrighetti L. A risk score for predicting perioperative blood transfusion in liver surgery. Br J Surg. 2007;94(7):860-865. https://doi.org/10.1002/bjs.5731

17. Roubinian NH, Murphy EL, Swain BE, Gardner MN, Liu V, Escobar GJ. Predicting red blood cell transfusion in hospitalized patients: role of hemoglobin level, comorbidities, and illness severity. BMC Health Serv Res. 2014;14:213. https://doi.org/10.1186/1472-6963-14-213
18. Maempel JF, Wickramasinghe NR, Clement ND, Brenkel IJ, Walmsley PJ. The pre-operative levels of haemoglobin in the blood can be used to predict the risk of allogenic blood transfusion after total knee arthroplasty. Bone Joint J. 2016;98-b(4):490-497. https://doi.org/10.1302/0301-620x.98b4.36245
19. Sima CS, Jarnagin WR, Fong Y, et al. Predicting the risk of perioperative transfusion for patients undergoing elective hepatectomy. Ann Surg. 2009;250(6):914-921. https://doi.org/10.1097/sla.0b013e3181b7fad3
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-383. https://doi.org/10.1016/0021-9681(87)90171-8
21. Lakomkin N, Goz V, Lajam CM, Iorio R, Bosco JA, 3rd. Higher Modified Charlson Index Scores Are Associated With Increased Incidence of Complications, Transfusion Events, and Length of Stay Following Revision Hip Arthroplasty. J Arthroplasty. 2017;32(4):1121-1124. https://doi.org/10.1016/j.arth.2016.11.014
22. Safiri S, Kolahi A-A, Noori M, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. Journal of Hematology & Oncology. 2021;14(1):185. https://doi.org/10.1186/s13045-021-01202-2
23. Zwiep TM, Gilbert RWD, Moloo H, et al. Improving the treatment of pre-operative anemia in hepato-pancreato-biliary patients: a quality improvement initiative. Patient Safety in Surgery. 2020;14(1):18. https://doi.org/10.1186/s13037-020-00239-5
24. Clevenger B, Richards T. Pre-operative anaemia. Anaesthesia. 2015;70(s1):20-e28. https://doi.org/https://doi.org/10.1111/anae.12918
25. Kooby DA, Stockman J, Ben-Porat L, et al. Influence of transfusions on perioperative and long-term outcome in patients following hepatic resection for colorectal metastases. Ann Surg. 2003;237(6):860-869; discussion 869-870. https://doi.org/10.1097/01.Sla.0000072371.95588.Da
26. Baker L, Park L, Gilbert R, et al. Intraoperative Red Blood Cell Transfusion Decision-making: A Systematic Review of Guidelines. Ann Surg. 2021;274(1):86-96. https://doi.org/10.1097/sla.0000000000004710
27. Prochaska M, Salcedo J, Berry G, Meltzer D. Racial differences in red blood cell transfusion in hospitalized patients with anemia. Transfusion. 2022;62(8):1519-1526. https://doi.org/10.1111/trf.16935

Managing the Difficult Airway

i-gel®

www.i-gel.com

- 2nd generation supraglottic airway
- Conduit for intubation with fibreoptic guidance
- Rescue device

INTERSURGICAL®
COMPLETE RESPIRATORY SYSTEMS

Quality, innovation and choice

Interact with us

www.intersurgical.co.uk

© Malaysian Journal of Anaesthesiology 2024; 3:42-54
Review article
https://doi.org/10.35119/myja.v3i1.71

Optimal nutritional therapy in critically ill patients: a narrative review

Mohd Basri **Mat Nor**

Department of Anaesthesiology and Critical Care, Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan, Malaysia

Abstract

Inadequate nutrition delivery remains a pervasive issue in critically ill patients, with significant challenges in accurately measuring nutritional requirements and personalising nutrition. Current medical nutrition therapy is constrained by difficulty in objectively measuring nutritional requirements and patient responses. Both enteral (EN) and parenteral nutrition (PN) are effective, but achieving and assessing nutritional targets pose substantial challenges. The adoption of computerised nutrition monitoring is on the rise, with future strategies potentially incorporating advanced muscle monitoring tools such as ultrasound and bioelectrical impedance analysis (BIA). Early enteral nutrition has been shown to reduce complications and shorten ICU stays; however, it should be delayed in specific conditions such as gastrointestinal bleeding. When EN is not feasible, PN serves as a safe alternative. Indirect calorimetry (IC) offers a method to measure energy expenditure and guide nutritional interventions, though larger trials are necessary to validate its benefits in personalised nutrition strategies. Significant muscle mass loss is prevalent in ICU patients, necessitating optimal amino acid delivery. Protein intake should be tailored to lean mass rather than total body weight, and bedside techniques like BIA and muscle ultrasound can aid in personalising protein delivery. While high protein intake may help mitigate muscle loss, its effect on clinical outcomes remains debated. Further trials are essential to enhance personalised ICU nutrition and improve patient outcomes throughout their ICU and post-ICU care journey.

Correspondence: Kulliyyah of Medicine, International Islamic University Malaysia, Bandar Indera Mahkota, 25200, Kuantan, Pahang, Malaysia
E-mail: m.basri@iium.edu.my

Keywords: critically ill patients, malnutrition, nutrition assessment, optimal nutrition delivery, personalised nutrition therapy

Introduction

Traditionally, nutrition support for critically ill patients was regarded as adjuvant care aimed at providing an exogenous energy source to preserve lean body mass (LBM) and support patients during stress response. Recently, this strategy has evolved into medical nutrition therapy (MNT), where feeding is believed to mitigate the metabolic response to stress, prevent oxidative cellular injury, and favourably modulate immune response. Optimal MNT is an essential component of care for critically ill patients, impacting recovery, morbidity, and mortality. Successful nutritional management requires a comprehensive strategy involving thorough assessment, precise energy requirement estimation, continuous monitoring, and personalised interventions. Nutritional strategies should be adapted to the patient's characteristics, diagnosis, ongoing treatments, and state of metabolism during intensive care unit (ICU) stay and convalescence. A personalised nutrition plan may prevent detrimental over- or underfeeding and attenuate muscle wasting. These patients frequently experience hypermetabolism, catabolism, and inflammation, which can worsen malnutrition and have adverse effects on clinical outcomes.[1]

In the ICU, critically ill patients are highly susceptible to developing malnutrition due to the rapid deterioration of their nutritional status following admission. In a recent meta-analysis encompassing 20 studies and 1,168 patients, the prevalence of malnutrition among ICU patients ranged from 38% to 78%.[2] Inflammation, undernutrition-driven catabolism, and inadequate dietary intake are key drivers of malnutrition. If left untreated, disease-related malnutrition is linked to unfavourable outcomes, including increased mortality rates and prolonged ICU and hospital stays. Critical illness often leads to immediate and significant muscle mass (MM) loss, ranging from 17.7% to 21.8% within 10 days.[3] This substantial muscle loss is associated with an increased incidence of complications and, ultimately, mortality. Early initiation of MNT is recommended for all patients who are admitted to the ICU for over 48 hours. The FASTHUG mnemonic is widely recognised and encompasses key aspects of the general care of critically ill patients in the ICU. It starts with the letter "F" for feeding, emphasising the importance of commencing nutrition early upon ICU admission and regularly reviewing the nutritional plan.[4]

This narrative review aims to provide an overview of nutritional therapy for critically ill patients, covering various aspects such as nutritional assessment, malnutrition risk, estimation of energy needs, monitoring, and personalised approaches in general adult ICU patient. The complex interplay of various factors affecting the nutritional needs of critically ill patients, coupled with variations in outcomes and research methodologies, poses significant challenges in formulating effective guidelines.

Nutritional assessment

Critically ill patients are at increased risk of developing malnutrition, which is linked to unfavourable clinical outcomes. The nutritional status of critically ill patients deteriorates rapidly after admission, irrespective of their initial nourishment status. Nutritional status is crucial in determining several patient outcomes, including the duration and expenses of hospitalisation, as well as morbidity and mortality rates. Nutritional assessment serves as a tool to evaluate a patient's nutritional status and needs, identify existing nutritional risks, and detect signs of malnutrition.[5] The World Health Organization defines malnutrition as encompassing both insufficient and excessive or imbalanced nutritional intake. In hospital settings, malnutrition is commonly referred to as undernutrition (inadequate intake or absorption of nutrients), a deficiency that affects bodily functions.[6] The European Society of Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as "a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease".[7] Critically ill patients are at high risk of malnutrition due to factors such as increased metabolic demands, inflammation, gastrointestinal dysfunction, and prolonged periods of fasting or inadequate nutrient intake. Malnutrition risk in critically ill patients refers to the likelihood that a patient will develop malnutrition during their stay in the ICU or while recovering from a critical illness. Recent recommendations suggest that any critically ill patient staying more than 48 hours in the ICU should be considered at risk for malnutrition. To establish an adequate and personalised nutritional regimen, conducting an individualised nutritional assessment in the initial hours of ICU admission is crucial. This approach enables the early identification of malnutrition risk and promptly initiating appropriate nutritional therapy.[8]

Nutritional assessment in critically ill patients is a multifaceted process that requires a thorough evaluation of various parameters. Traditional methods include clinical judgment, anthropometric measurements (*e.g.*, weight, height, body mass index [BMI]), and biochemical markers (*e.g.*, serum albumin, prealbumin,

transferrin). However, these markers can be influenced by acute phase responses and may not accurately reflect nutritional status in critically ill patients. Advanced tools such as bioelectrical impedance analysis (BIA) and dual-energy X-ray absorptiometry can provide more precise body composition measurements.[3,5]

ESPEN's updated guidelines of clinical nutrition for ICU patients recommend conducting a general clinical assessment to evaluate malnutrition in ICU settings until a specific tool is validated. This clinical evaluation may include gathering patient history, noting unintentional weight loss or reduced physical function before ICU admission, performing a physical examination, and conducting a general assessment of body composition, MM, and strength, if feasible. While no specific nutritional scoring system has been validated for use in the ICU, existing tools such as the Nutrition Risk Screening (NRS) 2002 and the Malnutrition Universal Screening Tool (MUST)5 score have not been developed specifically for critically ill patients. The NUTRIC (Nutritional Risk In Critically) tool is a novel risk assessment tool primarily based on disease severity. The Global Leadership Initiative on Malnutrition (GLIM) consensus statement outlines a set of risk factors that characterise malnutrition in a clinical context. According to the GLIM criteria, diagnosing malnutrition in critically ill patients necessitates the presence of at least 1 phenotypic criterion and 1 aetiologic criterion. After screening, the diagnostic assessment links a phenotype (weight loss percentage, BMI, decrease in appetite, and/or low MM) with an aetiology, *e.g.*, critical illness.[9]

A systematic review examining the significance of nutritional assessment tools in critically ill patients analysed 14 scientific articles that met selection criteria from 7 countries.[10] The reviewed instruments included mNUTRIC, NUTRIC, SGA, MUST, and the ESPEN and American Society for Parenteral and Enteral Nutrition (ASPEN) criteria. All studies highlighted beneficial effects following a nutritional risk assessment, with mNUTRIC being the most utilised tool, showing superior predictive validity for mortality and adverse outcomes. The review emphasised that employing nutritional assessment tools enables a comprehensive understanding of patient's nutritional status and facilitates tailored interventions to enhance their nutritional well-being. Notably, tools such as mNUTRIC, NRS 2002, and SGA have demonstrated the most effective outcomes.

Several techniques are now available to assess MM, LBM, or fat-free mass in ICU patients. MM can be assessed by ultrasound, computerised tomography (CT) scan, or BIA.[11] Sarcopenia is commonly observed in undernourished patients admitted to the ICU. Muscle function can be measured using handgrip dynamometry. BIA effectively evaluates body composition and is valuable for prognostic assessment in critically ill patients.[12] Studies indicate that patients demonstrating low MM upon admission, as determined by a CT scan, tend to experience longer hospital stays and

higher mortality rates.[13] Identifying patients at malnutrition risk and detecting MM loss are simple ways to contribute to better patient outcomes.

Evaluating the nutritional status of critically ill patients is challenging as there is no universally accepted gold standard assessment tool. Nonetheless, utilising the most effective tools for assessing these patients and implementing the best possible nutrition strategies is crucial.[14] Further research is needed to develop a better-validated screening tool for assessing nutrition in critically ill patients.

Malnutrition risk and outcome

In a systematic review, the prevalence of malnutrition in critically ill patients varied from 38% to 78%.[2] This review established an independent association between malnutrition and poorer clinical outcomes. Upon hospital admission, around one-third of patients already exhibit signs of malnutrition, and without adequate nutrition therapy, two-thirds of them will experience a worsening of their condition. Furthermore, during their hospital stay, two-thirds of initially non-malnourished patients will develop malnutrition. Malnutrition in critically ill patients is associated with a range of adverse outcomes, including increased infection rates, delayed wound healing, muscle wasting, prolonged mechanical ventilation, and higher mortality rates.[14] The pathophysiology of malnutrition in this population is complex, involving factors such as poor dietary intake, increased nutrient losses, and altered nutrient metabolism.[1] Early identification and management of malnutrition are critical to mitigate these risks. Studies have shown timely nutritional intervention can significantly improve clinical outcomes, highlighting the importance of proactive nutritional support in critically ill patients. According to the GLIM criteria, 2 steps are needed to diagnose malnutrition. The first step requires a validated screening tool to identify patients at risk, and the second step involves diagnosing and grading the severity of malnutrition.[9]

Malnutrition is more common in critically ill patients, mainly due to several contributing factors. Factors such as immobility, prolonged mechanical ventilation, and high levels of inflammation exacerbate the problem, putting patients at risk of skeletal muscle loss and weakness. Energy deficit in critically ill patients is closely linked to longer stays in the ICU, higher likelihood of infections, and increased mortality rates. The relationship between malnutrition and adverse outcomes is complex, influenced by factors such as age, the severity of the disease process, and other underlying medical illnesses.[15]

Malnutrition can be explained through 2 main factors: stress-induced breakdown

of the body and insufficient food intake. In cases of severe illness, the body releases catabolic hormones and proinflammatory agents to increase the breakdown of nutrients. Hormones such as glucagon, cortisol, and catecholamines are produced, releasing stored nutrients such as glucose, amino acids, and fatty acids to support essential organ functions. Inflammatory agents such as interleukin (IL)-1, IL-6, and tumour necrosis factor-alpha, triggered by infection or injury, further contribute to this breakdown process. The primary focus during such conditions is to provide adequate nutrition to sustain organ function and bolster the immune response. Moreover, critically ill patients often have limited nutrient reserves, exacerbated by challenges such as reduced food intake in the ICU, extended periods without eating, and interruptions in feeding schedules, which can inadvertently worsen malnutrition. Detecting and starting feeding protocols early can speed up recovery from severe illness.[16]

Most critically ill patients are in hypercatabolic condition, characterised by increased glycogenolysis, reduced protein synthesis, increased protein breakdown, increased insulin resistance, and lipolysis. These processes result in protein breakdown, hyperglycaemia, sarcopenia, weight loss, and undernutrition. The hypercatabolic condition progresses through different phases, starting with an early acute phase within the initial 48 hours, then a late acute phase spanning the subsequent 3–7 days, and then a chronic phase after 8 days.

In critically ill patients, significant physical stress triggers a catabolic response, resulting in muscle wasting and weakness. The longer the stay in the ICU, the higher the risk of weakness and the poorer the outcome. As stated in GLIM guidelines, MM is a new and innovative marker of malnutrition. Therefore, employing a rapid, non-invasive technique to assess both the quantity and quality of skeletal muscle in critically ill patients could have significant prognostic implications for the diagnosis of malnutrition.

A prospective, observational, multicentre study (EPNIC) conducted by Servia-Goixart *et al.* aimed to evaluate the influence of nutritional therapy on mortality rates among 639 critically ill patients. The study found that old age, higher organ failure scores, and elevated nutritional risk appear to be associated with higher mortality. Additionally, patients who required parenteral nutrition (PN) after initially starting enteral nutrition (EN) were identified as a high-risk subgroup for mortality, likely due to the severity of illness and challenges in receiving adequate nutritional therapy.[17] The average intake of calories and protein also seemed to affect outcomes. Moreover, the prognosis of ICU patients suffering from pre-existing malnutrition and sarcopenia is further complicated by the acute catabolic response typical of critical illness, which leads to rapid loss of LBM, resulting in muscle wasting, weakness, and functional decline.

Assessment of energy expenditure requirements

Accurate estimation of daily resting energy expenditure (REE) is crucial for determining the caloric requirements of critically ill patients to prevent harmful under- or overfeeding. As ICU patients typically engage in minimal physical activity, REE will be close to the total energy expenditure (EE). EE may vary during different phases of critical illness. Indirect calorimetry (IC) is considered the gold standard for measuring REE, as it directly assesses oxygen consumption and carbon dioxide production. However, its use may be limited by availability and practicality in ICU. Predictive equations (PEs) such as the Harris-Benedict, Mifflin-St Jeor, and Penn State equations are commonly used as alternatives. It is widely recognised that PEs are not reliable in predicting EE in the ICU, showing correlations ranging from 0.24 to 0.73 across 12 different equations.[18] Recent data indicates that the metabolic rate measured by IC in COVID-19 patients significantly differed from the values predicted by all commonly used PEs.[19]

Nevertheless, the precision of PEs can exhibit considerable variability depending on the patient population and clinical state. EE estimations derived from PEs can markedly diverge from measurements obtained through IC, potentially resulting in discrepancies of up to 1000 kcal/day from the actual EE. Research conducted by Duan *et al.* demonstrated that the implementation of IC-guided energy provision reduced short-term mortality rates by 23%, likely by averting detrimental effects of under- or overfeeding. Recent meta-analyses published in 2021 reported that patients receiving isocaloric nutrition guided by IC exhibited significantly decreased short-term mortality rates.[20] However, the outcomes of the recent TICACOS-II trial failed to replicate this observed reduction in mortality.[21]

Factors such as fever, sepsis, and mechanical ventilation can significantly alter energy expenditure, necessitating frequent reassessment and adjustment of caloric goals. In a local study recently published by Tah *et al.*, PEs tended to either over- or underestimate REE at different phases of critical illness. PEs with dynamic variables and respiratory data had better agreement with REE measured by IC compared with PEs developed for healthy adults or PE based on static variables.[22] Limited evidence suggests that certain equations are more specific for certain ICU populations. For example, the Penn State equations are considered by some experts as the most appropriate for ICU patients on mechanical ventilation.[15] Tah *et al.* found that even though none of the REEs calculated from PEs had excellent agreement, Swinamer (1990) appears to provide relatively good agreement across 3 phases and could be used to predict REE when IC is unavailable.[22]

Due to the shortcomings of current PEs, there is a continuous discussion

regarding the need for new models to better account for the specific metabolic demands of critically ill patients. The current formulas frequently underestimate energy requirements, increasing the risk of over- or underfeeding. Tah *et al.* developed and validated a new PE from acute phase data and found that it could provide optimal estimates of REE for patients in acute and late phases.[23] However, the equation has not been tested in multicentre trials. Emerging research suggests that artificial intelligence (AI) and machine learning may provide more advanced and individualised predictive tools. AI-driven models can potentially increase the accuracy of EE predictions by analysing large datasets and identifying complex patterns. AI-driven models would ultimately improve the effectiveness of nutritional therapy for patients in critical condition.

According to guidelines outlined by ESPEN and ASPEN on mechanically ventilated critically ill patients, EE assessment should be conducted through IC following stabilisation post- ICU admission.[24] Multiple meta-analyses have underscored the limited utility of PEs, variability exacerbated by challenges in assessing body weight. If IC is used, isocaloric nutrition rather than hypocaloric nutrition can be progressively introduced after the early phase of acute illness. When IC is unavailable, deriving EE evaluations from oxygen consumption (VO2) measurements via a pulmonary arterial catheter or carbon dioxide production (kcal/24 h = VCO_2 x 8.19) from the ventilator is recommended over reliance on PEs.[25] Applying basic weight-based formulas, such as 20-25 kcal/kg/day, may be preferred in cases where both methods are not feasible. If PEs are employed, a preference for hypocaloric nutrition (below 70% of estimated needs) over isocaloric nutrition is recommended during the initial week of ICU admission.[8]

Optimal nutritional delivery

Poor nutrition delivery in ICUs remains a global issue. One potential solution is the objective diagnosis of nutritional needs and personalisation of nutrition delivery for patients. Current ICU nutrition therapy has remained at the “beginning of knowledge”. Accurately measuring ICU patients’ nutritional requirements and their metabolic and clinical responses to nutritional interventions remains challenging. Although EN is preferred, PN is also adequate and produces comparable outcomes. The 3 main challenges in ICU nutrition delivery include:

1. Determining the nutritional target.
2. Achieving this target.
3. Assessing the impact on patient outcomes.

Healthcare providers must know the energy and protein delivered and how this compares to the targets. The availability of computerised nutrition monitoring systems is increasing. Future strategies may involve using muscle monitoring such as ultrasound, CT scans, and BIA to evaluate nutritional risk and monitor responses. In the post-ICU phase, continued use of IC and other muscle assessments should be considered to guide nutrition. Ideally, nutrition should be personalised, incorporating "ready-to-feed" indicators and markers showing when energy delivery is optimised, and protein is used to build lean mass. It is also important to determine the adequacy of energy intake while avoiding overfeeding or underfeeding. Therefore, current and future devices for measuring energy needs and body composition must be developed to achieve these goals.[26]

Current guidelines advocate early EN due to the observation that changes in the gut barrier can occur within 24 hours, manifesting as signs of gut ischaemia, increased permeability, bacterial translocation, and gut microbial imbalance (dysbiosis). Recent meta-analyses reveal that early EN, as opposed to delaying, is associated with reduced complications, lower rates of infectious morbidity, and shorter stays in ICU/hospital. It is advisable to postpone or slow down the advancement of EN in cases of gastrointestinal bleeding, mesenteric ischaemia, gastrointestinal intolerance, risk of aspiration, bowel obstruction, abdominal compartment syndrome, risk of refeeding syndrome (or phosphate levels < 0.65 mmol/L), or when there is unresuscitated haemodynamic instability while on vasopressors. However, no delay is recommended for patients on vasopressors (with norepinephrine infusion < 0.3 mcg/kg/min) who have been adequately resuscitated (evidenced by normal levels of lactate), those with an open abdomen, undergoing neuromuscular blockade, therapeutic hypothermia, extracorporeal membrane oxygenation, or in a prone position. In situations where EN is not viable, ASPEN guidelines emphasise that providing PN for a short period is safe, effective, and yields outcomes comparable to EN. Feeding intolerance is a frequent issue that can usually be effectively managed with prokinetic medications and by providing postpyloric feeding for patients who do not respond to prokinetics. There is no evidence of the superiority of intermittent feeding over continuous EN to support the practice change.[8]

Routine objective measurement EE in the ICU is now feasible due to IC technology advancements. The respiratory quotient (RQ) can reveal underfeeding (RQ < 0.7) or overfeeding (RQ > 1.0).[27] Utilising IC to guide nutritional targets and measure EE may be crucial for future personalised nutrition in the ICU, but should be applied carefully. Measurements are recommended after adequately resuscitating patients, typically after the third day in the ICU. The global availability and advancement of IC technology have made these measurements more accurate and easier to obtain, making it practical for many centres to consider incorporating IC into their practices.

Proper use of IC in suitable patients can help prevent the common issues of underfeeding or overfeeding in the ICU. This approach could enhance the focus on the importance of nutrition therapy in both the ICU and post-ICU settings. Larger trials are needed to confirm the potential benefits of using IC for personalised nutrition and to determine energy requirements across different patient populations accurately.

Significant MM loss is commonly observed during ICU stays. The optimal delivery of amino acids is crucial for maintaining protein homeostasis and counteracting catabolism in healthy individuals. International guidelines suggest increasing protein intake to 1.3–2.0 g/kg/day. However, these recommendations are based on retrospective and prospective cohort studies and lack data on how protein provision affects functional and metabolic outcomes. Despite normal gut protein absorption, it is important to note that increased amino acid provision may not enhance muscle protein synthesis during the acute phase.[28] The anabolic response in the ICU may be diminished due to factors such as anabolic resistance, immobilisation, insulin resistance, inflammation, and low muscle ATP levels. Even though protein can help preserve MM, this does not necessarily lead to improved muscle function. Early resistance training might help maintain MM and reduce muscle loss during critical illness. Recent studies suggest that the timing of protein intake is also important. Protein intake is typically calculated based on total body weight, but it should ideally be based on LM.[29]

In cases of sarcopenic obesity, using total body weight can result in protein overdosing, while it can lead to underdosing in non-sarcopenic obesity. Therefore, it makes sense to base protein provision on absolute LBM, and body composition measurements should be considered. BIA and muscle ultrasound are reliable, affordable, and accessible methods for assessing body composition at the bedside to estimate LBM. Tailoring protein provision to individual ICU protein requirements is challenging and still in the early stages. Bedside techniques such as BIA, muscle ultrasound, and new biomarkers for muscle breakdown, autophagy, inflammation, and insulin resistance may further help personalise protein delivery. Ongoing debate exists about whether high protein intake improves clinical outcomes; however, it may mitigate MM loss. Although protein absorption is normal in critically ill patients, severe skeletal muscle anabolic resistance may limit the benefits of high protein intake.[28] There is an urgent need for trials to evaluate the devices and technologies to determine the best ways to personalise ICU nutrition and improve outcomes throughout the entire ICU patient journey. Developing new markers and technologies to identify when patients can tolerate increased protein/calorie delivery and to measure substrate utilisation is essential.[26]

Conclusion

Malnutrition is a significant and prevalent issue in the ICU, affecting a substantial proportion of critically ill patients. The objective delivery of EE is crucial for managing the nutritional needs of these patients effectively. Ensuring optimal nutrition, particularly concerning adequate caloric and protein intake, is fundamental for ICU patients' recovery and overall health. Implementing personalised nutritional strategies tailored to the specific needs of each critically ill patient can play a vital role in preventing the adverse effects associated with both underfeeding and overfeeding. These strategies should consider each patient's unique metabolic and physiological demands to provide the most appropriate nutritional support. Additionally, comprehensive assessment tools are essential in determining the best approaches to optimise nutritional interventions. These tools can help healthcare providers identify patients at risk of malnutrition, monitor nutritional status, and adjust nutritional plans accordingly. By leveraging these assessment tools, clinicians can improve the efficacy of nutritional support and ultimately enhance clinical outcomes for critically ill patients.

Declarations

Ethics approval and consent to participate
Not required as this is a review.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

References

1. Stumpf F, Keller B, Gressies C, Schuetz P. Inflammation and Nutrition: Friend or Foe? Nutrients. 2023;15(5). https://doi.org/10.3390/nu15051159
2. Lew CCH, Yandell R, Fraser RJL, Chua AP, Chong MFF, Miller M. Association Between Malnutrition and Clinical Outcomes in the Intensive Care Unit: A Systematic Review [Formula: see text]. JPEN J Parenter Enteral Nutr. 2017;41(5):744-58. https://doi.org/10.1177/0148607115625638
3. Fazzini B, Märkl T, Costas C, et al. The rate and assessment of muscle wasting during critical illness: a systematic review and meta-analysis. Crit Care. 2023;27(1):2. https://doi.org/10.1186/s13054-022-04253-0
4. Vincent JL. Give your patient a fast hug (at least) once a day. Crit Care Med. 2005;33(6):1225-9. https://doi.org/10.1097/01.ccm.0000165962.16682.46
5. Ferrie S. What is nutritional assessment? A quick guide for critical care clinicians. Aust Crit Care. 2020;33(3):295-9. https://doi.org/10.1016/j.aucc.2020.02.005
6. World Health Organization. Malnutrition [Internet]. 2024 [cited 2024 May 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/malnutrition
7. Di Vincenzo O, Luisi MLE, Alicante P, et al. The Assessment of the Risk of Malnutrition (Undernutrition) in Stroke Patients. Nutrients. 2023;15(3). https://doi.org/10.3390/nu15030683
8. Singer P, Blaser AR, Berger MM, et al. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023;42(9):1671-89. https://doi.org/10.1016/j.clnu.2023.07.011
9. Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. Clin Nutr. 2019;38(1):1-9. https://doi.org/10.1016/j.clnu.2018.08.002
10. Domenech-Briz V, Gea-Caballero V, Czapla M, et al. Importance of nutritional assessment tools in the critically ill patient: A systematic review. Front Nutr. 2022;9:1073782. https://doi.org/10.3389/fnut.2022.1073782
11. Moonen H, Van Zanten ARH. Bioelectric impedance analysis for body composition measurement and other potential clinical applications in critical illness. Curr Opin Crit Care. 2021;27(4):344-53. https://doi.org/10.1097/mcc.0000000000000840
12. Koo BK. Assessment of Muscle Quantity, Quality and Function. J Obes Metab Syndr. 2022;31(1):9-16. https://doi.org/10.7570/jomes22025
13. Gallagher D, Heymsfield SB, Heo M, Jebb SA, Murgatroyd PR, Sakamoto Y. Healthy percentage body fat ranges: an approach for developing guidelines based on body mass index. Am J Clin Nutr. 2000;72(3):694-701. https://doi.org/10.1093/ajcn/72.3.694
14. Narayan SK, Gudivada KK, Krishna B. Assessment of Nutritional Status in the Critically Ill. Indian J Crit Care Med. 2020;24(Suppl 4):S152-s6. https://doi.org/10.5005/jp-journals-10071-23617
15. Al-Dorzi HM, Arabi YM. Nutrition support for critically ill patients. JPEN J Parenter Enteral Nutr. 2021;45(S2):47-59. https://doi.org/10.1002/jpen.2228
16. Dixit SB, Tiwari NR, Zirpe KG, et al. How Have Nutrition Practices in the ICU Changed in the Last Decade (2011-2020): A Scoping Review. Cureus. 2021;13(6):e15422. https://doi.org/10.7759/cureus.15422

17. Servia-Goixart L, Lopez-Delgado JC, Grau-Carmona T, et al. Evaluation of Nutritional Practices in the Critical Care patient (The ENPIC study): Does nutrition really affect ICU mortality? Clin Nutr ESPEN. 2022;47:325-32. https://doi.org/10.1016/j.clnesp.2021.11.018
18. Oshima T, Berger MM, De Waele E, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. Clin Nutr. 2017;36(3):651-62. https://doi.org/10.1016/j.clnu.2016.06.010
19. Niederer LE, Miller H, Haines KL, et al. Prolonged progressive hypermetabolism during COVID-19 hospitalization undetected by common predictive energy equations. Clin Nutr ESPEN. 2021;45:341-50. https://doi.org/10.1016/j.clnesp.2021.07.021
20. Pertzov B, Bar-Yoseph H, Menndel Y, et al. The effect of indirect calorimetry guided isocaloric nutrition on mortality in critically ill patients-a systematic review and meta-analysis. Eur J Clin Nutr. 2022;76(1):5-15. https://doi.org/10.1038/s41430-021-00919-0
21. Singer P, De Waele E, Sanchez C, et al. TICACOS international: A multi-center, randomized, prospective controlled study comparing tight calorie control versus Liberal calorie administration study. Clin Nutr. 2021;40(2):380-7. https://doi.org/10.1016/j.clnu.2020.05.024
22. Tah PC, Lee ZY, Poh BK, et al. A Single-Center Prospective Observational Study Comparing Resting Energy Expenditure in Different Phases of Critical Illness: Indirect Calorimetry Versus Predictive Equations. Crit Care Med. 2020;48(5):e380-e90. https://doi.org/10.1097/ccm.0000000000004282
23. Tah PC, Poh BK, Kee CC, et al. Do we need different predictive equations for the acute and late phases of critical illness? A prospective observational study with repeated indirect calorimetry measurements. Eur J Clin Nutr. 2022;76(4):527-34. https://doi.org/10.1038/s41430-021-00999-y
24. Compher C, Bingham AL, McCall M, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr. 2022;46(1):12-41. https://doi.org/10.1002/jpen.2267
25. Koekkoek WAC, Xiaochen G, van Dijk D, van Zanten ARH. Resting energy expenditure by indirect calorimetry versus the ventilator-VCO(2) derived method in critically ill patients: The DREAM-VCO(2) prospective comparative study. Clin Nutr ESPEN. 2020;39:137-43. https://doi.org/10.1016/j.clnesp.2020.07.005
26. Wischmeyer PE, Bear DE, Berger MM, et al. Personalized nutrition therapy in critical care: 10 expert recommendations. Crit Care. 2023;27(1):261. https://doi.org/10.1186/s13054-023-04539-x
27. Zusman O, Theilla M, Cohen J, Kagan I, Bendavid I, Singer P. Resting energy expenditure, calorie and protein consumption in critically ill patients: a retrospective cohort study. Crit Care. 2016;20(1):367. https://doi.org/10.1186/s13054-016-1538-4
28. Chapple LS, Kouw IWK, Summers MJ, et al. Muscle Protein Synthesis after Protein Administration in Critical Illness. Am J Respir Crit Care Med. 2022;206(6):740-9. https://doi.org/10.1164/rccm.202112-2780OC
29. Hermans AJH, Laarhuis BI, Kouw IWK, van Zanten ARH. Current insights in ICU nutrition: tailored nutrition. Curr Opin Crit Care. 2023;29(2):101-7. https://doi.org/10.1097/mcc.0000000000001016

© Malaysian Journal of Anaesthesiology 2024; 3:55-63
Case series
https://doi.org/10.35119/myja.v3i1.62

Erector spinae plane block with ropivacaine 0.2% in children: a single-centre case series in a tertiary paediatric centre in Malaysia

Jie Cong **Yeoh**[1], Noor Hasimah Binti **Mohd Sahroni**[2], Ye Yun **Phang**[2], Nirawanti **Binti Mohd Said**[2]

[1]Department of Anaesthesiology and Critical Care, Hospital Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur, Malaysia; [2]Department of Anaesthesiology and Intensive Care Unit, Hospital Tunku Azizah, Wilayah Persekutuan Kuala Lumpur, Malaysia

Abstract

Erector spinae plane block (ESPB) was first described in 2016 by Forero *et al.* as a modified interfascial plane block used for patients with chronic neuropathic thoracic pain. It was applied in the paediatric population for postoperative pain management as early as 2017. Most evidence on the efficacy of ESPB as postoperative analgesia in the literature is mainly found in case reports, but very few trials had been conducted. This case series describes 4 paediatric patients who received ESPB as part of multimodal analgesia while undergoing different types of surgery, *i.e.*, 1 Kasai procedure, 1 closure of stoma, and 2 thoracotomies. All 4 patients had general anaesthesia for the surgery. No complications were observed in relation to the regional anaesthetic technique. Pain control was achieved with a pain score of 0–2 for 3 patients and 2–4 for 1 patient (thoracotomy) on Day 1 postoperatively, while all of them a had pain score of 0–2 on postoperative Day 2. We found ESPB with ropivacaine 0.2% to be a safe and effective analgesia as part of multimodal

Correspondence: Jie Cong Yeoh, Department of Anaesthesiology and Critical Care, Hospital Kuala Lumpur, Jalan Pahang, 50586, Wilayah Persekutuan Kuala Lumpur, Malaysia
E-mail: yeohjiecong@gmail.com

management of postoperative surgical pain. Further studies are needed to validate this observation.

Keywords: erector spinae plane block, paediatric anaesthesia, pain management, regional anaesthesia, ropivacaine

Introduction

Forero *et al.* first described the erector spinae plane block (ESPB) in 2016.[1] However, the exact mechanism of this technique is still unknown. Ultrasound-guided ESPB is a safe[2] and effective method as part of multimodal postoperative analgesia.[3] To our knowledge, paediatric ESPB has appeared in the literature mainly in case reports and case series, with very few well-designed trials.[4-6] To date, there is no standard recommendation on the choice and dosage of local anaesthetic for ESPB in children.[4-5] We report a series of cases of variable age ranges with different types of surgeries performed in our centre with ropivacaine 0.2%.

Case presentation

Case 1

A 1.5-month-old baby boy weighing 4.12 kg was admitted with prolonged jaundice and a clinical diagnosis of biliary atresia, presenting signs of obstructive jaundice with abnormal liver function test results and a prolonged activated partial thromboplastin time (APTT). The patient underwent an on-table cholangiogram (OTC) followed by Kasai procedure under general anaesthesia. Due to deranged liver function tests and prolonged APTT, regional analgesia was preferred over central neuraxial blockade during surgery. Maintenance of anaesthesia consisted of sevoflurane/oxygen/air mix along with intravenous (IV) morphine 0.15 mg/kg intraoperatively. ESPB with ultrasound guidance and aseptic technique via Stimuplex A 22-G needle (B Braun Medical S.A, Uriburu, Argentina) was administered with 4 ml ropivacaine 0.2% in total (maximum total dose of 5 ml, 2.5 mg/kg) at T6 level on each side of the ESP with 2 ml each, in lateral position (Fig. 1, labelled as Case 1), as the incision was a rooftop incision. The procedure was performed post-surgery under general anaesthesia prior to extubation without any immediate complications. Morphine infusion at a rate of 15 mcg/kg/hr with face, leg, activity, cry, consolability (FLACC) score = 2 was initiated in the first 12 hours postoperatively and was reduced to 10 mcg/kg/hr by Day 1 and 2 after surgery was completed. This dosage was ceased once feeding became feasible on postoperative Day 3.

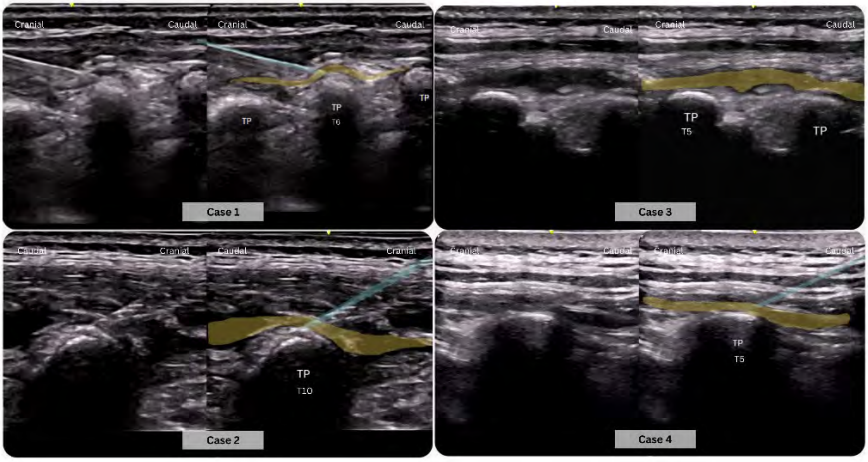


Fig. 1. The spread of local anaesthetic at the erector spinae plane. Yellow: local anaesthetic; blue: needle trajectory, TP: transverse process.

Case 2

An 8-year-old female with a weight of 18.4 kg was electively admitted for stoma closure due to post-perineal canal repair on colostomy. The patient had previously undergone sigmoid colostomy and lay open surgery 3 months prior and was undergoing treatment for relapsed pre-B-cell acute lymphoblastic leukaemia complicated by blinatumomab-induced central nervous system complications. Anaesthesia was maintained via mixed sevoflurane/oxygen and air. ESPB was performed with ropivacaine 0.2% 9 ml (maximum total dose of 23 ml, 2.5 mg/kg) with preservative-free clonidine (1.5 mcg/kg), administered via Stimuplex Ultra 360 20-G (B Braun Aesculap Japan Co Ltd, Ogaki, Japan) needle under ultrasound in-plane technique at the level of T10 in lateral position (Fig. 1, labelled as Case 2). The procedure was conducted under general anaesthesia before extubation. The child experienced no immediate complications and was observed in the regular ward after full recovery from general anaesthesia. Intravenous paracetamol 15 mg/kg was prescribed every 6 hours for a day, then switched to oral once the patient could tolerate oral medication. The postoperative pain score ranged from 0 to 1 on Day 1, and the child sat up in bed on postoperative Day 2.

Case 3

A 15-year-old girl weighing 46.3 kg was electively admitted for left thoracotomy and lung nodulectomies due to metastasis from osteosarcoma of the left proximal tibia, which had been treated with chemotherapy followed by resection and mega prosthesis reconstruction 3 months prior to this surgery. The surgery was performed under general anaesthesia with inhalational agents (sevoflurane, oxygen/air mix) using a double lumen endobronchial tube, with IV morphine analgesia (0.15 mg/kg) and a supplement with intercostal nerve block administered by the surgeon at its conclusion. Postoperatively, ESPB with ultrasound-guided in-plane technique via Stimuplex A 21-G needle and aseptic condition administered ropivacaine 0.2% 20 ml (maximum total dose of 57 ml, 2.5 mg/kg) at T5 level in lateral position (Fig. 1, labelled as Case 3), corresponding with the surgical incision site. The child was extubated without any complications. Post-surgery, patient-controlled analgesia (PCA) morphine was prescribed with a dosage of 1 mg/kg/day for the first 24 hours (pain score 2–4), followed by a reduced dosage of 0.6 mg/kg/day on Day 2 (pain score 0–2) before being discontinued entirely on Days 2 and 3 (pain score also 0–2). Multimodal analgesia comprising paracetamol, diclofenac, and oxycodone was introduced before the discontinuation of PCA morphine. There were episodes of vomiting postoperatively (Days 1 and 2) that required additional doses of metoclopramide and ondansetron, likely due to opioid use.

Case 4

A 13-year-old girl, weighing 32.1 kg, was admitted for a left thoracotomy for lung nodulectomies to address recurrent lung metastasis from proximal tibia osteosarcoma. One month prior, she had undergone the same procedure on her right side without complications or decreased effort tolerance. General anaesthesia with double-lumen endobronchial tube insertion was used during surgery, along with IV morphine and intercostal nerve block, under direct visualisation by the surgeon. Postoperative pain management included ESPB using ultrasound-guided technique via Stimuplex A 21-G needle with ropivacaine 0.2% 20 ml (maximum total dose of 40 ml, 2.5 mg/kg) administered at T5 level in lateral position (Fig. 1, labelled as Case 4), corresponding to the surgical incision site. The procedure was performed during general anaesthesia before extubation with no observed complications. Post-operation, PCA morphine was prescribed and her usage within 24 hours ranged from 0.5 mg/kg/day (pain score: 0–2) to 0.2 mg/kg/day on Day 2 (pain score: 0–1). The patient achieved the ability to sit up by Day 2 and was PCA-free on Day 3 with multimodal analgesia including paracetamol, diclofenac, and morphine administered as necessary.

Table 1. Summary of case series described

Variables	Case 1	Case 2	Case 3	Case 4
Age/ Body weight	1.5 months/ 4.12 kg	8 years/ 18.4 kg	15 years/ 46.3 kg	13 years/ 32.1 kg
Type of surgery	Kasai procedure for biliary atresia	Closure of stoma	Thoracotomy for lung nodulectomies	Thoracotomy for lung nodulectomies
Surgical incision	Rooftop incision	Left flank (at the level of umbilicus)	Left thoracotomy (~level T5)	Left thoracotomy (~level T5)
Level of injection	T6	T10	T5	T5
Preop or postop block*	Postop	Postop	Postop	Postop
Choice and volume of local anaesthetic	4 ml ropivacaine 0.2% (2 ml on each side of ESPB) (maximum dose: 5 ml, 2.5 mg/kg)	9 ml ropivacaine 0.2% + 1.5 mcg/kg clonidine as additive (maximum dose: 23 ml, 2.5 mg/kg)	20 ml ropivacaine 0.2% (maximum dose: 57 ml, 2.5 mg/kg) Intercostal nerve block (direct visualization) by surgeon prior to closure	20 ml ropivacaine 0.2% (maximum dose: 40 ml, 2.5 mg/kg) Intercostal nerve block (direct visualization) by surgeon prior to closure
Postoperative choice of analgesia and PS	Morphine infusion: 15 mcg/kg/hr during the 1st 12 hr; reduced to 10 mcg/kg/hr subsequently Opioid free POD 3	Intravenous paracetamol 15 mg/kg for 1 day and switched to oral paracetamol once tolerated orally	PCAM: 1 mg/kg/day for 1st 24 hr (PS 2–4) 0.6 mg/kg/day (PS 0–2) weaned POD 2-3 Oral paracetamol + diclofenac + oxycodone initiated prior to PCAM discontinuation	PCAM: 0.5 mg/kg/day for 1st 12 hr (PS 0–2) 0.2 mg/kg/day (PS 0–2) weaned POD 3 Oral paracetamol + diclofenac + oxycodone initiated prior to PCAM discontinuation
Complication(s)	Nil	Nil	Nil	Nil

*Preop refers to block prior to surgical incision; postop refers to block prior to extubation.
PCAM: Patient-controlled analgesia morphine; POD: Postoperative day; PS: Pain score

Discussion

Paediatric postoperative pain management poses a challenge, especially in infants and young children due to the subjective and complex nature of pain. Distinguishing between various emotional responses, such as anxiety or distress, can be tricky in some cases. Multimodal analgesia has emerged as an alternative approach to reduce opioid consumption during perioperative pain treatment. Regional anaesthesia using ultrasound-guided nerve blocks has gained popularity since its development in the 1990s for use alongside general anaesthesia as multimodal analgesic therapy during surgery.

In 2016, Forero *et al.* introduced the erector spinae plane nerve block,[1] which has since become a reliable and safe technique of multimodal postoperative analgesia. Nevertheless, evidence in relation to paediatric patients remains limited and primarily reliant on case reports.[4-6] In this case series, we present 4 cases (Table 1) wherein the application of an ESPB was utilised during intra-abdominal and thoracic surgery procedures performed on paediatric patients.

In the first case, ESPB was preferred over an epidural block due to the patient's coagulopathy.[7] This technique is deemed safe because it involves administering injections at a site distant from vascular and nerve structures. ESPB served as postoperative analgesia alongside IV morphine administration. The FLACC score was utilised to gauge the pain levels in this patient. A score of 0 for 3 days after surgery is an indication of good pain management. This case study supports the use of ESPB as effective multimodal analgesic combined with a reduced need for IV opioids.

The second case involved the utilisation of ESPB as a form of multimodal analgesia in conjunction with IV paracetamol after surgery. Pain evaluation was conducted by means of the Malaysian Ministry of Health face scale,[8] revealing that the patient experienced minimal discomfort rated between 0 and 1 from the postoperative period up to 2 days following the procedure, allowing for prompt mobilisation (sitting). ESPB was implemented as supplementary support for postoperative pain management without resorting to opioid administration, supporting its potential use as an alternative method for avoiding opioids and diminishing their undesirable effects. Consequently, this approach can be classified under opioid-sparing surgery techniques.

The third and fourth case studies focused on the use of ESPB during thoracic surgery in the adolescent age group. Administering a thoracic epidural to adolescents in lateral position after general anaesthesia is challenging due to the thoracic spine curvature becoming more prominent in adolescents, which further narrows the space for Tuohy needle introduction, unlike in younger children where

the thoracic vertebrae spines remain almost horizontal.[9] However, utilising ESPB can effectively decrease postoperative pain when combined with IV opioids and other multimodal analgesia methods for thoracic surgeries. These cases showed reduced opioid consumption per day, which ranged between 0.5 and 1.0 mg/kg/day, along with lower immediate postoperative to postoperative Day 2 pain scores in the range of 0–2.

Positioning

ESPB is often performed in the preoperative stage for adult patients, usually when they are seated and cooperative. However, in paediatric cases, this procedure can only be conducted after the child has been anesthetised, similar to other regional anaesthesia techniques. As a result, we have the option to administer this block with the patient positioned either prone or lateral; we tend to use the lateral position at our centre. These positions pose some challenges in obtaining a clear view during block application but can be overcome with practice.

Equipment (transducer and needle choice)

The selection of ultrasound probe and needle size relies on the patient's body structure, which varies from newborns to young adults. For neonates, we prefer to use a hockey stick transducer, a high-frequency probe with a smaller footprint for ultrasound-guided regional anaesthetic administration, as it provides more space for needle entry and allows better control of probe angulation. Additionally, there are several options in needle choices between young adolescents and neonates; typically, we use a 25–50 mm Stimuplex echogenic needle (*i.e.*, Stimuplex Ultra 360 20-G needle) for these procedures as it offers improved visualisation of the needle tip during in-plane ultrasound visualisation.

Conclusion

ESPB with ropivacaine 0.2% is safe and effective analgesia as part of multimodal management of postoperative surgical pain in children. Further research is required to better elucidate best practices for paediatric ESPB.

Declarations

Informed consent for publication

The patients and/or their guardian have provided informed consent for the publication of the clinical data contained in this case series.

Competing interests

None to declare.

Funding

None to declare.

Acknowledgements

We would like to thank the Director General of Health Malaysia for his permission to publish this article.

References

1. Forero M, Adhikary SD, Lopez H, Tsui C, Chin KJ. The erector spinae plane block: a novel analgesic technique in thoracic neuropathic pain. Reg Anesth Pain Med. 2016;41:621-627. https://doi.org/10.1097/AAP.0000000000000451
2. Ecoffey C, Lacroix F, Giaufré E, Orliaguet G, Courrèges P; Association des Anesthésistes Réanimateurs Pédiatriques d'Expression Française (ADARPEF). Epidemiology and morbidity of regional anesthesia in children: a follow-up one-year prospective survey of the French-Language Society of Paediatric Anaesthesiologists (ADARPEF). Paediatr Anaesth. 2010 Dec;20(12):1061-9. https://doi.org/10.1111/j.1460-9592.2010.03448.x
3. Aksu C, Gurkan Y. Defining the Indications and Levels of Erector Spinae Plane Block in Pediatric Patients: A Retrospective Study of Our Current Experience. Cureus. 2018;11(8):e5348. https://doi.org/10.7759/cureus.5348
4. Elkoundi A, Bentalha A, Kettani SEE, Mosadik A, Koraichi AE. Erector spinae plane block for pediatric hip surgery - a case report. Korean J Anesthesiol. 2019 Feb;72(1):68-71. https://doi.org/10.4097/kja.d.18.00149
5. Lucente M, Ragonesi G, Sanguigni Met al. Erector Spinae Plane Block in Children: a Narrative Review. Korean J Anesthesiol. 2022 Jul 5. https://doi.org/10.4097/kja.22279
6. Aksu C, Şen MC, Akay MA, Baydemir C, Gürkan Y. Erector Spinae Plane Block vs Quadratus Lumborum Block for pediatric lower abdominal surgery: A double blinded, prospective, and randomized trial. J Clin Anesth. 2019 Nov;57:24-28. https://doi.org/10.1016/j.jclinane.2019.03.006

7. Ayub A, Talawar P, Kumar R, Bhoi D, Singh AY. Erector Spinae Block a safe, simple and effective analgesic technique for major hepatobiliary surgery with thrombocytopenia. Egyptian Journal of Anaesthesia. 2018 Oct;34(4):169–72.
8. Ministry of Health Malaysia. Pain as the 5th Vital Sign Guideline: 3rd Edition [Internet]. 2018. Available from: https://www.moh.gov.my/moh/resources/Penerbitan/Program%20Bebas%20Kesakitan/Garis%20Panduan/2_in_1_P5VS_Guideline_3rd_Edition_Corrected_2020.pdf
9. Epidural Anaesthesia in Children [Internet]. WFSA Resource Library. [cited 2024 Mar 16]. Available from: https://resources.wfsahq.org/atotw/epidural-anaesthesia-in-children

© Malaysian Journal of Anaesthesiology 2024; 3:64-71
Case report
https://doi.org/10.35119/myja.v3i1.49

Propofol-induced postoperative unconsciousness in hepatocellular carcinoma

Mohammad Faiz Taqiyuddin **Mohd Nor**, Nurul 'Aifaa **Mohd Azmi**, Wan Fadzlina **Wan Muhd Shukeri**, Shamsul Kamalrujan **Hasan**

Department of Anaesthesiology and Critical Care, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Abstract

Although propofol is a commonly used medication for inducing general anaesthesia, it is not without side effects. In this case report, we present a patient with hepatocellular carcinoma who experienced postoperative unconsciousness following general anaesthesia induction using propofol. While this is a rare occurrence, it underscores the importance of remaining vigilant and understanding propofol's pharmacokinetic properties. The drug can be redistributed from fat tissues into the systemic circulation, resulting in delayed recovery and potential adverse effects. We also discuss the possible impact of disease interactions, particularly hepatic impairment with possible CYP450 deficiency, on propofol metabolism. We stress the necessity of closely monitoring patients during anaesthesia induction and maintenance.

Keywords: CYP450 deficiency, postoperative unconsciousness, propofol

Correspondence: Mohammad Faiz Taqiyuddin Bin Mohd Nor, Department of Anaesthesiology and Intensive Care, School of Medical Sciences, Universiti Sains Malaysia, Jalan Raja Perempuan Zainab 2, 16150, Kubang Kerian, Kelantan, Malaysia.
E-mail: faiztaqiu@usm.my

Introduction

Postoperative unconsciousness with propofol induction is a rare incident that occurs in 1/10,000 cases.[1] Recovery from anaesthesia with the use of propofol is usually rapid. However, in our case, the redistribution of propofol from fat tissues into the systemic circulation after propofol induction and maintenance of anaesthesia caused our patient to experience a loss of consciousness post-extubation. Here, we will discuss propofol and its side effects, as well as disease interactions with propofol that may interfere with drug metabolism and pharmacokinetics.

Case presentation

A 37-year-old Malay female, weighing 55 kg, with a known case of hepatocellular carcinoma (HCC) presented to our centre on 25 October 2022 for a scheduled computerised tomography (CT)-guided microwave coagulation therapy (MCT) of HCC under general anaesthesia. The patient had previously been diagnosed with hepatitis B in April 2022 but was otherwise healthy, with all blood test results being normal and classified as Child Pugh A. Her blood results are shown in Table 1.

Table 1. Results of admission investigations

Haematology		**Biochemistry**		**Liver function test**	
Hb	11.4 g/dL	Urea	1.8 (mmol/L)	ALB	31 g/L
WBC	5.72 (x 109/L)	Sodium	138 (mmol/L)	ALP	166 U/L
Platelets	299 (x 109/L)	Potassium	3.8 (mmol/L)	ALT	15 U/L
PT	15.6 secs	Chloride	109 (mmol/L)	AST	70 U/L
INR	1.16	Creatinine	54 (µmol/L)	Bilirubin	23 µmol/L
APTT	42 secs				

ALB: albumin; ALP: alkaline phosphatase; APTT: activated partial thromboplastin time; AST: aspartate aminotransferase; ALT: alanine transaminase; Hb: haemoglobin; INR: international normalized ratio; PT: prothrombin time

On the day of the event, she was electively intubated at the operating theatre and induced with intravenous (IV) fentanyl 100 mcg, IV propofol 150 mg, and IV rocuronium 50 mg. She was then transported with IV injection (IVI) of fentanyl and propofol to the radiology department for the procedure.

Upon arrival, however, there was a technical error with the ventilator machine; hence, we were unable to maintain anaesthesia using sevoflurane gas. As the patient's sedation weaned off after transitioning from IV sedation to gas sedation, the patient required multiple boluses of IV propofol to deepen the sedative effect. For the first hour of the procedure, anaesthesia was maintained with IVI propofol 1% (5–20 ml/h) (as no target-controlled infusion pump was available) and IVI fentanyl (10 mcg/ml) run at 2–4 ml/h.

The ventilator issue was resolved after a while, and we were able to switch back to sevoflurane to maintain anaesthesia. The intraoperative period was uneventful, with stable haemodynamic parameters and no desaturation episodes observed throughout the procedure. The patient successfully underwent MCT of liver lesions in segments II/III and VI. Intraoperative analgesia included IV paracetamol (1 g), IV magnesium sulfate (2.47 g), and IV morphine (6 mg). She was then transported back to the operating theatre for extubation and reversed with IV sugammadex 200 mg. Her Aldrete and Post Anaesthetic Discharge Scoring System scores post-extubation were 8 and 6, respectively, and she was sent to the ward after 30 minutes of monitoring in the recovery bay area.

However, upon arrival at the ward, the patient was unresponsive to calls and reported having laboured breathing. Glasgow Coma Scale (GCS) documented E1V1M1, but hemodynamically stable, with no desaturation episode and normal serum glucose (10.6 mmol/L). She was then transferred to the intensive care unit (ICU) and re-intubated for poor GCS. She received intermittent positive pressure ventilation overnight, and her GCS improved to E4VTM6 the next day, allowing her to be successfully extubated. As no significant causes for her unconsciousness were identified, we postulated that her GCS drop might have been due to remnants of the propofol effect, unmetabolised due to liver impairment. This was further evidenced by her liver enzymes rising from baseline upon ICU admission (Table 2).

The patient was also scheduled for a CT scan of the brain to rule out any potential pathology that may have contributed to the event, but she died due to advanced HCC with lung metastasis in January 2023.

Table 2. Serial liver function test investigation

Variable	25/10/22	26/10/22 (post MCT)	27/10/22 (2nd day ICU)	9/11/22 (Clinic follow-up)	Normal range
AST (U/L)	70	152	195	76	5–34
ALT (U/L)	15	34	47	15	< 34
ALP (U/L)	166	144	134	165	42–98
ALB (g/L)	31	28	28	31	38–44
Total protein (g/L)	69	62	62	70	

ALB: albumin; ALP: alkaline phosphatase; AST: aspartate aminotransferase; ALT: alanine transaminase; MCT: microwave coagulation therapy

Discussion

Propofol, chemically described as 2,6-diisopropylphenol, is a commonly used IV anaesthetic agent that can produce a rapid onset of unconsciousness and amnesia in patients. IV infusion of a therapeutic dose of propofol induces anaesthesia with minimal excitement within 40–60 seconds of the injection (the time it takes the injected dose in 1 arm to reach the brain). The half-time of blood-brain equilibration, like that of other fast-acting IV anaesthetic drugs, is roughly 1 to 3 minutes, accounting for the rate of anaesthesia induction. The mechanism of action, as with all general anaesthetics, is poorly known. Propofol is believed to cause its sedative and anaesthetic effects by positively modulating the inhibitory activity of the neurotransmitter GABA through the beta subunit GABAα receptors.[1,2]

Propofol pharmacokinetics is well represented by a 3-compartment linear model, with compartments representing plasma, fast-equilibrating tissues, and slowly equilibrating tissues. Following an IV bolus dosage, there is quick equilibration between the plasma and the brain, which explains the rapid onset of anaesthesia. Plasma levels first fall quickly as a result of both distribution and metabolic clearance. After a propofol bolus, distribution contributes to approximately half of the reduction. However, distribution does not remain constant throughout time; rather, it declines as tissues throughout the body equilibrate with plasma and become saturated. The rate at which equilibration occurs varies depending on the pace and length of the infusion. When equilibration occurs, there is no longer any net transport of propofol between tissues and plasma. Whereas about 1% of total plasma propofol is unbound, the free fraction of propofol in the cerebrospinal fluid (CSF) is approximately 31%. After 30 minutes, the blood and brain concentrations reach equilibrium, yielding a

total blood-to-CSF propofol ratio of 0.01 to 0.02. Because of the rapid initial distribution of a single bolus or short infusion, the time to neutralise clinical effects is brief. Because of its high lipid solubility, propofol can be redistributed to and from a slow compartment. This compartment has a high capacity to absorb propofol, resulting in a very large apparent volume of distribution at steady state (3–4 multiples of total body volume), even in non-obese individuals. Nonetheless, even after extended administration, the clinical effects are neutralised rather quickly as compared to other IV hypnotics because drug redistribution from the slow compartment is slower than metabolism and excretion.[2]

In contrast to other hypnotics, propofol has a typically favourable context-sensitive decrement time. Short infusions (< 3 h) have an 80% decrement time of < 50 min, but the decrement for larger infusions (> 12 h) can reach up to 3.5 hours. Propofol clearance in adults ranges from 23 to 50 mL/kg/min (1.6 to 3.4 L/min in individuals weighing 70 kg). It is primarily removed through hepatic conjugation into inactive metabolites that are excreted by the kidney (Fig. 1). A glucuronide conjugate accounts for nearly half the delivered dosage. In healthy humans, the steady-state volume of distribution for propofol (10-day infusion) is approximately 60 L/kg. In a typical adult, immediate post-anaesthesia recovery occurs after approximately 10 minutes of induction; however, recovery may be slightly delayed in cirrhotic patients.[2]

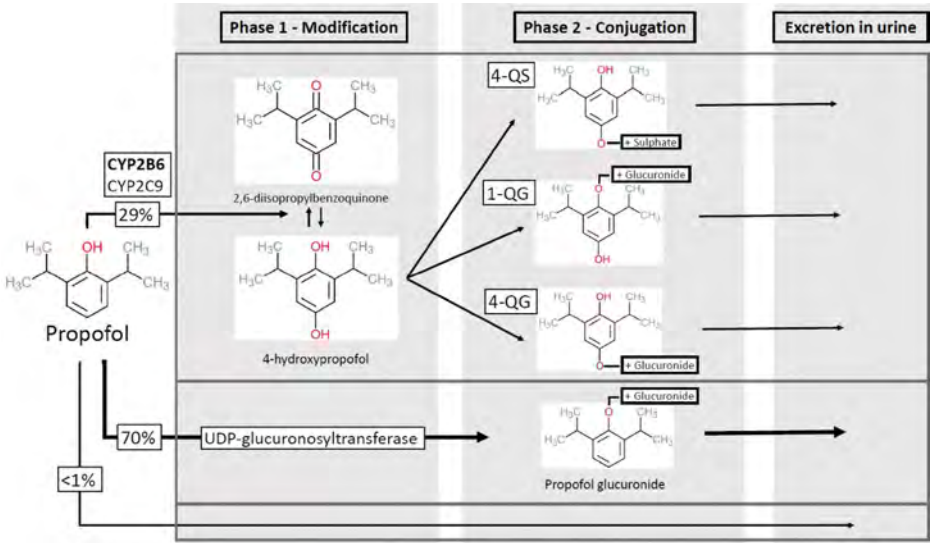


Fig. 1. Propofol metabolic pathway. CYP; cytochrome P450; UDP: uridine 5′-diphosphate; 4-QS: 4-hydroxypropofol sulphate; 1-QG: 1-hydroxypropofol glucuronide; 4-QG: 4-hyroxy-propofol-glucoronide. Reproduced from Sahinovic *et al.*[3]

Of all types of liver cancer, HCC is the most prevalent. Overall, primary liver cancer ranks as the fifth most frequently diagnosed cancer and the third most common cause of cancer-related deaths globally.[6] Of the various methods that can be used to treat liver cancer, MCT was chosen for our patient. Skin burns, liver capsule bleeding, and intense discomfort are 3 of the most prevalent MCT consequences. When a tumour is larger than 5 cm in diameter, cancer cells may become thermoresistant and undergo active proliferation, encouraging tumour spread and recurrence. Nonetheless, MCT may outperform conventional therapy options for HCC.[7] Therefore, the procedure shows no correlation with our patient's unfortunate event.

However, as we go back to the disease itself, the activity and protein levels of 7 major cytochrome P450 enzymes have been shown to be significantly and sometimes severely reduced in HCC tumours, most likely due to reduced transcription or mRNA stability. Hence, all the major drug-metabolising CYPs are severely dysregulated by liver cancer carcinogenesis, although the different drugs will be affected differently in different patients.[8] As we discussed earlier, propofol is redistributed from its slow compartment back into circulation after an initial bolus or infusion. If the rate of metabolism of propofol is impaired due to CYP enzyme deficiency, the active metabolite can still exert its full effect even after the patient appears to have recovered from the general anaesthetic effect. Given the absence of other plausible explanations for our patient's postoperative unconsciousness, it is reasonable to conclude that the redistribution of propofol was the cause.

Another likely explanation for our patient's loss of consciousness is propofol infusion syndrome. Propofol infusion syndrome, an uncommon and possibly fatal illness, was initially observed in children in 1990 and more recently in adults undergoing long-term (> 48 h) high-dose propofol infusions (> 5 mg kg^{-1} h^{-1}). Typical signs of propofol infusion syndrome include lactic acidosis, haemodynamic instability (arrhythmia and hypotension), acute renal injury, rhabdomyolysis, hypertriglycaeridemia, and liver failure.[10]

The exact cause of propofol infusion syndrome is not fully understood, but it is believed to be related to mitochondrial dysfunction. Early theories proposed that propofol might act as a mitochondrial uncoupler or interfere with fatty acid oxidation. Studies have shown that propofol may disrupt the respiratory chain, leading to decreased ATP production and metabolic acidosis.[10] It is thought that propofol inhibits enzymes like carnitine palmitoyl transferase I, causing an accumulation of fatty acids in the mitochondria and impairing energy production. Experiments in rats suggest that propofol's structure, similar to that of coenzyme Q, allows it to inhibit electron transfer in the respiratory chain.[9] Microscopic evidence has also indicated mitochondrial damage in cardiac muscle due to propofol. Case

studies have highlighted the importance of the cumulative dose of propofol, with higher rates and longer infusions increasing the risk of the syndrome.[10] However, even low doses can cause issues in individuals with genetic mitochondrial defects.

Mitochondrial dysfunction is a critical contributor to muscle weakness. Mitochondria are the powerhouses of cells, providing the energy necessary for muscle function. When mitochondria are damaged or dysfunctional, they cannot produce sufficient energy, leading to muscle fatigue and weakness, which, in our case, mimicked the "collapse" state of our patient. However, because our patient did not me*et all* the criteria for propofol infusion syndrome, we did not consider it to be the primary cause of our patient's decrease in GCS.

Conclusion

Propofol is an IV anaesthetic agent primarily metabolised by the liver through the CYP enzyme system, which also metabolises other drugs. CYP450 deficiency can slow propofol clearance, resulting in higher plasma concentrations of propofol, which in turn can lead to prolonged sedation and respiratory depression. However, it is important to note that CYP450 deficiency is a relatively rare condition and not all patients will exhibit this phenotype. Overall, CYP450 deficiency, such as presumed in our patient, can lead to altered pharmacokinetics of propofol, including impaired metabolism and altered redistribution, which can result in prolonged sedation and anaesthesia. Hence, close monitoring is crucial to ensure patient safety.

Declarations

Informed consent for publication
The patient provided informed consent for the publication of the clinical data contained in this case report.

Competing interests
Dr. Wan Fadzlina Wan Muhd Shukeri serves as Section Editor for Malaysian Journal of Anaesthesiology. She has not been involved in any part of the publication process prior to manuscript acceptance. The remaining authors have no competing interests to declare.

Funding
None to declare.

Acknowledgements
None to declare.

References

1. MIMS Online Team. Fresofol 1% MCT/LCT Full Prescribing Information, Dosage & Side Effects | MIMS Hong Kong. MIMS Hong Kong [Internet]. n.d. Available from: https://www.mims.com/hongkong/drug/info/fresofol%201percent%20mct-lct?type=full
2. Suh SJ, Yim HJ, Yoon EL, et al. Is propofol safe when administered to cirrhotic patients during sedative endoscopy? Korean J Intern Med. 2014;29(1):57. https://doi.org/10.3904/kjim.2014.29.1.57
3. Sahinovic MM, Struys MM, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. Clin Pharmacokinet. 2018;57(12):1539-1558. https://doi.org/10.1007/s40262-018-0672-3
4. Iwersen-Bergmann S, Rösner P, Kühnau HC, Junge M, Schmoldt A. Death after excessive propofol abuse. Int J Legal Med. 2001;114:248-251. https://doi.org/10.1007/s004149900129
5. Propofol - LiverTox - NCBI Bookshelf. Propofol - LiverTox - NCBI Bookshelf. 2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK547909/#:~:text=Propofol%20has%20been%20associated%20with,an%20enlarged%20or%20fatty%20liver
6. Bosetti C, Turati F, La Vecchia C. Hepatocellular carcinoma epidemiology. Best Pract Res Clin Gastroenterol. 2014;28(5):753-70. https://doi.org/10.1016/j.bpg.2014.08.007
7. Chen X, Liu HP, Li M, Qiao L. Advances in non-surgical management of primary liver cancer. World J Gastroenterol. 2014;20(44):16630. https://doi.org/10.3748/wjg.v20.i44.16630
8. Yan T, Lu L, Xie C, et al. Severely impaired and dysregulated cytochrome P450 expression and activities in hepatocellular carcinoma: implications for personalized treatment in patients severely impaired and dysregulated activities of CYPs in HCC. Mol Cancer Ther. 2015;14(12):2874-2886. https://doi.org/10.1158/1535-7163.MCT-15-0274
9. Vanlander AV, Menten B, Smet J, et al. Possible pathogenic mechanism of propofol infusion syndrome involves coenzyme Q. Anesthesiology. 2015;122(2):343-352. https://doi.org/10.1097/ALN.0000000000000484
10. Hemphill S, McMenamin L, Bellamy MC, Hopkins PM. Propofol infusion syndrome: a structured literature review and analysis of published case reports. Br J Anaesth. 2019;122(4):448-459. https://doi.org/10.1016/j.bja.2018.12.025

© Malaysian Journal of Anaesthesiology 2024; 3:72-78
Case report
https://doi.org/10.35119/myja.v3i1.57

Misoprostol-induced seizures following self-abortion: a rare, but repeated occurrence

Darshelaan **Purushotmanan**

Department of Anaesthesiology and Intensive Care, Hospital Wanita dan Kanak Kanak, Sabah, Malaysia

Abstract

Misoprostol is a synthetic prostaglandin E1 (PGE) analogue used for medical termination of pregnancy, managing miscarriage, inducing labour, cervical ripening, and treating postpartum haemorrhage. Generally, it is safe and well-tolerated, with dose-dependent adverse effects such as nausea, vomiting, diarrhoea, abdominal pain, fever, and headache that usually resolve within a few days. However, seizures are a rare complication, occurring primarily in patients with a history of epilepsy or a predisposition to seizures and is associated with high doses and rapid administration. This case report highlights the repercussions of a misoprostol overdose used for pregnancy termination, leading to seizures induced by hyperthermia. The first patient required temporary invasive ventilation and resuscitation but recovered, whereas the second patient receiving a lower dose, exhibited milder symptoms. Both patients received psychosocial counselling prior to discharge.

Keywords: early pregnancy, misoprostol, pregnancy termination, seizure

Correspondence: Dr. Darshelaan Purushotmanan, 1086, JLN BPJ 2/23, Bandar Puteri Jaya, 08000, Sungai Petani, Kedah, Malaysia.
E-mail: darshelaanpurushotmanan@gmail.com

Introduction

There is an increasing trend of individuals turning to non-medical sources for abortifacients, which can lead to the misuse and abuse of medically approved drugs such as misoprostol. Despite being illegal in Malaysia, the widespread availability and affordability of the drug have contributed to its misuse, resulting in severe complications and morbidity in some cases. This report presents two cases of patients who presented with seizures after allegedly self-administering excessive amounts of misoprostol orally and vaginally. Treatment of such cases involves stabilising the patient's condition, monitoring vital signs, and addressing any complications that may arise.

Case presentation

Case 1

A 32-year-old lady, gravida 2 para 1 (with 1 set of twins), was brought to the emergency department by her husband with complaints of severe abdominal pain and behavioural changes after ingesting an unknown medication at midnight. The patient had no known medical illnesses; however, the husband claimed that she had postpartum depression following her first pregnancy, which required admission for 4 days. Subsequently, she was discharged home with psychoeducation and counselling. Upon further history, the husband revealed that the patient had self-administered misoprostol orally and vaginally, with a total dosage of 1400 mcg.

In the emergency room, the patient was delirious, agitated, and aggressive, prompting the emergency response team to initiate a red alert. The initial impression was meningoencephalitis, as the patient had a high-grade fever with a temperature of 42.5°C and exhibited bizarre behaviour. Clinically, she was tachycardic, with a heart rate of 140 beats per minute (bpm); tachypnoeic, with a respiratory rate of 30–40 breaths per minute; and hypotensive, with blood pressure (BP) of 80/40 mmHg. She was pale with minimal vaginal bleeding and premature uterine contractions. There were no other features of anaphylaxis. The patient suddenly developed unusual seizure symptoms, including spasmodic incurving of fingers resembling carpopedal spasms of the hand in hypocalcaemia, lip-smacking phenomena, and blank staring eyes. This occurred approximately 6 times, with no regaining of postictal consciousness in between.

A decision was made to intubate her, with a rapid sequence intubation using intravenous (IV) fentanyl 100 mcg, IV midazolam 5 mg, and IV succinylcholine 100 mg to prevent impending collapse and airway protection. Following intubation, she received a fluid bolus of 30 ml/kg of crystalloid and 10 ml/kg of colloid. Low-dose inotropes were started, parenteral antipyretics were administered, and tepid sponging was performed to reduce fever. An urgent bedside ultrasound performed by the obstetric team revealed an estimated gestational age of 16 weeks with no foetal heartbeat present and no free fluid observed. At this point, the differential diagnosis included meningoencephalitis, septic shock due to septic abortion with disseminated features, electrolyte imbalance, anaphylactic shock, and possible misoprostol-induced seizure.

Blood tests showed mild hypomagnesaemia. Cultures from blood and vaginal swabs were negative and the brain CT scan was normal. She received a loading dose of IV phenytoin 1 g over 1 hour and was transferred to the ICU for monitoring and ventilatory support. She had no further convulsions and was extubated the same day. The medically induced delivery of the non-viable foetus was uneventful. She was given IV ceftriaxone for 3 days, followed by IV ampicillin-sulbactam for a week. Based on the evidence, the final diagnosis was misoprostol-induced convulsions. The patient completed her antibiotic regimen and was referred to the psychiatric team for assessment. She received non-pharmacological treatments such as relaxation therapy and behavioural therapy, along with coping therapy. She was administered intramuscular etonogestrel 68 mg as contraception and was discharged after a week of observation in the ward.

Case 2

A previously healthy 15-year-old mother with an unintended and undesired pregnancy, in her second trimester was brought to casualty with a generalised tonic-clonic seizure after a self-induced abortion attempt by self-administering 3 oral doses and 2 vaginal doses of misoprostol with a total dosage of 1000 mg.

The patient's vital signs were BP 110/80 mmHg, heart rate of 125 bpm and a high-grade fever of 40°C. Otherwise, she was saturating well and not tachypnoeic, with a respiratory rate of 18 breaths per minute. The seizure she experienced was of modest intensity and lasted for 3 minutes. It exhibited a similar semiology to that of our initial patient but was successfully aborted with a single dose of IV diazepam 5 mg. Her vitals and presentation were less severe than those of the first patient, likely due to a lower cumulative dosage of misoprostol. However, the drugs were taken all at once, which led to hyperthermia and seizures.

Her vital signs improved within 4 hours, and she was closely monitored using a fit chart, remaining seizure-free. The induced infant weighed about 200 g, which was not viable. She stayed physically well for the next 24 hours under observation. Like the first patient, her septic workup, CT brain, and serum electrolytes were normal, leading to a diagnosis of misoprostol-induced seizure. Despite symptoms like acute kidney injury and mild transaminitis, she recovered quickly, managed her grief, and was discharged. She was referred for counselling on adolescent pregnancy and psychoeducation was provided to both her and her partner. Contraception was also offered, and the patient was reviewed in the nearest health clinic for further follow up.

Discussion

Misoprostol is a synthetic PGE analogue that is converted into the active metabolite misoprostol acid after desulfation, and it replaces protective prostaglandins consumed during therapies that inhibit prostaglandin synthesis. It inhibits gastric acid secretion and protects the gastric mucosa. Initially used to treat peptic ulcers induced by non-steroidal anti-inflammatories, it has become widely used in obstetric practice for medical termination of pregnancy in the first and second trimesters, management of missed abortion, medical management of incomplete abortion, and treatment of postpartum haemorrhage due to its uterotonic and cervical ripening effects.[1]

The World Health Organization recommends a dose of 800 mcg via buccal, vaginal, or sublingual route for patients less than 13 weeks of gestation, while patients with gestational age greater than 13 weeks are recommended to take 400 mcg every 3 hours until abortion occurs, up to 5 doses in 24 hours. The toxic dose in humans has not yet been determined, but studies have shown that the maximum cumulative dose tolerated is 1600 mcg.[2] Though both of our patients took less than the maximum tolerated dose, they experienced severe adverse effects, likely due to the drugs being taken excessively at once. Misoprostol can cause side effects such as fever, chills, nausea, vomiting, and diarrhoea. Uncommon side effects include delirium and confusion. In this case report, our first patient presented with compensated shock likely due to hypotension caused by peripheral vasodilatation as a result of circulating prostaglandin, leading to compensatory tachycardia that was further exacerbated by high-grade fever. Patients are typically not very responsive to fluid therapy, and early initiation of vasopressors is recommended to meet the transiently increased metabolic demand state.

Hyperpyrexia in both of these patients was likely due to PGE2, which is a primary mediator of fever induction by binding to PGE receptors and shifting hypothalamic set points upwards, triggering temperature elevation.[3] Durocher *et al.* found that 35.6% of patients who received misoprostol for post-partum haemorrhage developed a fever of ≥ 40.0°C.[3] Our patients' temperatures on arrival ranged from 40–42°C, consistent with these findings. Regular antipyretics and aggressive cooling therapy are essential. Few studies examine prostaglandin E analogues' seizure pathophysiology, but one study on mice reveals Misoprostol lowers seizure threshold.[4]

It is crucial not to overlook other potential causes of recurrent seizures and status epilepticus. Epilepsy can be ruled out, given that this is a provoked, first-episode seizure with no previous history. A diagnosis of meningoencephalitis is supported by fever, altered mental state, and seizures; this condition is also characterised by neck rigidity, photophobia, and indications of elevated intracranial pressure. Contrast-enhanced CT (CECT) of both patients' brains were normal, ruling out this possibility. Conversely, leptomeningeal enhancement would have been detected if meningoencephalitis were the probable diagnosis. Lumbar puncture was not performed because the patients and spouse had declined.

Septic shock secondary to septic abortion was also considered but ruled out due to the absence of specific signs such as foul-smelling vaginal discharge and growth of organisms from high vaginal, placental and foetal swab culture. Despite presenting with features of sepsis such as fever, tachycardia, and hypotension, further investigations did not support this diagnosis. Electrolyte imbalances such as hyponatremia, hypernatremia, hypocalcaemia, and hypomagnesemia can potentially cause seizures. Therefore, it is essential to rule out these imbalances before further evaluation.

A seizure is an abrupt and transient surge of electrical activity in the brain, while epilepsy is a neurological disorder marked by the occurrence of 2 or more unprovoked seizures. After the initial evaluation at the emergency department, a thorough medical and neurological examination is conducted, along with blood tests. It is crucial to position the head in a way that opens the airway. If there are problems with oxygenation or ventilation, intubation with rapid sequence induction should be performed. Supplemental oxygen therapy should be administered for those not requiring intubation. Seizure control can be achieved by administering benzodiazepines, such as lorazepam 2 mg or diazepam 5 mg, at 5-minute intervals.[5] If the seizure is reoccurring, it is recommended to administer a bolus of an antiepileptic drug (AED) together with benzodiazepines. One option is to administer phenytoin at a dose of 15–20 mg/kg for 25–50 minutes.[5] In cases where phenytoin is contraindicated, IV levetiracetam of 40-60 mg/kg over 15 minutes is preferred.

Recovery times for both cases described in this report were within 4 to 6 hours, which is consistent with the results of a pharmacokinetic study conducted by Zieman *et al.*[6] Plasma concentration of misoprostol gradually increases after vaginal administration, reaching its maximum level after 70–80 minutes, before slowly declining after 6 hours.[6] Therefore, it is essential to provide aggressive and optimal resuscitative and supportive therapy in the early stages to prevent further morbidity and mortality, as this condition is easily reversible if well managed. The ultimate goal of treating these patients is to refer to a psychiatric team for assessment, psychoeducation, and psychotherapy to address their concerns and issues. Proper contraception advice should also be given until they are ready for conception.

Conclusion

Despite its widespread off-label use in obstetrics and gynaecology, it is crucial to consider misoprostol's potential adverse effects, including rare events like hyperpyrexia and convulsions, as observed in our cases. Misuse of misoprostol for self-induced abortion can have severe consequences and should be strongly discouraged. Ensuring access to safe, legal abortion services, alongside education and awareness campaigns, can mitigate such incidents. Healthcare professionals must remain vigilant about medication misuse, educate patients on the risks, and ensure early recognition and optimal supportive care to reduce morbidity and mortality.

Declarations

Informed consent for publication
The patients provided informed consent for the use of the clinical data contained in this case report.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements

The author would like acknowledge Hospital Likas for providing the facilities and healthcare staff in the management of these patients. The authors would like to thank the Director General of Health Malaysia for their permission to publish this article.

References

1. Sharma N, Das R, Ahanthem SS, Reddy K. Misoprostol induced convulsion - A rare side effect of Misoprostol. J Clin Diagn Res. 2017;11(2): https://doi.org/10.7860/JCDR/2017/23396.9189
2. Pfizer Medical Information. Cytotec® Overdosage (Misoprostol). Available from: https://www.pfizermedicalinformation.com/en-us/cytotec/overdose
3. Durocher J, Bynum J, León W, Barrera G, Winikoff B. High fever following postpartum administration of sublingual Misoprostol. BJOG. 2010;117(7):845-852. https://doi.org/10.1111/j.1471-0528.2010.02564.x
4. Medeiros FC, Medeiros MA, Rao VS, Figueiredo EG. Effects of Misoprostol on pentylenetetrazol-induced seizures in mice. Arq Neuropsiquiatr. 1997;55(4):677-679. https://doi.org/10.1590/s0004-282x1997000500001
5. Müllges W. Diagnosis and treatment of status epilepticus in the intensive care unit. Med Klin Intensivmed Notfmed. 2019;114(5):475-484. https://doi.org/10.1007/s00063-019-0581-8
6. Zieman M, Fong SK, Benowitz NL, Bankster D, Darney PD. Absorption kinetics of Misoprostol with oral or vaginal administration. Obstet Gynecol. 1997;90:88-92. https://doi.org/10.1016/S0029-7844(97)00111-7

© Malaysian Journal of Anaesthesiology 2024; 3:79-88
Case report
https://doi.org/10.35119/myja.v3i1.63

Bradycardic peri-arrest after electrical cardioversion for atrial fibrillation: a case report

Jinxuan **Cai**[1], Vu **Nguyen**[2], Shameer **Ahmed**[2], Benjamin **Cheung**[3,4]

[1]School of Medicine and Dentistry, Griffith University, Gold Coast, Australia; [2]Department of Cardiology, St Andrew's Hospital Toowoomba, Toowoomba, Australia; [3]Department of Anaesthesia, St Andrew's Hospital Toowoomba, Toowoomba, Australia; [4]School of Medicine, University of Queensland, Toowoomba, Australia

Abstract

Electrical cardioversion can precipitate prolonged bradycardia and cardiac arrest when the sinoatrial node is dysfunctional, and the escape rhythms from the atrioventricular node and ventricles fail to take over. We report the case of an elderly male who rapidly progressed into bradycardic peri-arrest after electrical cardioversion for persistent atrial fibrillation. Despite the immediate initiation of intravenous atropine and transcutaneous pacing, 2 minutes of cardiopulmonary resuscitation with further boluses of atropine and adrenaline were required before the return of spontaneous circulation. The patient was transferred to the intensive care unit, and a permanent pacemaker was implanted before discharge. Advanced age, long duration of atrial fibrillation, previous aortic valve replacement, use of anti-arrhythmic drugs, and intravenous propofol bolus were all contributing factors to this event. We summarise the relevant clinical features, risk factors, and management considerations, in the hope of promoting awareness of this rare complication of a common procedure.

Keywords: atrial fibrillation, cardiac arrest, cardiac pacing, electrical cardioversion

Correspondence: Benjamin Cheung, MBBS, 280 North Street, Toowoomba, Queensland 4350, Australia.
E-mail: bencheungaustralia@gmail.com

Introduction

Electrical cardioversion is a relatively safe and efficient procedure that has been used to terminate atrial fibrillation (AF) since the 1960s.[1] However, bradyarrhythmia is a known complication of electrical cardioversion for AF.[2] A retrospective multicentre study conducted by Gronberg *et al.* investigating 7,660 cases of electrical cardioversion for AF showed that bradyarrhythmia occurred in 0.9% of cases, with 0.2% being bradycardia alone and the rest being asystole followed by a period of bradycardia.[2] Among the cases that resulted in asystole, most of them were of brief duration and recovered spontaneously, though 7 (0.09%) required resuscitation and 2 (0.02%) required external pacing. Another study by Shin *et al.* evaluated a total of 1,100 cases of electrical cardioversion and showed a bradyarrhythmia rate of 0.7%, where 0.3% received permanent pacemaker implantation.[3] Despite the rareness of this complication, it has the potential to cause serious harm to the patient, which marks the need for educational effort regarding its clinical features and prompt management.

Case presentation

An 83-year-old man underwent his first elective electrical cardioversion after failed pharmacological treatment for persistent rate-controlled AF, which lasted for at least 12 months and was symptomatic with shortness of breath. Past medical history included gastro-oesophageal reflux disease, hypothyroidism, aortic valve replacement, and ischaemic heart disease requiring angioplasty and coronary artery bypass grafts. His regular medications were amiodarone, bisoprolol, clopidogrel, apixaban, furosemide, ezetimibe, rosuvastatin, rabeprazole, thyroxine, and paroxetine. There was no history of presyncope or syncope suggesting bradyarrhythmia. Recent echocardiography reported normal left ventricular size and function, moderate mitral regurgitation, biatrial enlargement, and normal right ventricular size with mildly reduced systolic function. The bioprosthetic aortic valve replacement was well seated with normal haemodynamics. There was no previous anaesthetic complication. Besides the narrow-complex AF shown on electrocardiogram (ECG), the patient's physical examination and investigations were otherwise unremarkable. He consented to electrical cardioversion under monitored sedation.

In the catheterisation laboratory, the patient's monitoring included ECG, non-invasive blood pressure, pulse oximetry, and capnography through the side port of a Hudson oxygen mask (Salter Labs, MI, USA). His observations were within normal limits, and AF with a rate of 72 beats per minute (bpm) was confirmed on

cardiac monitoring. Sedation was induced with 100 mg of intravenous propofol, and the patient's blood pressure, heart rate, and capnography were maintained within normal limits after loss of consciousness.

After synchronisation, a direct current shock of 200 J was discharged through pads placed on the anterior chest wall and upper back. The slow AF rapidly progressed into a ventricular escape rhythm at a rate of 25 bpm without any signs of atrioventricular (AV) node escape rhythm. The cardiologist was able to initiate transcutaneous pacing through the cardioversion pads with minimal delay, while intravenous atropine was administered simultaneously by the anaesthetist. The demand pacing heart rate was set to 50 bpm with a maximum output of 140 mA. ECG connections and pacing pads were confirmed to be in the correct position with good skin contact. The femoral arterial pulse was palpated with a gloved hand to check for mechanical capture of external pacing.

Despite the presence of spontaneous breathing confirmed with capnography, no palpable femoral pulse or brachial blood pressure could be obtained after administration of 1.2 mg intravenous atropine. The patient was therefore considered to be in a state of bradycardic peri-arrest, and cardiopulmonary resuscitation (CPR) was initiated along with an intravenous bolus of 500 mcg of adrenaline. A laryngeal mask airway (i-gel, Intersurgical® Berkshire, UK) was inserted with minimal interruption. Return of spontaneous circulation, as evidenced by a strong central pulse, was achieved at 2 minutes after starting CPR. The first systolic blood pressure recorded after the return of spontaneous circulation was 220 mmHg with a heart rate of 120 bpm still in AF. An urgent focused echocardiogram was performed that showed an ejection fraction of approximately 50%. He was transferred to the intensive care unit after regaining consciousness.

During his intensive care stay, he developed sinus bradycardia at a rate of 40 bpm with intermittent junctional bradycardia that required isoprenaline and noradrenaline infusion to maintain his blood pressure. A permanent pacemaker was implanted 2 days later for persistent bradyarrhythmia.

Discussion

This unexpected case of bradycardic peri-arrest highlights the risk where profound bradycardia with compromised cardiac output can result from a combination of delayed sinoatrial (SA) node recovery and failure of AV node junctional rhythm.

The bradycardic peri-arrest was not anticipated in this patient, who was at narrow complex AF with a rate of 72 bpm and no history suggestive of unstable ischaemia or bradycardia. The low-to-medium dosage of amiodarone 200 mg daily and bisoprolol 2.5 mg daily in this patient with normal renal and hepatic functions was unlikely to be a direct causative factor in this event. In hindsight, the long duration of AF, advanced age, previous aortic valve replacement, use of anti-arrhythmic drugs, especially amiodarone, and the bolus dose of propofol may have all cumulatively contributed to this event.[4]

A list of causes for dysfunctional SA node, AV node, and ventricular escape are shown in Table 1. The duration of AF is one of the major predictive factors for arrhythmic complications after electrical cardioversion, which should be taken into consideration in this case given the patient's long history of AF.[5] It is also important to note that patients with underlying degenerative cardiac conduction disease such as AF with controlled ventricular response, in the absence of rate controlling agent on board, can develop significant bradycardia or sustained ventricular arrhythmias upon cardioversion.[6] Age-related degeneration and fibrosis are among the most common causative factors, while cardiac ischaemia and various cardiac procedures can also pose risks to the intrinsic pacemakers depending on the area involved.[7] A study involving 20,725 patients with AF undergoing their first electrical cardioversion found that the rate of developing bradyarrhythmia within 30 days ranges from 0.5% to 5.1% as the patient's age increases from 40 to 90 years.[8]

This case also points out the possibility that transcutaneous pacing can be inefficacious despite measures to reduce impedance, in which scenario anaesthetists should be vigilant and prepared to initiate resuscitation. Figure 1 demonstrates our modified approach to resuscitation for bradycardic peri-arrest, incorporating recommendations from guidelines and senior clinicians. It is not intended to be a substitute of current guidelines, but a summary of experience gained from reflecting on the case described in this report. It suggests that electrical treatments can be initiated simultaneously with pharmacological treatments in the setting of bradycardic peri-arrest. Failed mechanical capture, which resembles pulseless electrical activity, may occur in myocardial stunning or metabolic derangements that raise the pacing threshold.[9] Failed electrical capture may occur when there is suboptimal electrode placement or poor skin contact due to sweat or hair.[9] Early recognition of the high-risk patients and allocation to appropriate care settings, such as the catheterisation laboratory, is required to facilitate temporary or permanent transvenous pacing that may be initiated under expert guidance.

Table 1. Risk factors for intrinsic cardiac pacemaker dysfunction[4-8]

	Sinoatrial node	**Nodal escape (atrioventricular node)**	**Infra-Hisian escape (including Purkinje and ventricular escape)**
Depolarisation rate (bpm)	60–100 Narrow complex	40–60 Narrow complex	20–40 Broad complex
Common risk factors for dysfunction	• Long-standing conduction disorders • Advanced age/idiopathic fibrosis • Medication toxicities: beta-blocker, calcium-channel blocker, digoxin, amiodarone, local anaesthetic systemic toxicity • Metabolic derangements: hyperkalaemia, hypermagnesaemia, thyroid dysfunction, hypocalcaemia, hypoxia, hypothermia • Infiltrative disorders: amyloidosis, sarcoidosis, haemochromatosis • Infectious diseases: infective endocarditis, Lyme disease, Chagas disease • Inflammatory and autoimmune conditions: rheumatic heart disease, scleroderma, systemic lupus erythematosus		
Specific risk factors for dysfunction	• Excessive vagal tone • Spinal cord injury • Carotid sinus syncope • Sodium channel mutations • Ischaemia involving proximal right coronary artery	• Excessive vagal tone • Spinal cord injury • Carotid sinus syncope • Sodium channel mutations • Tricuspid valve replacement • Transcatheter aortic valve implantation • Aortic valve replacement or repair • Hypertrophic obstructive cardiomyopathy • Inferior wall ischaemia • Ticagrelor-induced bradycardia • Pre-existing left bundle branch block	• Myocarditis • Congenital heart disease • Septal ischaemia

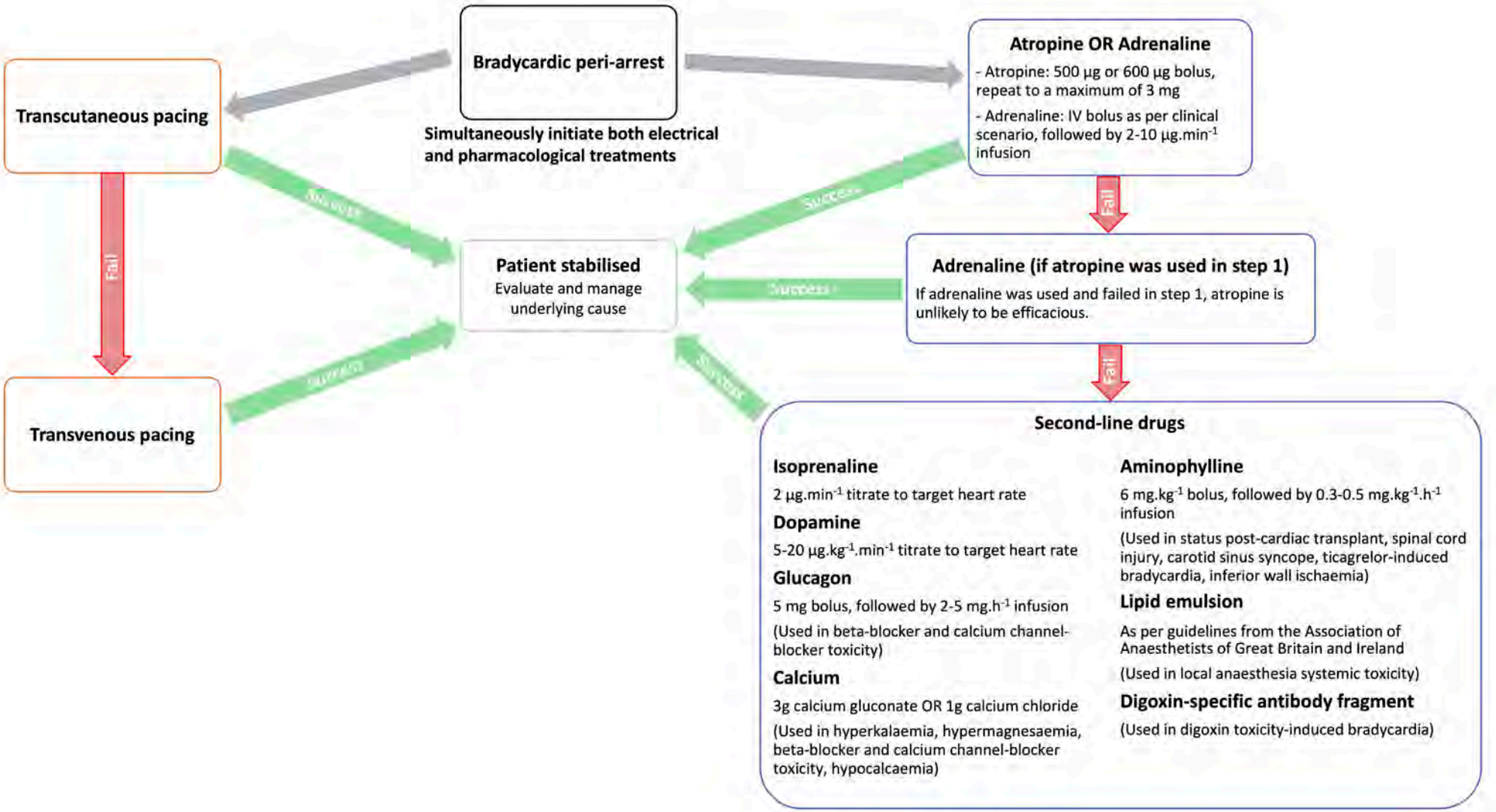


Fig. 1. Modified resuscitation for bradycardic peri-arrest.[4,10]

Atropine and adrenaline are the mainstay pharmacological treatments for bradycardic peri-arrest, as they can achieve rapid reversal of the pathophysiology. Atropine is the preferred first-line drug in many guidelines, it is readily available and can quickly counteract nodal dysfunction due to excessive vagal tone but may be ineffective in other situations, such as Mobitz type II second-degree heart block and third-degree heart block with a low Purkinje or ventricular escape rhythm.[4] Atropine may also be inefficacious in patients with cardiac transplants, as the denervated heart will not respond to vagal blockade, and probably will not work if adrenaline has already failed as the first-line drug. The role of intravenous adrenaline bolus in this case is probably more significant as it stimulates the entire myocardium despite the cause of the bradyarrhythmia.[4] Under circumstances where atropine is potentially inefficacious, such as the aforementioned higher degree heart block with ventricular escape rhythm, adrenaline may be used as an alternative first-line agent during the early course of CPR without contradicting the current guidelines.[10]

Second-line medications may be appropriate in some clinical scenarios, such as glucagon in beta-blocker or calcium channel-blocker toxicity and lipid emulsion in local anaesthetic systemic toxicity.[10] Bradyarrhythmia induced by electrolyte disturbances may be treated with calcium chloride or calcium gluconate. Aminophylline should be considered in bradyarrhythmia complicated by spinal cord injury, inferior wall myocardial infarction, and status post-cardiac transplant.[10] Other second-line options, including isoprenaline and dopamine, may be used at the clinician's discretion. Moreover, the sinus and junctional bradycardia reported during intensive care stay could be further complicated by Torsades de Pointes as a result of QT interval prolongation. The use of isoprenaline infusion and subsequent pacemaker implantation have effectively reduced the risk of this potential complication.

Conclusion

This report highlights the risk factors contributing to the development of bradycardic peri-arrest after electrical cardioversion for AF and discusses potential treatment options. Simultaneous initiation of electrical and pharmacological interventions is encouraged. Failure to capture can occur during pacing, in which scenario anaesthetists should be prepared to initiate resuscitation. Atropine and adrenaline are generally used first line, though the choice of drug may vary depending on the underlying cause.

Declarations

Informed consent for publication
Informed, sufficient, and express consent from the patient for the use of their clinical data, images, and/or other medical information consigned in the article was obtained.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

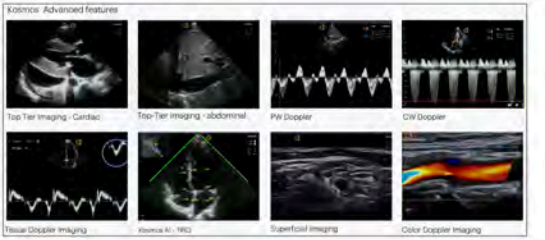
References

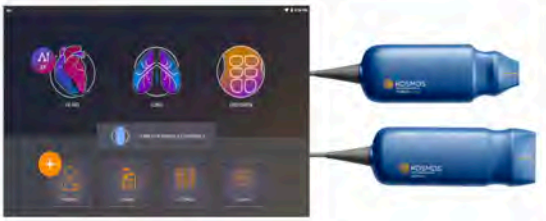
1. Pisters R, Nieuwlaat R, Prins MH, et al. Clinical correlates of immediate success and outcome at 1-year follow-up of real-world cardioversion of atrial fibrillation: the Euro Heart Survey. Europace. 2012;14(5):666-674. https://doi.org/10.1093/europace/eur406
2. Grönberg T, Nuotio I, Nikkinen M, et al. Arrhythmic complications after electrical cardioversion of acute atrial fibrillation: the FinCV study. Europace. 2013;15(10):1432-1435.
3. Shin DG, Cho I, Hartaigh B, et al. Cardiovascular Events of Electrical Cardioversion Under Optimal Anticoagulation in Atrial Fibrillation: The Multicenter Analysis. Yonsei Med J. 2015;56(6):1552-1558. https://doi.org/10.3349/ymj.2015.56.6.1552
4. Farkas J. Internet Book of Critical Care. EMCrit. [updated 2021 Nov 20. Available from: https://emcrit.org/ibcc/bradycardia/#other_medications
5. Toso E, Blandino A, Sardi D, et al. Electrical cardioversion of persistent atrial fibrillation: acute and long-term results stratified according to arrhythmia duration. Pacing Clin Electrophysiol. 2012;35(9):1126-1134. https://doi.org/10.1111/j.1540-8159.2012.03453.x
6. Park J, Seol SH, Kim DK, et al. Safety concern with electrical cardioversion of persistent atrial fibrillation with slow ventricular response. Pacing Clin Electrophysiol. 2022;45(8):963-967. https://doi.org/10.1111/pace.14483
7. Jones SA, Boyett MR, Lancaster MK. Declining Into Failure. Circulation. 2007;115(10):1183-1190. https://doi.org/doi:10.1161/CIRCULATIONAHA.106.663070
8. Rasmussen PV, Blanche P, Dalgaard F, et al. Electrical cardioversion of atrial fibrillation and the risk of brady-arrhythmic events. American Heart Journal. 2022;244:42-49. https://doi.org/https://doi.org/10.1016/j.ahj.2021.10.182
9. Doukky R, Bargout R, Kelly RF, Calvin JE. Using transcutaneous cardiac pacing to best advantage: How to ensure successful capture and avoid complications. J Crit Illn. 2003;18(5):219-225.
10. Soar J, Böttiger BW, Carli P, et al. European Resuscitation Council Guidelines 2021: Adult advanced life support. Resuscitation. 2021;161:115-151. https://doi.org/10.1016/j.resuscitation.2021.02.010

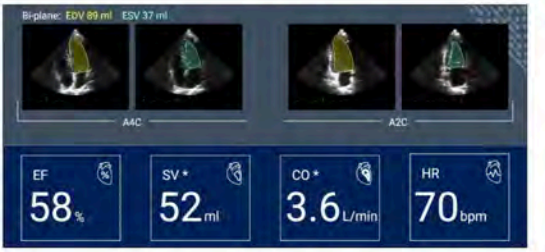
KOSMOS
by EchoNous

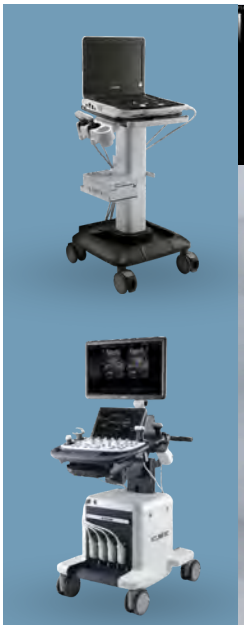
Top Tier Imaging - Kosmos imaging is benchmarked against advanced cart-based systems and delivers clinical clarity at the bedside. It is the only ultraportable device providing advanced feature sets such as PW & CW Doppler with TDI.

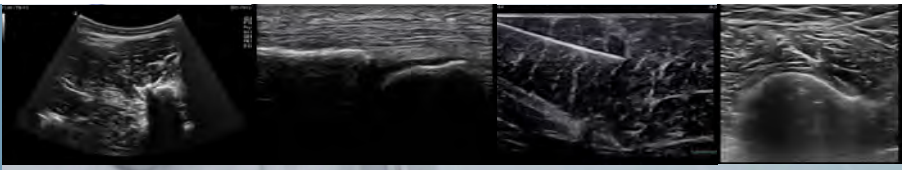
Kosmos AI Solutions - Kosmos is enabled with extensive AI capabilities to help provide a more complete diagnosis at the bedside. It supports novice and advanced users with real-time probe positioning guidance, image grading, and auto-labeling while also providing automatic calculations ranging from a simple ejection fraction to complete complex systolic and diastolic function analysis and assessment of valve disease.



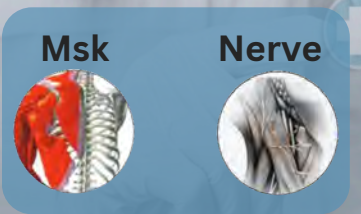


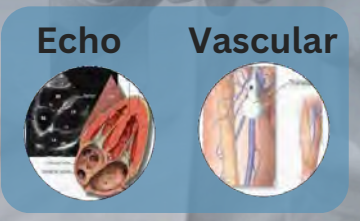






ALPINION





CommerMega Sdn Bhd
No. 12A Ground Floor, Jalan Impian Makmur 3/A , Taman Saujana Impian, 43000 Kajang, Selangor, Malaysia
Tel: +603 8741 1772 / +603 8741 1722 Fax: +603 8741 3382 Email: info@commermega.com

Loke: +013-364 9788 Hj. Roslan: +6012-322 7044

Malaysian Society of
Anaesthesiologists

College of
Anaesthesiologists, AMM

www.myja.pub
P-ISSN: 2772-9524
KUGLER PUBLICATIONS
www.kuglerpublications.com