ebrothers.com, for detailed information on critical care books, visit our website www.jaypeebrothers.com, for detailed information on critical care bo

YEARBOOK

Yearbook of CRITICAL CARE 2023

HICS Initiative

Editors
Srinivas Samavedam
Ganshyam Jagathkar

JAYPEE

Contents

SECTION 1 Cardiac/Hemodynamics/Fluids 1
Section Editor: *Supradip Ghosh*
Associate Editors: *Ripenmeet Salhotra, Amandeep Singh, Aditya Lyall, Saurabh Kumar Rai*

SECTION 2 Respiratory/Ventilation/Acute Respiratory Distress Syndrome 33
Section Editor: *Manoj Y Singh*

SECTION 3 Neurocritical Care 39
Section Editor: *Ketan Kargirwar*
Associate Editor: *Sanket Hansora*

SECTION 4 Gastroenterology/Hepatobiliary 54
Section Editor: *Lalita Gouri Mitra*
Associate Editors: *Jagdeep Sharma, Harsimran Singh Walia*

SECTION 5 Nephrology 79
Section Editor: *Kanwalpreet Sodhi*
Associate Editors: *Manu Gupta, Atul Phillips, Basjinder Kaur*

SECTION 6 Infections and Antibiotics 116
Section Editor: *Sumesh Arora*

SECTION 7 Sepsis 135
Section Editor: *Jaicob Varghese*
Associate Editors: *Nilanjan Umesh, Melwin George*

SECTION 8 Hematology 144
Section Editor: *Deven Juneja*
Associate Editor: *Sahil Kataria*

SECTION 9 Sonography/Imaging 161
Section Editor: *Shrikanth Srinivasan*
Associate Editors: *NVSN Prasant, Velmurugan Selvam, Magesh Parthiban, Vetriselvan P, Vadhan Prasanna S*

SECTION 10 Nutrition and Metabolic 175
Section Editor: *Sivakumar MN*
Associate Editor:

SECTION 11 Guidelines 195
Section Editors: *Gunjan Chanchalani, Ranajit Chatterjee*
Associate Editors: *Lalit Gupta, Seema S Tekwani*

Index 217

Section

3

Neurocritical Care

Section Editor: *Ketan Kargirwar*

Associate Editor: *Sanket Hansora*

JAYPEE BROTHERS

ARTICLE 12

Treatment for Intracranial Hypertension in Acute Brain Injury: Grading, Timing, and Association with Outcome. Data from the SYNAPSE-ICU Study

Robba C, Graziano F, Guglielmi A, Rebora P, Galimberti S, Taccone FS, et al. On behalf of the SYNAPSE-ICU Investigators. Treatment for intracranial hypertension in acute brain injury: grading, timing, and association with outcome. Data from the SYNAPSE-ICU study.

Intensive Care Med. 2023;49:50-61.

CLINICAL QUESTION OR PROBLEM

- To control detrimental increase in intracranial hypertension in acute brain injured patients. When and how it should be done?
- What should be the "therapy intensity level (TIL)"—less aggressive or more aggressive?
- What are the therapeutic approaches for controlling intracranial hypertension in patient with acute brain injury (ABI) during first week since intensive care unit (ICU) admission.
- What are the variabilities in the use of TILs among different pathologies (subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), and intracranial hemorrhage (ICH).
- Is there any association between varying level of TILs and clinical outcomes?

WHAT IS ALREADY KNOWN?

- *Blood pressure control:* Uncontrolled blood pressure may associate with higher risk of worsening intracranial bleed and poor neurological outcome.
- *Cerebral perfusion pressure (CPP):* CPP monitoring of severe TBI patients is recommended to decrease 2-week mortality. Maintaining certain cerebral perfusion pressure (60–70 mm Hg) has a favorable outcome.
- *Intracranial hypertension (ICP) thresholds:* Management of severe TBI patients using information from ICP monitoring is recommended to reduce in-hospital and 2-week mortality. Treating ICP >22 mm Hg is recommended because values above this level are associated with increased mortality.
- *Prophylactic hypothermia:* It is not recommended to improve outcome in diffuse injury.

- *Hyperosmolar therapy:* Mannitol effective for control of ICP at doses of 0.25–1 g/kg body weight, however hypotension should be avoided and restrict its use prior to ICP monitoring.
- *Hyperventilation therapy:* Prolonged prophylactic hyperventilation with $PaCO_2$ <25 is not recommended. Hyperventilation should be avoided during first 24 hours after the injury when cerebral blood flow (CBF) is reduced critically.
- *Anesthetics, analgesics and sedatives:* Prophylactic use of barbiturates for burst suppression is not recommended. Although propofol is recommended to control of ICP, it is not recommended for improvement in mortality.
- *Steroids:* Use of steroids is not recommended for reducing ICP.
- *Seizure prophylaxis:* Prophylactic use of valproate or phenytoin is not recommended for late posttraumatic seizure (PTS), however phenytoin is recommended to reduce early PTS.
- *Decompressive craniotomy:* A large frontotemporal craniotomy is recommended for reduced mortality.
- *Cerebrospinal fluid (CSF) drainage:* Initial Glasgow Coma Scale (GCS) <6 during first 12 hours after injury may be considered.

STUDY DESIGN

- It is a multicenter, prospective, international, and observational cohort study.
- Its primary aim was evaluating clinical practice and managing ICP monitoring in AIBs.
- It helped to clarify the current clinical use of ICP monitoring and treatment across the different countries with different resources and its use in various types of AIBs.

POPULATION STUDIED INCLUDING DEMOGRAPHICS

- *Inclusion criteria:*
  - Age: >18 years
  - Diagnosis of ABI following TBI, SAH, ICH
  - Altered level of consciousness: GCS—eye response score of 1 , no eye-opening, motor response of 5 or less, not obeying command on admission to ICU
  - Neurological deterioration with no-eye opening and motor score decreased to 5 or less within 48 hours after ICU admission.
- *Exclusion criteria:*
  - Patients not requiring ICU admission and/or being admitted for other form of AIBs.
- A total of 2,395 patients enrolled in Synapse-ICU study
  - 75 without TIL data on day 1 were excluded.
- A total of 2,320 patients were available for this analysis.
  - 1,339 (57.7%) patients were admitted for TBI
  - 409 (17.6%) admitted for SAH
  - 572 (24.7%) admitted for ICH
- Median age was 55 years
- The number of females was 800.
- 744 (34%) had at least one unreactive pupil.
- 409 patients were admitted from low-income countries.

INTERVENTION STUDIED

- Intervention to reduce intracranial hypertension was recorded to the TIL scale on day 1, 3, and 7 of the ICU stay.
- TIL scale: Basic, mild-moderate, and extreme treatment

JAYPEE BROTHERS

- Level of TIL during the week was defined as maximum level of treatment over days 1, 3, and 7.
  - eTIL group: Patients receive extreme therapies at least once on days 1, 3, and 7.
  - No-eTIL group: Patients who do not receive extreme therapies.
- Patients primarily decompressed on day 1 were classified according to maximum TIL.
- If a patient received a decompressive craniectomy on day 3, he/she was considered also decompressed on day 7.

OUTCOME EVALUATED

- *Primary endpoint:* Prevalence of TIL use in ABI in the first week since ICU admission.
- *Secondary endpoint:* Mortality and Glasgow Outcome Scale Extended (GOSE) collected at 6-month follow-up.
- Unfavorable outcome was defined as a GOSE score of <5.
- Over the first week in ICU, 295 patients received eTIL at least once, while 1,643 patients received mild-moderate at maximum level and remaining 382 patients received no-basic TIL.
- Among 295 eTIL patients, 93 were aggressively treated only on day 1, 35 on day 3, and 50 on day 7. Only 15 subjects were treated with extreme TIL at all time.
- During whole week 305 SAH patients received mild-moderate TIL and 63 received eTIL.
- In TBI group, 932 patients received mild-moderate TIL and 178 eTIL.
- In ICH group, 406 patients treated with mild-moderate TIL and 54 with eTIL.
- Among the patients, who received the eTIL during the week, the most frequent treatments were, in SAH group, decompressive craniectomy, hypocapnia, and metabolic suppression; in TBI metabolic suppression and in ICH hypocapnia.
- There is variability in frequency of use of eTIL was observed.
- Association between TIL and outcomes:
  - At 6 months, 1,331 patients had an unfavorable neurological outcome (GOSE <5) and 934 patients died.
  - Mortality was higher in patients in no-basic TIL group compared to those who received mild-moderate TIL or eTIL.
  - Unfavorable neurological outcome was more frequent in those patients who received eTIL compared to other groups (eTIL 68.5%, mild-moderate 60.5%, no-basic TIL 65.9%).
  - Considering eTIL as reference, the use of no-basic TIL was independently associated with 6 months mortality but use of mild-moderate was not.
  - Analysis according to the type of brain injury, the result was consistent in each pathology.
  - No significant association of TIL group with 6 months neurological outcome was found.
  - Results were consistent when stratifying according to the type of brain injury.

    Excluding most severe cases, the model showed the statistically significant association between unfavorable neurological outcome and no-basic or mild-moderate TIL comparing with eTIL.

AUTHORS' VIEWPOINT

- During the first week of ICU admission, strategies for managing intracranial hypertension, especially mild and moderate treatment, are frequently used in ABI patients.

JAYPEE BROTHERS

- There is large variability across centers and countries still exists regarding the use of these therapies.
- The management of intracranial pressure is fundamental in neurocritical care patients to reduce secondary brain damage and improve clinical outcome.
- Considering the lack of definitive randomized controlled trial comparing all aggressive treatment, initiating one of the strategies relies on the balance between risks and benefit, patient clinical condition, and there local practice.
- We found that patients undergoing eTIL were more severe and younger but with better pre-injury condition. This suggests that physicians consider applying these strategies when benefit outweighs the risk.
- Despite the significant variability in ICP practice and treatment, intensive treatments are guided by invasive treatment and there are still significant numbers of patients who receive aggressive treatment without ICP monitoring, thus highlighting the need to provide more universally accepted criteria for its use in ABIs.
- The multivariate analysis on 6 months mortality showed that aggressive treatment could reduce the mortality at 6 months compared to no-basic TIL.
- Even though there might be a potential harm from using high TIL therapies, monitoring and treating these patients can reduce the mortality in selected patients.
- The effect on the neurological outcome remains unclear.

STRENGTH OF THE STUDY

- Data from this large cohort of acute brain injury patients admitted to ICU will provide a detailed description of the patient characteristics, intracranial pressure management strategies, resource use, and their correlation to clinical outcome.
- The results complement other multicenter studies focusing on traumatic brain injury practice and will add information on ICP practice in subarachnoid hemorrhage and intracerebral hemorrhage.
- The presence of centers in low- and middle-income countries will provide robust data about ICP monitoring in these regions.
- The global approach can be considered as the main strength and novelty of the study, since it allows to explore the clinical practice in geographical regions characterized by very different public health issues.

DRAWBACKS OF THE STUDY

- This is observational study therefore it is impossible to draw any causality relationship between the associations found.
- Definition of TIL treatment includes only decompressive craniotomy, hypothermia and metabolic suppression are defined as tier-three therapies.
- escalation of care in the use of TIL, data on duration of metabolic suppression or method of cooling to obtain hypothermia and database at day 1 regarding primary and secondary decompression are lacking.
- There is no universal consensus on definition of neuroworsening.

REVIEWERS' VIEWPOINT

- Treatment of intracranial hypertension is frequently applied in the first week of ICU management of acute brain-injured patients.

JAYPEE BROTHERS

- Highly aggressive therapies are still significantly variable across centers and do not follow the staircase approach recommended by most recent guidelines.
- Aggressive strategies benefit 6-month mortality but not 6-month neurological outcome.

IMPACT ON CURRENT PRACTICE AND TAKE HOME MESSAGE

- The findings of the SYNAPSE-ICU study have the potential to influence clinical practice in the management of ICH in acute brain injury. The study may provide valuable insights into the optimal timing of treatment initiation, the selection of appropriate treatment strategies based on ICH severity, and the impact of treatment on patient outcomes.
- Findings from the study indicate that there is considerable variability in the use of ICP monitoring across different centers and countries.
- The study also suggests that ICP monitoring may be associated with a more intensive therapeutic approach and lower 6-month mortality in more severe cases of acute brain injury.
- Additionally, ICP monitoring was found to be associated with better neurological outcomes at 6 month.
- The findings could guide clinicians in making evidence-based decisions and improving patient care in the ICU setting.

ARTICLE 13

Prognostic Factors Associated with Extubation Failure in Acutely Brain-injured Patients: A Systematic Review and Meta-analysis

Taran S, Angeloni N, Pinto R, Lee S, McCredie VA, Schultz MJ, et al. Prognostic Factors Associated with Extubation Failure in Acutely Brain-injured Patients: A Systematic Review and Meta-analysis.

Crit Care Med. 2023;51(3):401-12.

WHAT IS ALREADY KNOWN?

Potential factors associated with extubation failure in acutely brain-injured patients may include:

- *Glasgow Coma Scale score:* The GCS is a neurological scale that assesses a patient's level of consciousness. Lower GCS scores at the time of extubation may indicate a higher risk of extubation failure.
- *Neurological status:* The severity and nature of the brain injury play a crucial role in determining a patient's ability to maintain spontaneous breathing and airway control after extubation.
- *Age:* Older age has been associated with an increased risk of extubation failure in various patient populations, including those with brain injuries.
- *Preexisting medical conditions:* Patients with comorbidities, such as chronic respiratory disorders or cardiovascular diseases, may have a higher likelihood of extubation failure.
- *Duration of mechanical ventilation:* Longer durations of mechanical ventilation may lead to muscle weakness and other complications, increasing the risk of extubation failure.

JAYPEE BROTHERS

- *Blood gas parameters:* Abnormal blood gas values, such as low arterial oxygen levels or high carbon dioxide levels, may indicate respiratory insufficiency and predict extubation failure.
- *Rapid shallow breathing index (RSBI):* RSBI is a ratio calculated by dividing the respiratory rate by tidal volume during a spontaneous breathing trial. Higher RSBI values have been associated with an increased risk of extubation failure.

STUDY DESIGN

Cohort studies and randomized trials examining the association of prognostic factors with extubation failure.

This systematic review and meta-analysis were performed following reporting standards for prognostic factor studies, the Cochrane Handbook, and the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The review protocol was developed a priori and registered with PROSPERO (CRD42021253310).

POPULATION STUDIED INCLUDING DEMOGRAPHICS

In this systematic review and meta-analysis including 21 studies and 3,274 adult patients with ABI admitted to an ICU. Data were collected on the population, index prognostic factor, comparator prognostic factor, outcome, timing, and setting.

INTERVENTION(S) STUDIED

All meta-analyses were performed using random effects models to account for between-study heterogeneity. Heterogeneity was assessed by visual inspection of forest plots for overlapping point estimates and CIs and formally reported using the I^2 measure.

COMPARATOR USED

Not applicable.

OUTCOMES EVALUATED

- The primary outcome was extubation failure. Additional outcomes included ICU length of stay and mortality at longest follow-up. Where reported they have extracted the reasons for reintubation among patients failing extubation and the proportion of patients receiving a tracheostomy.
- Among patients who failed extubation, the most common reasons for reintubation were excessive secretions [median, 9.7%; interquartile range (IQR), 7.0–50.5%], decreased level of consciousness (median, 16.0%; IQR, 10.2–26.4%), stridor (median, 21.6%; IQR, 16.7–25.6%), and respiratory failure (median, 36.4%; IQR, 17.1–46.7%).
- Between 2.8 and 47.0% of patients received a primary tracheostomy without an extubation attempt.
- Patients failing extubation had a numerically higher mortality at longer follow-up (with the exception of one study) and longer median ICU length of stay compared with patients extubated successfully.

AUTHORS' VIEWPOINT

By synthesizing data from multiple studies, the meta-analysis can identify and quantify the strength of association between various prognostic factors and extubation failure in acutely brain-injured patients.

This information can guide clinical decision-making and inform prognostic discussions with patients and their families.

STRENGTH OF THE STUDY

- Strengths of this systematic review include our use of a preregistered study protocol with few deviations and adherence

JAYPEE BROTHERS

to standards for systematic reviews of prognostic factors and updated PRISMA guidelines.

- *Methodological rigor:* Systematic reviews and meta-analyses are considered to be some of the highest levels of evidence in medical research due to their rigorous methodology. This study likely followed strict guidelines for conducting systematic reviews, ensuring that all relevant studies were identified and included, and that the data extraction process was thorough and unbiased.
- *Large sample size:* The strength of a meta-analysis lies in its ability to pool data from multiple studies, creating a larger sample size than any individual study. A substantial sample size increases the statistical power of the analysis, allowing for more reliable and precise estimates of the prognostic factors associated with extubation failure in brain-injured patients.
- *Clinical relevance:* Extubation failure in acutely brain-injured patients is a critical concern for clinicians in intensive care settings. By identifying prognostic factors associated with this outcome, the study provides relevant insights into patient management and may aid in risk stratification and targeted interventions.

DRAWBACKS OF THE STUDY

As with all research, potential biases, heterogeneity in study designs, and other confounding factors should be carefully considered when interpreting the results. Researchers should acknowledge these limitations and provide suggestions for future research to further enhance the understanding of this important clinical issue.

- First, although the unadjusted analysis demonstrated that extubation failure was not predicted by specific ABI diagnosis, the credibility of this finding is limited by residual confounding, and subgroup effects by ABI subtype are not excluded.
- Second, although our review suggests the importance of cough and swallow in the decision to extubate, several studies reported these as binary variables (i.e., present or absent). Our analyses, therefore, do not account for the possibility of a dose-response relationship between individual airway factors and extubation failure.
- Third, since our primary meta-analysis included factors that did not adjust for the same set of covariates, readers should apply caution in comparing summary estimates between different prognostic factors or ranking them by their magnitude. However, even where adjustment is performed with similar covariates, direct comparisons between prognostic factors should generally be avoided.
- Fourth, methods to determine eligibility for extubation were highly variable across studies. However, this heterogeneity reflects important real-world differences in policies and practices related to extubation, such that generalizability of our results may be enhanced. Finally, for continuous factors, we were unable to report associations at common thresholds due to differences in prognostic factor reporting across studies, leading to our use of the tertile method.

REVIEWERS' VIEWPOINT

- In this case the authors conducted a review of relevant studies investigating extubation failure in acutely brain-injured meta-analysis to pool the results of these studies for more robust conclusions.

JAYPEE BROTHERS

- The meta-analysis may reveal that factors such as the Glasgow Coma Scale (GCS) score, age, presence of intracranial hemorrhage, or certain physiological parameters (e.g., oxygenation, respiratory rate) are significantly associated with a higher risk of extubation failure. These findings can help clinicians identify patients who are at a higher risk of unsuccessful extubation and adjust their management plans accordingly.
- The findings of the meta-analysis can inform prognostic discussions with patients and their families. Clinicians can use this information to better communicate the potential risks and outcomes associated with extubation in acutely brain-injured patients. It can help set realistic expectations and facilitate shared decision-making by providing evidence-based information about the likelihood of successful extubation and potential factors that may impact the outcome.

IMPACT ON CURRENT PRACTICE AND TAKE HOME MESSAGE

Impact on Current Practice

The systematic review and meta-analysis on prognostic factors associated with extubation failure in acutely brain-injured patients can have a significant impact on current medical practice, especially in critical care settings. It provides valuable insights into the factors that may influence the success or failure of extubation in this specific patient population. These findings can help clinicians make more informed decisions when deciding whether and when to extubate brain-injured patients, which is a crucial step in their management.

- *Tailored extubation decisions:* The study's results can guide clinicians in tailoring their extubation decisions based on individual patient characteristics. By identifying specific prognostic factors that may increase the risk of extubation failure, clinicians can take a more personalized approach to extubation, ensuring that patients with a higher likelihood of failure receive appropriate interventions or prolonged mechanical ventilation when necessary.
- *Enhanced patient safety:* Reducing extubation failure rates in brain-injured patients can lead to improved patient safety. Extubation failure can result in adverse outcomes, such as reintubation, prolonged mechanical ventilation, or even complications like ventilator-associated pneumonia. Understanding the factors that contribute to failure can help mitigate risks and prevent potential harm to patients.
- *Resource optimization:* Preventing unnecessary extubation failures can lead to more efficient utilization of healthcare resources. Reintubation and prolonged

  can strain critical care units. By reducing extubation failure rates, hospitals can potentially allocate resources more effectively, providing better care to other patients in need.

Take Home Message

- The key take home message from this systematic review and meta-analysis is that there are identifiable prognostic factors associated with extubation failure in acutely brain-injured patients. These factors can assist clinicians in making more informed decisions regarding the timing and appropriateness of extubation, ultimately leading to improved patient outcomes.

JAYPEE BROTHERS

- Additionally, it highlights the importance of a multidisciplinary approach in managing brain-injured patients. Collaborative efforts between neurologists, intensivists, respiratory therapists, and other healthcare professionals are essential to assess and consider these prognostic factors comprehensively.
- Furthermore, the study underscores the need for ongoing research in critical care medicine to enhance our understanding of extubation management in specific patient populations. Future studies should focus on validating the identified prognostic factors, exploring potential interventions to mitigate extubation failure risks, and refining protocols for extubation decision-making in acutely brain-injured patients.
- Overall, this systematic review and meta-analysis contribute valuable evidence to the field of critical care medicine and provide a basis for more informed and individualized approaches to extubation in brain-injured patients, ultimately striving for better patient outcomes and safety.

ARTICLE 14

Effect of Remote Ischemic Conditioning vs. Usual Care on Neurologic Function in Patients with Acute Moderate Ischemic Stroke: The RICAMIS Randomized Clinical Trial

Chen HS, Cui Y, Li XQ, Wang XH, Ma YT, Zhao Y, et al. Effect of Remote Ischemic Conditioning vs Usual Care on Neurologic Function in Patients with Acute Moderate Ischemic Stroke: The RICAMIS Randomized Clinical Trial.

JAMA. 2022;328(7):627-36.

WHAT IS ALREADY KNOWN?

The study aimed to assess the efficacy of remote ischemic conditioning (RIC) as a neuroprotective strategy for acute moderate ischemic stroke. Prior research had indicated the potential neuroprotective effects of RIC in preclinical studies, but robust clinical evidence for its effectiveness in patients with ischemic stroke was lacking.

STUDY DESIGN

This was a multicenter, open-label, blinded-endpoint, randomized clinical trial conducted at 55 hospitals in China from December 26, 2018, through January 19, 2021.

POPULATION STUDIED INCLUDING DEMOGRAPHICS

The study included 1,893 patients with acute moderate ischemic stroke, with a mean age of 65 years, and 34.1% of participants were women.

INTERVENTION(S) STUDIED

Eligible patients were randomly assigned to receive RIC treatment in addition to guideline-based treatment. RIC involved five cycles of cuff inflation for 5 minutes and deflation for 5 minutes to the bilateral upper limbs to 200 mm Hg. This was administered for 10–14 days.

JAYPEE BROTHERS

COMPARATOR USED

The control group received guideline-based treatment alone.

OUTCOMES EVALUATED

The primary endpoint was excellent functional outcome at 90 days, defined as a modified Rankin Scale score of 0–1. Secondary outcomes included favorable functional outcome (mRS scores 0–2), early neurologic deterioration, stroke-associated pneumonia, change in National Institutes of Health Stroke Scale (NIHSS) score, occurrence of stroke or other vascular events, and time to death within 90 days. The authors concluded that RIC significantly increased the likelihood of excellent neurologic function at 90 days for patients with acute moderate ischemic stroke. However, they emphasized the need for further trials to replicate these findings.

AUTHORS' VIEWPOINT

- Remote ischemic conditioning is a noninvasive and well-tolerated neuroprotective therapy that has shown promise in patients with acute moderate ischemic stroke.
- *Neuroprotection:* RIC activates endogenous tissue repair mechanisms, which can help protect the brain from further damage and promote neurological recovery.
- *Cardiovascular protection:* RIC has been shown to have cardiovascular benefits, including improving blood flow and reducing the risk of cardiovascular events.
- *Feasibility and safety:* RIC is a noninvasive and well-tolerated therapy that can be applied within 24 hours after stroke, including in patients receiving standard stroke treatments such as thrombolysis or mechanical thrombectomy.

STRENGTH OF THE STUDY

- *Rigorous methodology:* The Remote Ischemic Conditioning in Acute Moderate Ischemic Stroke (RICAMIS) study is designed with careful consideration of various factors, including appropriate inclusion criteria, random allocation of participants, standardized intervention protocols, and robust outcome measures. This rigorous methodology enhances the validity and reliability of the study's findings.
- *Targeted patient population:* The RICAMIS study focuses specifically on patients with acute moderate ischemic stroke. This targeted approach allows for a more precise evaluation of the potential benefits of RIC in this specific subgroup of stroke patients.
- *Functional outcome assessment:* The primary outcome measure of the RICAMIS study is functional outcome, assessed using validated stroke scales such as the modified Rankin Scale (mRS) or the NIHSS. By utilizing these standardized measures, the study aims to provide meaningful and clinically relevant data on the impact of RIC on patients' functional recovery.
- *Potential clinical relevance:* If the RICAMIS study demonstrates positive results, it has the potential to influence clinical practice and stroke management guidelines. The findings may support the adoption of RIC as an adjunctive therapy in the acute management of moderate ischemic stroke, potentially improving patient outcomes and enhancing the standard of care.
- *Ethical considerations:* The RICAMIS study adheres to rigorous ethical guidelines, ensuring informed consent, patient confidentiality, and protection of participants' rights. This commitment to

JAYPEE BROTHERS

ethical conduct demonstrates the study's integrity and further strengthens the credibility of its findings.

DRAWBACKS OF THE STUDY

- First, the open-label design did not allow blinding of the assigned treatment to participants and physicians. Blinded endpoint assessments were performed to reduce observer bias, but assessment of the success of outcome blinding was not performed.
- Second, a structured interview was used to assess the mRS disability score, which may have affected the accuracy of assessors in distinguishing how much of an individual's disability was due to stroke versus nonstroke.
- Third, there may have been outcome measurement bias in the full analysis set and selection bias in the exclusions after randomization.
- The relatively large amount of dropout after randomization may have introduced attrition bias, although there was a similar proportion of dropout in the RIC versus control group.
- Fourth, data regarding physiotherapy and speech language therapy were not collected and could not be assessed for possible confounding.
- Fifth, confirmation of these findings is required, including in non-Chinese populations, given potential differences compared with other populations in body mass, comorbid factors, and patterns of cerebrovascular disease of patients with AIS.

REVIEWERS' VIEWPOINT

- The RICAMIS study has the potential to bring about practice-changing implications in the management of acute moderate ischemic stroke if its findings demonstrate positive results.
- The target condition of acute ischemic stroke has a massive disease burden but limited treatment options currently beyond IV thrombolysis (which is only applicable to a small subset). Even minor benefits could impact many lives.
- Clinically relevant outcomes are being assessed—functional independence and disability at 90 days. Positive results on such patient-centered outcomes could strongly support implementation.
- An international, multi-center trial design will help minimize bias and ensure inclusion of a diverse population, supporting broader applicability of findings.

IMPACT ON CURRENT PRACTICE AND TAKE HOME MESSAGE

- *Integration of RIC in stroke management guidelines:* If the RICAMIS study shows that RIC improves functional outcomes in patients with acute moderate ischemic stroke, it may lead to the inclusion of RIC as a recommended neuroprotective strategy in stroke management guidelines. Healthcare professionals may be encouraged to consider RIC as part of the overall
- *Adoption of RIC as an adjunctive therapy:* Positive results from the RICAMIS study could lead to the adoption of RIC as an adjunctive therapy alongside standard care for acute moderate ischemic stroke. Healthcare providers may consider incorporating RIC protocols into the acute stroke management pathway to potentially enhance neuroprotection and improve patient outcomes.
- *Development of RIC protocols:* The RICAMIS study may provide insights into

JAYPEE BROTHERS

the optimal protocols for applying remote ischemic conditioning in acute moderate ischemic stroke. The study's findings, along with further research, could guide the development of standardized RIC protocols, including the duration, frequency, and intensity of RIC cycles, to maximize its neuroprotective effects.

- *Consideration of RIC in prehospital settings:* If RIC is shown to be beneficial in the RICAMIS study, there may be considerations for implementing RIC protocols in prehospital settings, such as during ambulance transport or in emergency medical services. This could provide an opportunity for early initiation of RIC and potentially extend the therapeutic window for neuroprotection.
- *Further research and refinement:* The RICAMIS study's findings, whether positive or negative, may stimulate further research and refinement of RIC protocols in acute moderate ischemic stroke. Subsequent studies could explore the optimal timing of RIC initiation, the potential benefits in different stroke subtypes, and the long-term effects of RIC on functional recovery and quality of life.

ARTICLE 15

Transfusion Guidelines in Traumatic Brain Injury: A Systematic Review and Meta-analysis of the Currently Available Evidence

Montgomery EY, Barrie U, Kenfack YJ, Edukugho D, Caruso JP, Rail B, et al. Transfusion Guidelines in Traumatic Brain Injury: A Systematic Review and Meta-analysis of the Currently Available Evidence.

Neurotrauma Rep. 2022;3(1):554-68.

WHAT IS ALREADY KNOWN?

- *Timing of transfusion:* Timing is an important consideration in transfusion management for TBI patients. Early initiation of transfusion, particularly in cases of severe hemorrhage, may help improve outcomes by maintaining adequate tissue oxygenation.
- *Transfusion thresholds:* The optimal transfusion threshold for TBI patients is still a matter of debate. The TRICC trial, which included ICU patients but not specifically TBI patients, found no difference in 90-day mortality between a restrictive transfusion threshold (hemoglobin level of 7 g/dL) and a liberal threshold (hemoglobin level of 10 g/dL).[1-3] However, more recent studies have not provided definitive superiority of one strategy over the other.
- *Outcomes:* Several studies have assessed the association of blood transfusion thresholds with clinical outcomes in TBI patients. On study found that transfusion when the initial hemoglobin level was >10 g/dL was associated with decreased survival. Another study suggested that transfusion was associated with worse outcomes with a hemoglobin threshold <9 or 10 g/dL, but improved outcomes in patients with a hemoglobin level <7 and 8 g/dL.
- *Risk factors:* Several risk factors have been identified for the need for blood transfusion in TBI patients. These include

JAYPEE BROTHERS

older age, lower GCS score, higher Injury Severity Score (ISS), and higher head Abbreviated Injury Scale (AIS) score.
- *Complications:* Blood transfusions in TBI patients can lead to various complications. These include acute respiratory distress syndrome (ARDS), infections, and adverse reactions to blood products.
- *Coagulopathy management:* Traumatic brain injury patients often experience coagulopathy, which increases the risk of bleeding and complications. The use of antifibrinolytic agents, such as tranexamic acid, has shown promise in reducing mortality and improving outcomes in TBI patients with coagulopathy.

STUDY DESIGN

A systematic review and meta-analysis was conducted using PubMed, Google Scholar, and Web of Science electronic database.

POPULATION STUDIED INCLUDING DEMOGRAPHICS

Traumatic brain injury patients who require blood transfusion and those did not require it. The transfusion triggers in traumatic brain injury. Studied population age, sex, Glasgow Coma Scale (GCS), ISS, and head AIS.

INTERVENTION(S) STUDIED

Traumatic brain injury patients who were not transfused blood, number of patients who were transfused blood, transfusion hemoglobin (Hgb) threshold, age, GCS on presentation, ISS on presentation, mean number of packed RBC (pRBC) transfusions, complication rate, and mortality rate.

COMPARATOR USED

Traumatic brain injury patients who did not require RBC transfusion.

OUTCOMES EVALUATED

Follow-up outcomes of interest included mortality, length of stay (LOS), and Glasgow Outcome Scale [GOS; or Glasgow Outcome Scale-Extended (GOSE)].

AUTHORS' VIEWPOINT

- Traumatic brain injury is a complex condition that can lead to significant morbidity and mortality. The management of TBI includes various aspects such as surgical intervention, prevention of secondary brain injury, and optimization of systemic factors.
- Transfusion of blood products, such as packed red blood cells (PRBCs), platelets, and fresh frozen plasma (FFP), is often considered in the management of TBI to maintain adequate oxygen delivery to the brain and prevent coagulopathy. However, the optimal transfusion thresholds and ratios in TBI remain a topic of debate.
- Several systematic reviews and meta-analyses have been conducted to evaluate the available evidence on transfusion guidelines in TBI, but the results have been somewhat conflicting. Some studies have suggested that a more liberal transfusion strategy with higher hemoglobin thresholds may improve outcomes in TBI patients, while others have not found a significant benefit or have even suggested potential harm with liberal transfusion practices.
- Standardized criteria regarding the definition of TBI severity, inclusion of anemic patients, Hgb monitoring, indications for transfusion, and consideration of the unique oxygenation requirements of cerebral tissue are important foundations on which to build future studies to more definitively answer this important question.

JAYPEE BROTHERS

STRENGTH OF THE STUDY

- *Comprehensive literature search:* The systematic review and meta-analysis will involve a comprehensive search of multiple electronic databases, ensuring a thorough identification of relevant studies. This approach minimizes the risk of missing important evidence.
- Transfusion status and GCS on admission were independent predictors for long-term functional outcome is important to consider these associations in the context of transfusion threshold analyses, given that outcomes between groups may simply be the result of transfused patients being sicker and more likely to receive transfusion.
- The meta-analysis determined that transfused patients have higher rates of mortality, which likely suggests that patients who require a transfusion have an inherently worse prognosis at baseline, but further clarification is warranted given the heterogeneity of included studies.
- *Inclusion of different study designs:* The article plans to include both randomized controlled trials (RCTs) and observational studies, allowing for a broader assessment of the available evidence. This inclusion of different study designs increases the robustness and generalizability of the findings.
- *Quality assessment:* The article mentions the use of appropriate tools to assess the quality of included studies, such as the Cochrane Risk of Bias Tool for RCTs and the Newcastle-Ottawa Scale for observational studies. This quality assessment helps ensure that the included studies are methodologically sound and minimizes the risk of bias.
- *Data extraction and analysis:* The article describes a standardized data extraction process, which involves two independent reviewers extracting data from the selected studies. This approach enhances the reliability and accuracy of the data. Additionally, the planned meta-analysis using appropriate statistical methods allows for the estimation of pooled effect sizes, providing a quantitative summary of the findings.
- *Potential impact on clinical practice:* The article highlights the potential impact of the study findings on clinical practice. By synthesizing the currently available evidence, the study aims to inform transfusion guidelines in traumatic brain injury and ultimately improve patient outcomes. This practical relevance enhances the significance of the research.

DRAWBACKS OF THE STUDY

Weaknesses of the article may include:

- Inclusion criteria are inconsistent regarding the definition of TBI, whether anemic versus non-anemic patients are eligible for inclusion, follow-up time, and the specific definitions "restrictive" and "liberal" transfusion thresholds.
  Variability in definitions: Definitions of transfusion triggers/thresholds, anemia levels, and outcomes were not standardized between studies, introducing some uncertainty.
- *Potential publication bias:* Additionally, only two included studies were RCTs that sought to directly compare outcomes in TBI patients between transfusion thresholds. The remaining studies were post hoc analyses of RCTs or unmatched retrospective analyses, which are more subject to selection and confounding bias. The inclusion of both RCTs and post hoc analysis may introduce heterogeneity in terms of study design, patient populations, and interventions.

JAYPEE BROTHERS

- *Variability in transfusion strategies:* Transfusion strategies may vary across studies, including thresholds for transfusion, type of blood products used, and timing of transfusions. This heterogeneity could limit the ability to draw firm conclusions and make specific recommendations for clinical practice.
- *Quality of included studies:* Although the article mentions the use of quality assessment tools, the overall quality of the included studies may vary. The inclusion of studies with high risk of bias or low methodological quality could introduce potential sources of bias and impact the reliability of the findings.
- *Potential confounding factors:* The observational studies included in the analysis may be prone to confounding, as they rely on existing data and may not have controlled for all potential confounders. This could introduce biases and affect the accuracy of the estimated treatment effects.

REVIEWERS' VIEWPOINT

- It is important to note that the management of TBI is highly individualized and depends on various factors, including the severity of the injury, the patient's clinical condition, and the presence of associated injuries. The decision to transfuse blood products in TBI should be based on a careful assessment of the patient's hemodynamic status, coagulation profile, and the presence of active bleeding.
- There is still a need for a systematic review and meta-analysis to comprehensively evaluate the currently available evidence and address the remaining uncertainties in transfusion guidelines for traumatic brain injury.

IMPACT ON CURRENT PRACTICE AND TAKE HOME MESSAGE

- Current literature appears to support restrictive transfusion protocols (Hgb <7 g/dL) compared to liberal thresholds (Hgb <10 g/dL), but the quality and consistency of evidence is mixed.
- The management of TBI is highly individualized, and the decision to transfuse RBCs should be based on the patient's specific needs. Factors such as the severity of the injury, presence of active bleeding, and hemodynamic stability should be taken into account.

REFERENCES

1. Gobatto ALN, Link MA, Solla DJ, Bassi E, Tierno PF, Paiva W, et al. Transfusion requirements after head trauma: a randomized feasibility-controlled trial. Crit Care. 2019;23(1):89.
2. Warner MA, O'Keeffe T, Bhavsar P, Shringer R, Moore C, Harper C, et al. Transfusions and long-term functional outcomes in traumatic brain injury. J Neurosurg. 2010;113(3):539-46.
3. McIntyre LA, Fergusson DA, Hutchison JS, Pagliarello G, Marshall JC, Yetisir E, et al. Effect of a liberal versus restrictive transfusion strategy on mortality in patients with moderate to severe head injury. Neurocrit Care. 2006;5(1):4-9.

JAYPEE BROTHERS

r detailed information on critical care books, visit our website www.jaypeebrothers.com, for detailed information on critical care books, visit our webs

Yearbook of
CRITICAL CARE 2023
HICS Initiative

The field of intensive care is very dynamic, and new evidence emerges almost on a daily basis. Keeping pace with all the new information, analyzing and assimilating it and implementing its gist is the key to the practice of evidence-based medicine. The Hyderabad Intensive Care Symposium (HICS) has been in the forefront of bringing such information into the midst of keen learners of intensive care every year. However, the time constraints of a didactic meeting make it impossible to convey every advance and guideline. The team therefore took upon itself the task of compiling all the major and interesting publications of the last 12 months and having them analyzed for publication. The endresult is this *Yearbook of Critical Care*.

- Comprehensive review of all major publications from July 2022 to July 2023
- Experienced and seasoned teachers as reviewers
- Systemwise compilation
- Reviewers' opinion at the end of each section
- Handy format

Srinivas Samavedam MD DNB FRCP FNB EDIC FICCM is currently the Chief Intensivist at Ramdev Rao Hospital, Hyderabad, Telangana, India. He has more than 20 years of experience as a practicing Intensivist and more than 15 years as a Teacher. He has been an Examiner for several critical care examinations and has a strong passion in sharing knowledge. He has served as the General Secretary and Vice President of the Indian Society of Critical Care Medicine (ISCCM) in the past.

Ganshyam Jagathkar MD FNB FICCM is currently the Director of Critical Care at Medicover Hospitals, Hyderabad, Telangana, India. He has been the organizing Secretary of the popular HICS symposium since inception. His passion for teaching students in a simple and crisp manner has made him a popular figure among students and young intensivists. He is currently serving as the Vice President of the Indian Society of Critical Care Medicine (ISCCM).

Printed in India

Available at all medical bookstores
or buy online at www.jaypeebrothers.com



JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
CRITICAL CARE

