



# JNIC

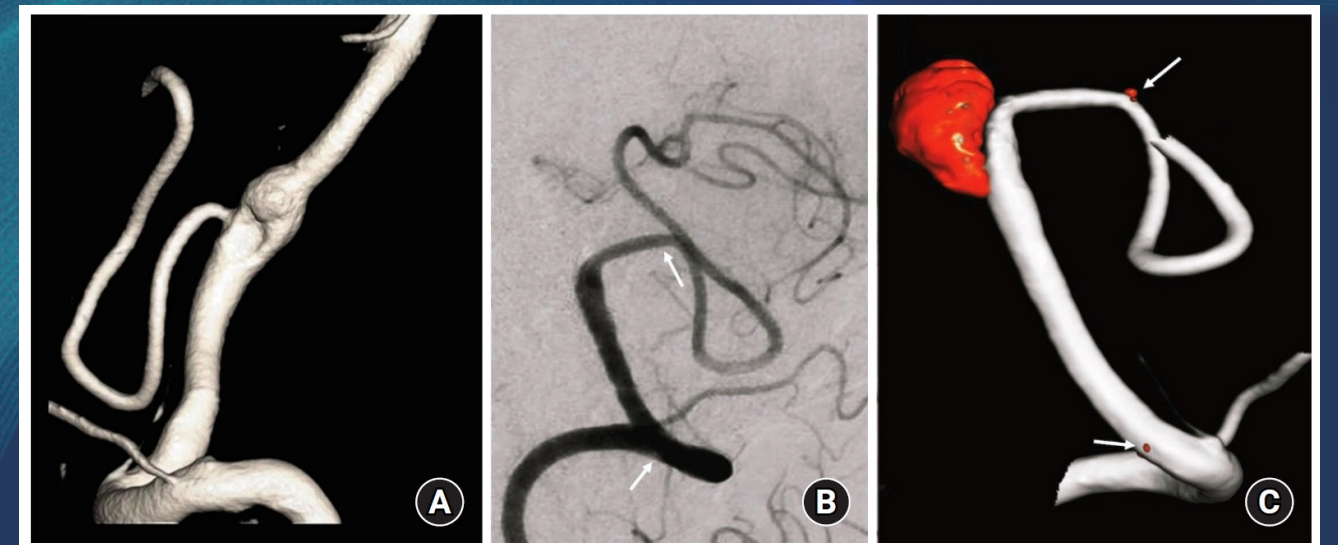
Journal of Neurointensive Care

Journal of Neurointensive Care

# JNIC

Journal of Neurointensive Care

Vol. 7 · No. 1 · April 2024



Pages 1-39

Vol. 7 · No. 1 · April 2024

Korean Neurointensive Care Society

e-jnic.org

# JNIC

Journal of Neurointensive Care

Vol. 7 • No. 1 • April 2024

---

## Aims and Scope

*Journal of Neurointensive Care (J Neurointensive Care, JNIC)* is the official journal of the Korean Neurointensive Care Society and is published biannually (the last day of April and October). It is a peer reviewed, open access journal aimed at publishing all aspects of neurointensive care medicine, such as stroke, brain and spine trauma, perioperative neurosurgical intensive care, neuro-pediatric severe anomaly, CNS infection, seizure, myelitis and etc. It is intended for all neurointensive care providers as neurosurgeons, neurologists, anesthesiologists, emergency physicians, and critical care nurses treating patients with urgent neurologic disorders.

## Open Access

This is an open-access article distributed under the terms of the Creative Commons Attribution Non- Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## Subscription Information

The Korean Neurointensive Care Society will send *J Neurointensive Care* for free to some important individuals and institutions. Full text PDF files are also available at the official website (<http://www.e-jnic.org>). To order a subscription to *J Neurointensive Care*, please contact our editorial office.

---

**Publisher:** Byung-Moon Cho

**Editors-in-Chief:** Dong-Hyuk Park

## Editorial Office

Department of Neurosurgery, Korea University College of Medicine  
73, Incheon-ro, Seongbuk-gu, Seoul 02841, Korea  
Tel: +82-2-920-6833 Fax: +82-2-929-0629 E-mail: [jnic.editor@gmail.com](mailto:jnic.editor@gmail.com)

## Printing Office M2PI

#805, 26 Sangwon 1-gil, Seongdong-gu, Seoul 04779, Korea  
Tel: +82-2-6966-4930 Fax: +82-2-6966-4945 E-mail: [support@m2-pi.com](mailto:support@m2-pi.com)

© 2024 by Korean Neurointensive Care Society

∞This paper meets the requirements of KS X ISO 9706, ISO 9706-1994 and ANSI/NISO Z39.48-1992 (Permanence of Paper)

## Editorial Board

### Editors-in-Chief

Dong-Hyuk Park *Korea University, Korea*

### Associate Editor

Jang Hun Kim *Korea University, Korea*

### Editorial Board

Jin Hwan Cheong *Hanyang University, Korea*  
Junseok W Hur *Korea University, Korea*  
Sung Pil Joo *Chonnam National University, Korea*  
Tae Gon Kim *CHA University, Korea*  
Young Woo Kim *The Catholic University of Korea, Korea*  
Doo-Sik Kong *Sungkyunkwan University, Korea*  
Hyon-Jo Kwon *Chungnam National University, Korea*  
Soon Chan Kwon *Ulsan University, Korea*  
Sang Weon Lee *Pusan National University, Korea*  
Taek Kyun Nam *Chung-Ang University, Korea*  
Keun Young Park *Yonsei University, Korea*  
Paul R. Sanberg *University of South Florida, USA*  
Rokuya Tanikawa *Sapporo Teishinkai Hospital, Japan*  
Chan Jong Yoo *Gachon University, Korea*

### Editorial Assistant

Do-Young Kim *Korea University Anam Hospital, Korea*

### Ethics Editor

Young Mo Ku *Ulsan University, Korea*

### Statistical Editor

Jae Won Lee *Korea University, Korea*

### English Editor

Dong-Wook Lee *Korea University, Korea*

### Manuscript Editor

Jeonghee Im *M2PI, Korea*

### Layout Editor

In A Park *M2PI, Korea*

### Website and JATS XML File Producers

Jeonghee Im *M2PI, Korea*

### Review Articles

- 1 Endovascular Treatment Strategies for Vertebral Artery Dissection: A Single-Center Experience and Literature Review  
Junhyung Kim, Sang Kyu Park, Joonho Chung
- 12 Cardiac Arrest in Traumatic Brain Injury  
Oday Atallah, Md Moshir Rahman, Bipin Chaurasia, Vishal Chavda, Amit Agrawal

### Original Articles

- 18 Intracranial Pressure Monitoring in Patients With Traumatic Brain Injury: An Umbrella Review of Systematic Review and Meta-Analysis  
William A Florez-Perdomo, Rakesh Mishra, Luis Rafael Moscote-Salar, Rafael Cincu, Ved Prakash Maurya, Amit Agrawal
- 29 Comparison the Perfusion/Diffusion Mismatching Judging From CT-Based and MR-Based Study  
Jae-Yong Shim, Do-Sung Yoo, Kwang-Wook Jo, Hae-Kwan Park

### Letter to the Editor

- 37 Virtual Neurosurgery Education Conferences on Social Medi: A Perspective  
Minaam Farooq, Noor Atiq, Amr Badary, Bipin Chaurasia

# Endovascular Treatment Strategies for Vertebral Artery Dissection: A Single-Center Experience and Literature Review

Junhyung Kim, Sang Kyu Park, Joonho Chung

Department of Neurosurgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Received: November 2, 2023

Revised: December 7, 2023

Accepted: December 22, 2023

## Corresponding Author:

Joonho Chung, MD, PhD  
Department of Neurosurgery,  
Gangnam Severance Hospital,  
Yonsei University College of  
Medicine, 211 Eonju-ro,  
Gangnam-gu, Seoul 06273, Korea  
Tel: +82-2-2228-3390  
E-mail: ns.joonho.chung@gmail.com

Although some vertebral artery dissection (VADs) cases heal naturally, others progress to stroke, necessitating intervention. Endovascular treatment (EVT) has gained prominence as a viable approach for addressing VADs owing to its perceived low risk of procedure-related complications and high effectiveness. In this review, we share our practical experience of this technique by incorporating the indications and methods for VAD treatment via EVT. Our EVT strategies covered the management of both ruptured and selected cases of unruptured VADs. Unruptured cases that require treatment include those complicated by lesions with recurring or progressive ischemia, large dissecting aneurysms with mass effects, early changes in the VAD structure during follow-up, and involvement of the basilar or bilateral vertebral arteries (VAs). In cases of ruptured VADs, we aimed to occlude the site of rupture through either VA occlusion or stent-assisted coiling. For unruptured VADs, the goal is to restore the original blood flow dynamics using a range of stenting techniques. The choice of EVT technique should be made on a case-by-case basis, considering factors such as the patient's presenting symptoms, hemodynamic status, adequacy of collateral blood supply, and anatomical characteristics of the important arteries and perforators.

**Keywords:** Endovascular procedures; Dissecting vertebral artery aneurysm; Stents

## INTRODUCTION

Intracranial vertebral artery dissection (VAD) is the most common form of brain arterial dissection. While some types of VAD heal naturally, others progress to stroke and require treatment. Stroke caused by VAD can present as brainstem dysfunction, cerebellar infarction, or subarachnoid hemorrhage (SAH)<sup>1</sup>. Spontaneous intracranial VAD can be categorized into three primary clinical types: headaches, non-hemorrhagic ischemic symptoms, and SAH<sup>2</sup>. Arterial dissection begins with sudden disruption of the in-

ternal elastic lamina and media, leading to the accumulation of blood within the arterial wall and the formation of an intramural hematoma. In patients with arterial dissection exhibiting a narrowed or blocked arterial pattern, a subintimal hematoma and intimal flap can restrict blood flow<sup>3,4</sup>.

Endovascular treatment (EVT) has recently gained popularity as a treatment option for VADs because of its low rates of procedure-related complications and high efficacy<sup>2,5-7</sup>. The choice of treatment for patients with VADs depends on the patency of the contralateral vertebral artery (VA) and the location of the dissec-

tion segment in relation to the origin of the posterior inferior cerebellar artery (PICA). Complete occlusion of the dissected segment has been deemed the optimal treatment for VAD<sup>5-8</sup>. If the dissection is located proximal or distal to the PICA without contralateral VA hypoplasia, the lesion can be treated through complete occlusion of the dissected segment using coils (internal trapping), to allow for PICA filling from the contralateral or ipsilateral VA<sup>9</sup>. However, when VADs involve the PICA origin, complete isolation of the dissected segment can be achieved through internal coil trapping with PICA revascularization via bypass surgery or PICA stenting. In such cases, EVT techniques such as VA trapping with VA-PICA stenting, multiple stenting, flow-diverting stenting (FDS), and stent-assisted coil embolization (SAC) have shown promising outcomes. In recent years, we have developed and refined strategies for VAD treatment. In this article, we aim to share our experiences with VADs, including their indications and EVT methods.

## DIAGNOSIS

### Inclusion criteria

(1) A history of acute clinical symptoms and/or signs relevant to intracranial VAD; (2) angiographic evidence of VAD (such as aneurysmal dilatation of the intracranial VA, pearl-and-string signs, or tapered steno-occlusion); and (3) available results from digital subtraction angiography (DSA), magnetic resonance (MR) imaging, and/or computed tomographic (CT) angiography conducted at symptom onset.

### Exclusion criteria

(1) Definitive traumatic VAD; (2) iatrogenic VAD; (3) incidental discovery of asymptomatic fusiform dilatations of the VAs; (4) laboratory or angiographic findings suggestive of vasculitis or fibromuscular dysplasia; or (5) lack of documented MR or CT angiography at the initial assessment.

## TREATMENT INDICATIONS

We performed EVT for intracranial VADs based on the following indications:

- (1) Ruptured VADs with SAH.
- (2) Unruptured VADs:
  - VAD with recurrent or progressive ischemia
  - Dissecting aneurysms > 7 mm, or those causing mass effects
  - Early unfavorable changes in VAD morphology during follow-up
  - Involvement of the basilar arteries
  - Bilateral VADs

### Ruptured VADs presenting with SAH

VADs presenting with SAH are considered unstable and carry a high risk of rebleeding, as the hemodynamic stress exerted on the vessel wall can lead to episodes of rebleeding. One study reported a rebleeding rate as high as 71.4% in a group of 42 untreated patients<sup>10</sup>. In cases of rebleeding, the mortality rate was notably elevated to 46.7%<sup>10</sup>. EVT can reduce hemodynamic stress and create a favorable environment for healing. The optimal approach for patients with SAH due to VADs involves complete isolation of the dissected segment from the circulation.

### Unruptured VADs

Currently, there is no consensus regarding the optimal management strategies for unruptured VADs. Nevertheless, EVT has gained preference as a treatment option for VADs owing to the significant risk of cranial nerve palsy and brainstem injury associated with microsurgery. Intracranial VADs can lead to narrowing and subsequent occlusion of the VA, resulting in thromboembolic ischemia<sup>1</sup>. Ischemic strokes in the posterior fossa involving the brainstem may lead to elevated mortality rates and substantial morbidity, resulting in a variety of neurological deficits<sup>11</sup>. Moreover, patients presenting with ischemic symptoms tend to have less favorable outcomes compared to those without such symptoms<sup>12</sup>. These findings suggest that EVT for VADs during the acute phase should predominantly focus on preventing the progression or recurrence of ischemic stroke (particularly in patients presenting with ischemic symptoms), rather than solely aiming to prevent SAH.

While most unruptured VADs can spontaneously heal, unruptured VADs subsequently leading to SAH have been reported<sup>13-15</sup>. Large dissecting aneurysms greater than 7 mm or with mass effect and lesions with adverse changes in shape and size during follow-up are associated with an elevated rupture risk. Therefore, EVT is advisable for patients with progressive ischemia or recurrent ischemic symptoms despite medication, as well as for those with an enlarged dissection aneurysm observed on follow-up angiographic imaging<sup>16-19</sup>.

In the case of unruptured VADs, involvement of the basilar artery appears to hold significant clinical importance in terms of patient outcomes. Previous studies have consistently demonstrated that VADs affecting the basilar artery are independent predictors of unfavorable outcomes<sup>12,20-23</sup>. Additionally, other factors such as the initial severity of ischemic symptoms (as indicated by a higher baseline National Institutes of Health Stroke Scale [NIHSS] score), dissections involving bilateral VAs, and intracranial VA involvement, have all been suggested as predictors of unfavorable outcomes in cases of unruptured VADs. Consequently, consider-

ing EVT for VADs involving the basilar artery, as well as those affecting both VAs seems reasonable<sup>12,24,25</sup>.

## ENDOASCULAR TREATMENTS

### Periprocedural management of antithrombotic therapy

Treatment of ruptured VADs generally involves the administration of loading doses of clopidogrel (300 mg) and aspirin (300 mg), delivered through a nasogastric tube following femoral artery puncture<sup>26</sup>. Post-procedural surgical management procedures, such as external ventricular drainage and ventriculoperitoneal shunt insertion, can be performed without interruption by antiplatelet agents.

For symptomatic unruptured VADs, patients are administered daily doses of 75 mg clopidogrel and 100 mg aspirin for more than 5 d before undergoing EVT. During the procedure, patients received an intravenous heparin load of 50 IU/kg immediately after guiding catheter placement, and the activated clotting time was maintained at twice the baseline level throughout the endovascular procedure. Heparin administration was discontinued immediately after completion of the procedure. In the event of thromboembolic complications during the procedure, an intra-arterial injection of 0.5–1.0 mg of the glycoprotein IIb/IIIa antagonist tirofiban is administered. After the procedure, patients who have undergone EVT with stents are prescribed daily doses of 75 mg clopidogrel for 3 months, and 100 mg aspirin daily for a minimum of 12

months. Patients previously taking anticoagulants continued to receive the same anticoagulant along with aspirin (100 mg/d). In cases involving FDS, patients were prescribed clopidogrel 75 mg daily for at least 6 months, and aspirin 100 mg daily for at least 24 months. Follow-up angiography is typically scheduled within one month, 3–6 months, and at 12–24 months for unruptured VADs. For symptomatic unruptured VADs, follow-up angiography was conducted at 3–6 months, and then at 12–24 months.

### Endovascular techniques

Treatment decisions and endovascular treatment techniques are summarized in Fig. 1.

#### Deconstructive technique

A deconstructive technique refers to occlusion of the parent artery achieved through methods such as internal coil trapping or proximal coil occlusion. This approach effectively halted blood flow into the dissected segment of the VA. If dissection is not completely excluded from the forward arterial circulation after proximal occlusion, a potential for rebleeding remains. Furthermore, rebleeding can occur if the dissection cavity expands following proximal occlusion. Ideally, the dissected segment should be occluded both proximally and distally to prevent the risk of rebleeding through retrograde filling of the dissecting aneurysm. Deconstructive techniques are preferred and offer advantages for treating ruptured VADs, as they can effectively prevent rebleeding, reduce the likelihood of recurrence, and allow for additional surgical proce-

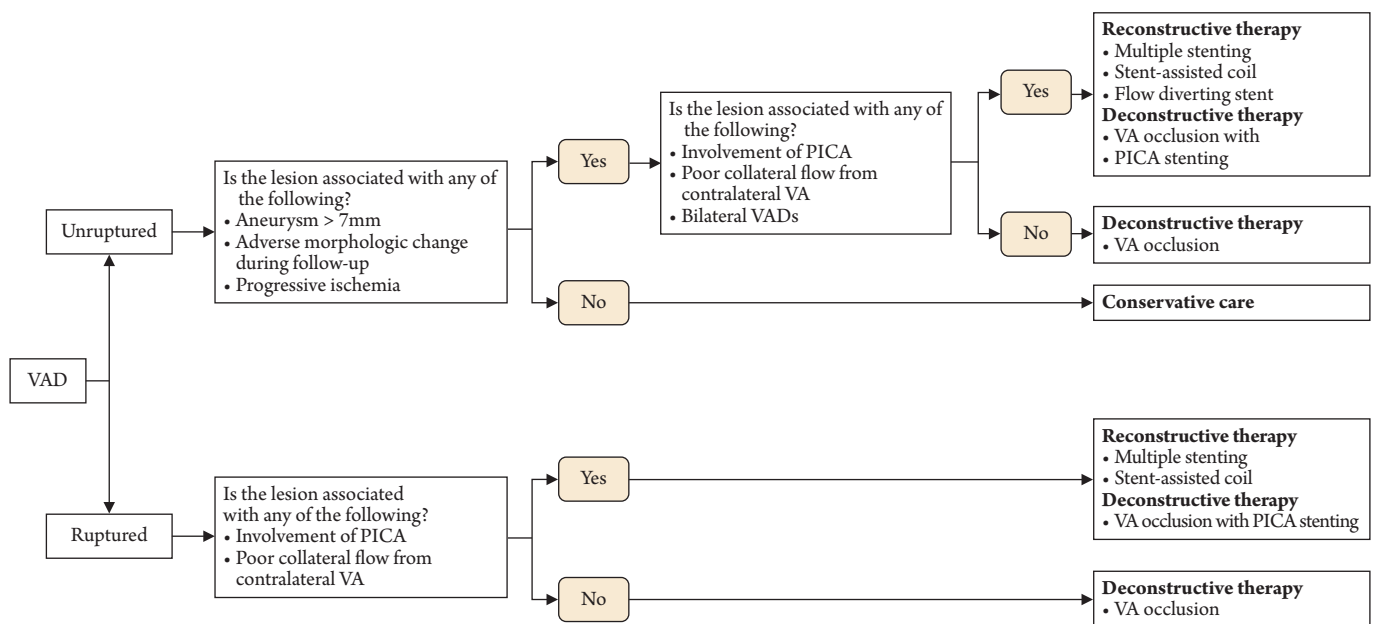


Fig. 1. A flowchart for the treatment decisions and endovascular treatment strategies for vertebral artery dissection. PICA: Posterior inferior cerebellar artery, VAD: Vertebral artery dissection, VA: Vertebral artery.

dures, including external ventricular drainage and decompressive surgery, as no antiplatelet medication is necessary. Deconstructive techniques carry the risk of ischemic stroke in cases where the collateral blood supply is insufficient; therefore, this method is recommended for VADs in nondominant VAs, or VAs with robust collateral circulation.

#### 1) VA trapping (occlusion) by coiling

If dissection occurs either proximal or distal to the PICA, without any significant narrowing (hypoplasia) of the contralateral VA, the lesion can be completely occluded using coils. In this approach, the PICA can subsequently receive blood flow from either the contralateral or ipsilateral VA. Our preferred method was VA trapping by coiling, which involves sacrificing the VA to completely isolate the dissected segment from the circulatory system. Typically, this method is applied to VADs that do not involve the PICA origin in the non-dominant VA using either internal coil trapping or proximal coil occlusion. Proximal occlusion of the VA entails the placement of coils in the segment proximal to the VAD, effectively blocking blood flow into the affected region. Conversely, internal coil trapping involves the embolization of the VA within the dissected segment itself. In cases where a deconstructive method was considered for dominant VAs, we performed balloon test occlusion at the ipsilateral VA, proximal to the affected segment, to assess the feasibility and safety of the procedure.

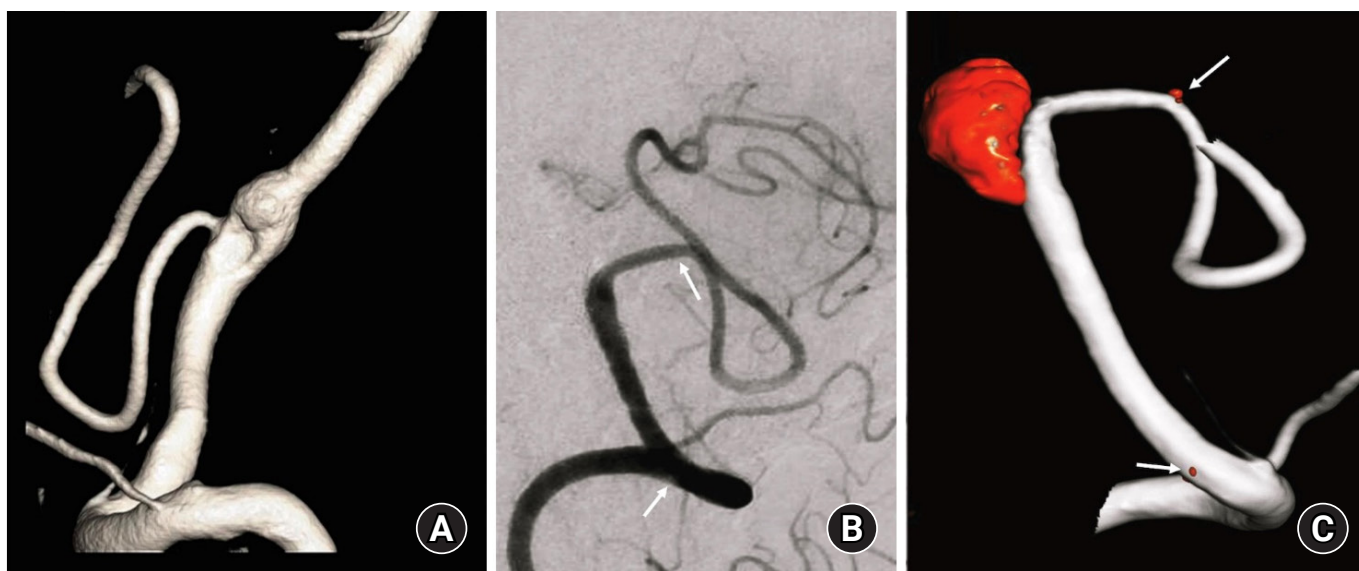
#### 2) VA trapping (occlusion) with PICA stenting

When VAD involves the origin of the PICA in the nondominant

VA, a substantial risk of PICA infarction is incurred if internal coil trapping is performed<sup>6,27</sup>. In the context of EVT, the preferred approach in such a case is reconstructive therapy. In our practice, occlusion of the dissected segment by coil embolization, while preserving the PICA through PICA stenting, was considered. We have previously reported a case in which we treated a patient with a self-expanding closed-cell Enterprise stent (Codman Neurovascular, FL, USA) deployed from the proximal VA to the PICA. We thereby achieved complete occlusion of the dissected segment through coiling (Fig. 2)<sup>6</sup>. When the origin of the PICA involves the distal segment of the VAD, we may perform internal coil trapping of the VAD and PICA stenting by deploying an Enterprise stent from the distal VA to the PICA, by approaching from the contralateral VA<sup>7</sup>.

When we assessed the clinical and radiological outcomes of VADs involving the PICA origin using different EVT approaches (VA trapping with VA-PICA stenting, multiple stenting, SAC, and FDS), we found that VA trapping with VA-PICA stenting resulted in the lowest recurrence rate and favorable neurological outcomes. In contrast, SAC displayed higher recurrence rates and a high potential for severe, disabling infarctions<sup>5</sup>.

Regarding PICA patency following VA-PICA stenting, we have previously shared our experience using Enterprise stents in small arteries (less than 2 mm in diameter)<sup>28</sup>. Among the 31 enrolled patients, three (9.7%) experienced procedure-related complications, all of which were asymptomatic. Follow-up angiography was performed in 27 patients (87.1 %) at an average of 15.5 months post-EVT. In cases where the parent arteries had two acute angles



**Fig. 2.** (A) Three-dimensional reconstruction image showing a ruptured vertebral artery dissection with involvement of the origin of the posterior inferior cerebellar artery (PICA) in a non-dominant vertebral artery (VA). (B) One-year follow-up angiography. (C) Three-dimensional reconstruction image showing PICA patency. Arrows indicate proximal and distal stent markers in the VA and the PICA.



(four cases), 75.0% were occluded on follow-up angiography. Conversely, parent arteries with either no acute angles (13 cases) or one acute angle (six cases) showed 100% patency on follow-up angiography. Further, a significant difference was found between the sizes of the parent arteries at follow-up and before EVT ( $p=0.037$ ). On multivariate logistic regression analysis, the tortuosity (number of acute angles) of the parent arteries was identified as the sole predisposing factor for size increments of the parent arteries on follow-up angiography. Successful stent navigation and deployment were achieved in all patients (100%) without symptomatic procedure-related complications. These results suggest that the angiographic configuration and course of the parent arteries are crucial factors in maintaining the patency of parent arteries with a diameter of less than 2 mm. Thus, stent deployment in small parent arteries is technically safe. Based on our findings, we believe that PICA patency can be ensured following VA-PICA stenting.

#### *Reconstructive technique*

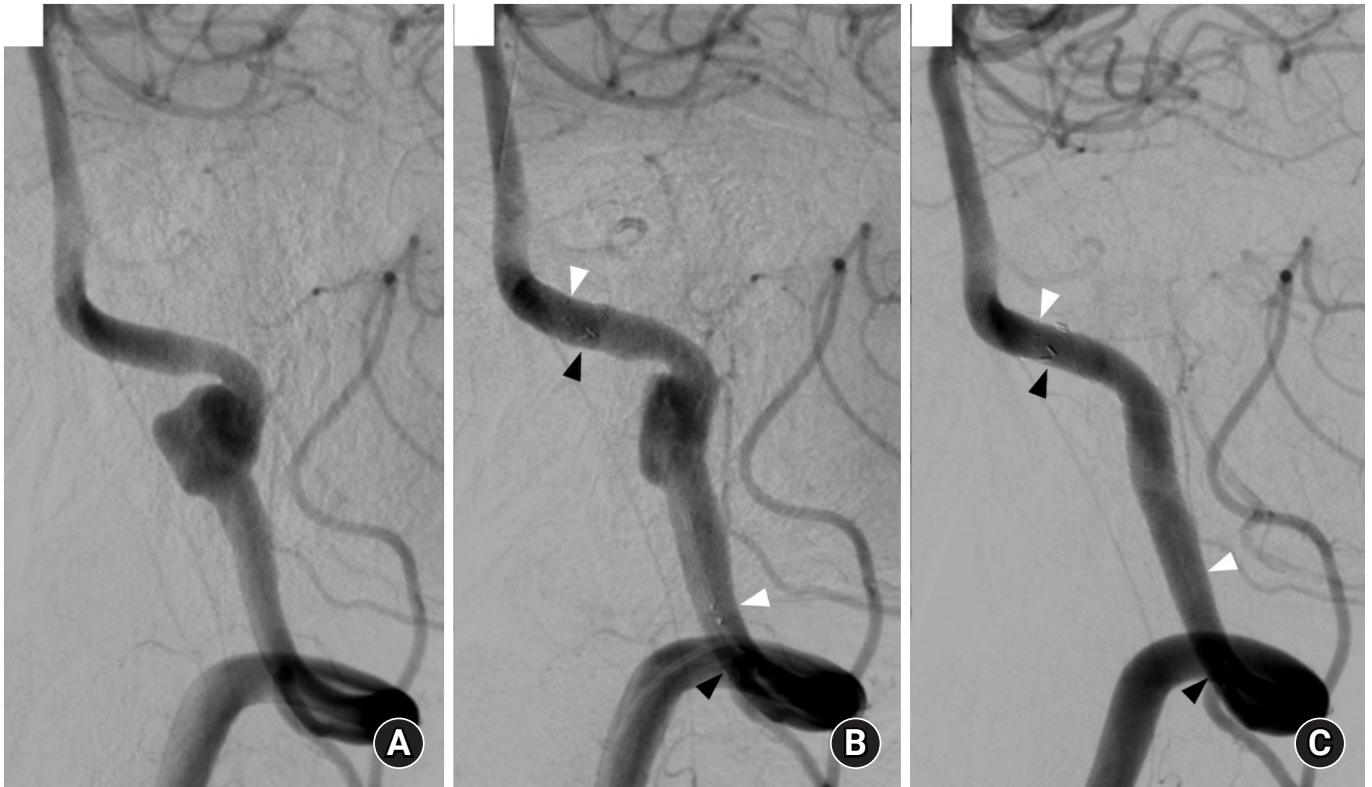
Deconstructive techniques may not always be feasible, especially in cases of VADs involving the dominant or solitary VA with limited collateral blood flow, or in instances of bilateral VADs. In such scenarios, reconstructive techniques that aim to preserve the parent artery by using stents alone or in combination with coiling have gained prominence as viable alternatives for vessel deconstruction. Reconstructive techniques offer potential benefits, particularly in cases in which complete angiographic occlusion is not the primary goal. Endovascular reconstruction of VADs employing methods such as multiple stenting (the stent-in-stent technique), SAC, and FDS have also become more common. The objective of these techniques is to prevent ischemic complications, while restoring the original hemodynamics of the affected artery. Notably, all reconstructive techniques require an extended period of dual antiplatelet therapy, particularly in the context of SAH, which may pose challenges for subsequent neurosurgical interventions, such as external ventricular drainage and craniectomy. However, reconstructive techniques offer the advantage of maintaining physiological blood flow in the ipsilateral VA, which may reduce the risk of periprocedural morbidity. Understanding the relationship between the dissected segment of the VA and critical structures such as the anterior spinal artery, PICA, and medullary perforators is of utmost importance to ensure a safe and enduring cure following EVT.

#### 1) Multiple stenting

In cases of symptomatic unruptured VADs or lesions with steno-occlusive angiographic features such as the pearl-and-string sign, multiple stenting is often considered. When a self-expanding

closed-cell stent is deployed to cover the dissected segment, it facilitates the reconstitution of the vessel lumen. This, in turn, aids in the stabilization of the intimal flaps, and promotes vessel wall repair by encouraging neointima formation. In instances where the VAD extends over a very long segment and reaches the basilar artery without the presence of a large dissecting aneurysm, employing multiple stents with a telescoping technique can prove to be an effective treatment method. We prefer using a laser-cut closed-cell Enterprise stent for multiple stents. This technique was found to be easy to deploy and exhibited a commendable chronic outward force, indicating its ability to maintain its diameter against external forces. Moreover, when using a closed-cell-design stent and opting for oversizing, the stent tends to possess a higher chronic outward force<sup>29)</sup>.

One approach we employed for multiple stenting without coiling, particularly when VAD occurred in the dominant or solitary VA, was the double-stenting technique. This method involves deploying a Low-profile Visualized Intraluminal Support (LVIS) Blue stent (Microvention, Tustin, CA, USA) within an Enterprise stent<sup>29)</sup>. LVIS Blue stent is a braided stent known for providing a high degree of metal coverage, typically ranging from 22–28%. This characteristic makes the LVIS Blue stent beneficial for achieving complete obliteration of a dissecting aneurysm, as it enhances the occlusion rate by exerting a flow diversion effect. Moreover, the overlapping LVIS Blue stents can potentially act as flow diverter devices because of their substantial metal coverage surface area. However, deploying an LVIS Blue stent in a VAD may result in a reduced metal coverage surface area, as the device often experiences a transition from a constrained to an unconstrained diameter<sup>30-32)</sup>. To overcome this limitation and capitalize on the flow diversion effect of the LVIS Blue stent, we utilized the structural properties of a laser-cut closed-cell Enterprise stent using a technique known as the LVIS Blue stent-within-an-Enterprise stent. The Enterprise stent exhibited minimal outward expansion at the unconstrained segment, and served as a scaffold to reduce the size of the unconstrained segment across the fusiform dissecting aneurysm neck. This ensured an even distribution of high metal coverage surface area and porosity without the presence of a transition zone at either end of the aneurysm neck. Consequently, the flow-diverting effect of the LVIS Blue stent remained intact. An Enterprise stent typically provides a metal coverage surface area ranging from 8 to 11%. After overlapping with the LVIS Blue stent, the metal coverage surface area increased to approximately 33% of the straight vessel. Using this technique, we were able to facilitate the complete obliteration of VA dissecting aneurysms, while promoting endothelial healing of the VA (Fig. 3)<sup>33)</sup>. This technique offers a cost-effective alternative to deploying dedicated flow divert-



**Fig. 3.** (A) Right vertebral artery (VA) angiography showing the dissecting aneurysm involving 360 degree of the dominant VA. (B) Flow stagnation inside the aneurysm immediately after performing a LVIS blue stent-within-an-Enterprise stent technique. (C) Right VA angiography at 6-month follow-up revealing complete obliteration of the aneurysm and remodeling of the VA. The VA shows good patency without in-stent stenosis. White arrowheads and black arrowheads indicate proximal and distal ends of the LVIS Blue and Enterprise, respectively.

ers. In addition, the delivery and deployment processes are relatively simple and straightforward. However, this technique requires an adequate time for complete healing of the dissected segment. Therefore, it may not be suitable for ruptured VADs, given the challenge of achieving immediate obliteration of the rupture point and the associated risk of hemorrhagic complications due to the use of dual antiplatelet agents during the acute phase.

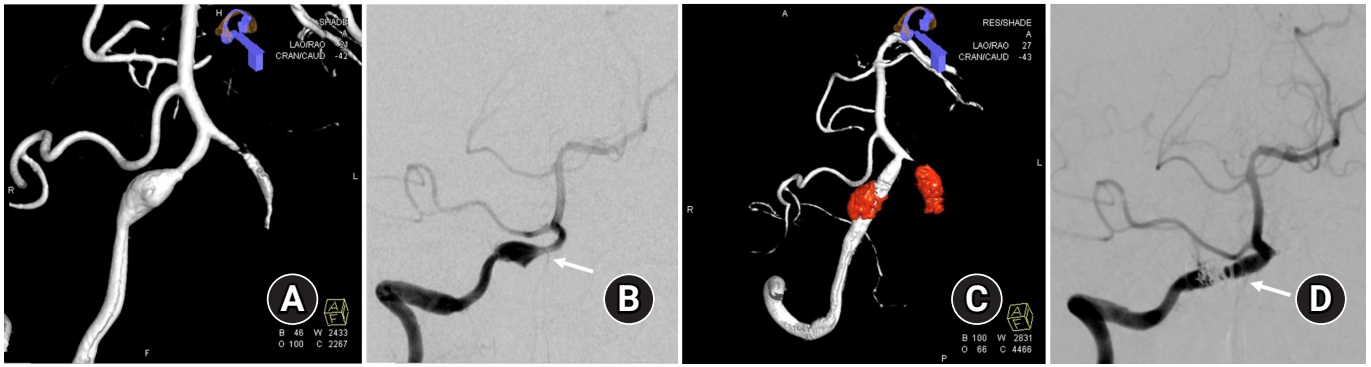
## 2) Stent-assisted coiling

In cases involving ruptured VADs associated with dissecting aneurysms within the dominant or single VA with limited collateral flow, multiple stenting or FDS may present a risk of rebleeding during the latent period when the dissecting flap stabilizes and thrombosis forms within the dissecting aneurysm. Owing to the non-saccular shape of the dissecting aneurysms, reconstructive techniques without coils are often challenging for ruptured VADs. As a result, our preferred approach for patients with ruptured VADs and aneurysmal dilatation in the dominant or single VA was the SAC (Fig. 4).

However, when performing SAC for VADs, considering the in-

volvement of critical branches such as the anterior spinal artery, PICA, or medullary perforators is crucial. Preserving these branches is paramount for safe reconstruction of the VA. In some cases, achieving complete SAC may be challenging, as dissecting aneurysms frequently exhibit fusiform rather than saccular dilatation. In such instances, if the rupture point of a dissecting aneurysm is identified, the coils can be packed densely into that specific area. SAC of VADs involving the PICA tends to experience a higher recurrence rate than other treatment options. One study conducted by Cho et al. assessed the clinical and radiologic outcomes of VADs involving the PICA based on different types of EVT<sup>5)</sup>. They observed that both the multiple stenting and VA-PICA stenting groups had the highest rate of postoperative infarction, followed by the SAC group. However, no infarction occurred in the FDS group during the follow-up period. Furthermore, dissecting aneurysm recurrence was noted in 25% of patients treated with SAC, probably because a strategic decision was made to leave a small portion of the dissecting aneurysm to ensure patency of the PICA.

To spare these critical branches originating from the VA, two LVIS Blue stents partially overlapping in the dissecting segment



**Fig. 4.** (A) Ruptured bilateral vertebral artery dissections with dominant vertebral artery (VA) on the right. (B) Right dominant VA had fusiform aneurysmal dilatation with the rupture point on the inferior part. (C) Left non-dominant VA was occluded by internal coil trapping and stent-assisted coiling with triple stenting was performed for the right dominant VA. (D) Follow-up angiography at 12-month showing complete obliteration of the dissecting aneurysm and well-reconstruction of right dominant VA. A white arrow indicates the anterior spinal artery is originated just distal to the dissecting aneurysm.

can be deployed, ensuring that the proximal and distal segments of the VA are covered by a single stent. This approach helps reduce the risk of perforator infarction from the normal VA segment, and enhances the flow-diverting effect to increase the chances of complete healing of the dissecting segment.

### 3) Flow diverting stenting

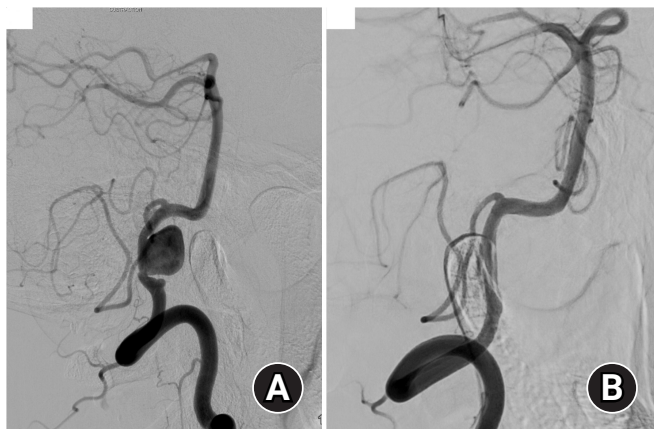
Reconstructive procedures involving FDS have become the preferred choice worldwide and are gradually replacing multiple stenting procedures (Fig. 5). One notable advantage of FDS is its potential to preserve the patency of branching vessels and perforators originating from the parent artery<sup>34-38</sup>. The presence of gaps between the stent strands facilitates blood flow into these branching vessels, while simultaneously disrupting flow into the dissecting aneurysm and promoting intrasaccular thrombosis. Recent meta-analyses have reported a perforator infarction rate of approximately 3%, with a slightly higher rate observed in patients with posterior circulation aneurysms compared to those with anterior circulation aneurysms<sup>39</sup>. The concept of wall reconstruction appears logical when considering a ruptured VAD as a diffuse defect of the vessel wall. However, comprehensive multicenter studies of the outcomes of these reconstructive techniques are limited. Most outcome data are derived from published case series<sup>38,40-43</sup>. As the use of FDS for VADs continues to grow, larger studies are warranted to determine long-term outcomes, including aneurysm occlusion rates, thromboembolic complications resulting from device insertion, and consequences of covered branch vessels and perforators.

## DISCUSSION

EVT has emerged as the preferred treatment for intracranial

VADs. However, a consistent and universally accepted strategy for determining when to reconstruct or occlude an affected VA segment has yet to be established. In this article, we share our real-world practices and experiences accumulated over the past decade in the treatment of VADs using EVT. Our approach was based on the specific clinical situation and anatomical characteristics of each patient. In cases of ruptured VADs, we generally occluded the rupture point by performing VA occlusion in the non-dominant VA or SAC occlusion in the dominant VA. For unruptured VADs, VA reconstruction using various stents is considered to maintain the original hemodynamics.

Notably, the current trend in treating VADs leans towards reconstructive techniques using FDS. However, it is essential to recognize that reconstructive techniques involving stents, particularly for ruptured VADs, pose the risks of procedure-related complications and recurrence. In a previous study, we reported our experience with SAC for ruptured wide-necked aneurysms in the acute period, and assessed the incidence and risk factors of procedure-related complications<sup>26</sup>. Among 72 patients treated with SAC, we found a periprocedural complication rate of 19.4%. The overall procedure-related thromboembolic complication rate regardless of symptoms was 12.5%, which exceeded the risk of hemorrhagic complications. Based on these findings, we concluded that microsurgical clipping or alternative endovascular techniques, such as the multiple-microcatheter or balloon-assisted technique, may be more appropriate first-line treatment options than SAC, particularly for patients with poor clinical grades or acute hydrocephalus. Furthermore, we evaluated the postoperative stroke risk and recurrence rate of both ruptured and unruptured VADs involving the PICA following different EVT modalities<sup>6</sup>. Our findings indicated that VA trapping with VA-PICA stenting showed the lowest rate of



**Fig. 5.** (A) Digital subtraction angiography of the left vertebral artery showing vertebral artery dissection (VAD) with a dissecting aneurysm. (B) A 6-month follow-up angiography showing complete healing of the VAD after treatment with a flow diverting stent, Pipeline Flex with Shield technology. Although the flow diverting stent covered the origin of the posterior inferior cerebellar artery (PICA), the flow of the PICA was patent.

aneurysm recurrence, but was associated with a higher rate of minor infarction and favorable neurologic outcomes. In contrast, SAC is associated with high recurrence rates and a risk of fatal disabling infarction. Importantly, the rate of post-treatment recurrence did not significantly differ between the reconstructive and deconstructive techniques. The involvement of the PICA origin by VADs was identified as the only independent risk factor for recurrence after EVT<sup>48</sup>. These findings underscore the importance of carefully considering the choice of treatment modality for VADs, the patient's clinical status, anatomical factors, and the potential risks and benefits associated with each technique.

In a prior meta-analysis examining patients with vertebrobasilar dissecting aneurysms treated using either reconstructive or deconstructive techniques, the immediate occlusion rate was found to be 75.0% (95% CI, 55.0–88.0%), while the long-term occlusion rate was 87.0% (95% CI, 74.0–94.0%)<sup>44</sup>. Additionally, the angiographic recurrence rate was estimated to be 7.0% (95% CI, 5.0–10.0%), with a retreatment rate of 3.0% (95% CI, 2.0–6.0%). The perioperative morbidity rate was 12.0% (95% CI, 9.0–16.0%), and the all-cause perioperative mortality rate was 8.0% (95% CI, 6.0–11.0%). The overall rebleeding rate in patients with ruptured dissecting aneurysms was 9.0% (95% CI, 6.0–13.0%). When comparing deconstructive and reconstructive techniques, we observed that patients treated with deconstructive methods had higher rates of complete occlusion not only immediately after the procedure (88.0% vs. 53.0%,  $p < 0.0001$ ), but also on long-term follow-up angiography (88.0% vs. 81.0%,  $p < 0.0001$ ). In contrast, perioperative morbidity was lower in the reconstructive group than in the deconstructive

group (4.0% vs. 12.0%,  $p = 0.04$ ). Although we observed a trend towards a lower perioperative mortality rate (4.0% vs. 10.0%,  $p = 0.11$ ) and a higher rate of good long-term clinical outcomes (92.0% vs. 86.0%,  $p = 0.10$ ) in the reconstruction group, these differences were not statistically significant. In summary, this meta-analysis suggests that EVT of vertebrobasilar dissecting aneurysms can achieve a high rate of complete occlusion and yield favorable long-term neurological outcomes. Deconstructive techniques may result in a higher rate of complete angiographic occlusion, whereas reconstructive techniques may be associated with lower perioperative morbidity. However, long-term neurological outcomes and retreatment rates were statistically similar between the two treatment modalities.

Radiologically, VADs can be categorized into three groups: dilatation without stenosis, pearl-and-string appearance, and stenosis without dilatation<sup>45</sup>. In the angiographic evaluation of symptomatic unruptured VADs, aneurysmal dilatation is more common than the steno-occlusive type. This distinction differs from that of extracranial vertebral artery dissection, in which the steno-occlusive type predominates. One possible explanation for this difference in lesion type is the absence of an external elastic lamina and a decreased amount of medial elastic tissue in the intradural artery. Subintimal dissections tend to result in luminal stenosis or occlusion, while subadventitial dissections often result in dilatation. The primary lesion morphology in symptomatic intracranial VADs may differ between unruptured and ruptured cases. Further, the morphology of symptomatic intracranial VADs may change during follow-up imaging. Ahn et al argued that ruptured VADs are more likely to present with dilatation without stenosis or a pearl-and-string appearance than with a stenosis without dilatation appearance<sup>45</sup>. In their study, intramural hematoma occurred in 33.9% (78 out of 230) of cases, developing most frequently in lesions featuring stenosis without dilatation (42 out of 60 [70%]), followed by lesions with a pearl-and-string appearance (27 out of 90 [30%]), and dilatation without stenosis appearance (9 out of 80 [11%]) ( $p < 0.05$ )<sup>45</sup>. The dilatation-without-stenosis group remained stable in 74% (25 out of 34) of cases, while the stenosis-without-dilatation group showed improvement in 91% (39 out of 43) of cases. Intracranial VADs with intramural hematoma exhibited progression at a four-fold higher rate than VADs without intramural hematoma (20% vs. 5%,  $p = 0.003$ )<sup>45</sup>.

## CONCLUSION

Determining the optimal course of action for VAD treatment is a complex decision-making process. Nevertheless, EVT is currently the primary approach for managing VADs. The EVT technique

should be selected on a case-by-case basis, considering clinical symptoms, hemodynamic conditions (including collateral blood supply adequacy), and anatomical characteristics of the neighboring major arteries and perforators. The decision-making process should be guided by both endovascular neurosurgeons and interventional neuroradiologists.

## NOTES

### ORCID

Junhyung Kim, <https://orcid.org/0000-0002-8908-978X>

Sang Kyu Park, <https://orcid.org/0000-0001-9231-0716>

### Ethics statement

This study was a literature review of previously published studies and was therefore exempt from institutional review board approval.

### Author contributions

Conceptualization: SKP, JC. Writing- original draft: JC. Writing, review & editing: JK, SKP.

### Conflict of interest

There is no conflict of interest to disclose.

### Funding

None.

### Data availability

None.

### Acknowledgements

None.

## REFERENCES

- Nam KH, Ko JK, Cha SH, Choi CH, Lee TH, Lee JI. Endovascular treatment of acute intracranial vertebral artery dissection: long-term follow-up results of internal trapping and reconstructive treatment using coils and stents. *J Neurointerv Surg* 2015; 7:829–834.
- Shin YS, Kim HS, Kim SY. Stenting for vertebrobasilar dissection: a possible treatment option for nonhemorrhagic vertebrobasilar dissection. *Neuroradiology* 2007;49:149–156.
- Hara M, Yamamoto I. Introduction to symposium: intracranial dissecting aneurysms. *Neuropathology* 2000;20:83–84.
- Sakata N, Takebayashi S, Kojima M, Masawa N, Suzuki K, Takatama M. Pathology of a dissecting intracranial aneurysm. *Neuropathology* 2000;20:104–108.
- Cho DY, Choi JH, Kim BS, Shin YS. Comparison of clinical and radiologic outcomes of diverse endovascular treatments in vertebral artery dissecting aneurysm involving the origin of PICA. *World Neurosurg* 2019;121:e22–e31.
- Chung J, Kim BS, Lee D, Kim TH, Shin YS. Vertebral artery occlusion with vertebral artery-to-posterior inferior cerebellar artery stenting for preservation of the PICA in treating ruptured vertebral artery dissection. *Acta Neurochir (Wien)* 2010;152:1489–1492.
- Kim MJ, Chung J, Kim SL, Roh HG, Kwon BJ, Kim BS, et al. Stenting from the vertebral artery to the posterior inferior cerebellar artery. *AJNR Am J Neuroradiol* 2012;33:348–352.
- Kim BM, Shin YS, Kim SH, Suh SH, Ihn YK, Kim DI, et al. Incidence and risk factors of recurrence after endovascular treatment of intracranial vertebrobasilar dissecting aneurysms. *Stroke* 2011;42:2425–2430.
- Iihara K, Sakai N, Murao K, Sakai H, Higashi T, Kogure S, et al. Dissecting aneurysms of the vertebral artery: a management strategy. *J Neurosurg* 2002;97:259–267.
- Mizutani T, Aruga T, Kirino T, Miki Y, Saito I, Tsuchida T. Recurrent subarachnoid hemorrhage from untreated ruptured vertebrobasilar dissecting aneurysms. *Neurosurgery* 1995;36:905–911; discussion 912–903.
- Moteki Y, Niimi Y, Okada Y, Kawamata T. Ruptured vertebral artery dissecting aneurysm as a risk factor for ocular symptoms accompanied with subarachnoid hemorrhage. *World Neurosurg* 2018;116:e505–e512.
- Kim BM, Kim SH, Kim DI, Shin YS, Suh SH, Kim DJ, et al. Outcomes and prognostic factors of intracranial unruptured vertebrobasilar artery dissection. *Neurology* 2011;76:1735–1741.
- Inagaki T, Saito K, Hirano A, Kato T, Irie S, Murakami T. [Vertebral arterial dissection with subarachnoid hemorrhage after ischemic onset]. *No Shinkei Geka* 2000;28:997–1002.
- Kawada S, Meguro T, Mandai S, Matsuhisa T, Moriyama E, Sakurai M, et al. A Case of Dissecting Aneurysm of the Vertebral-Basilar Artery with Brain Stem Ischemia and Subarachnoid Hemorrhage. *Surgery for Cerebral Stroke* 1994;22:485–489.
- Yamataki A, Kurashima Y, Ueda S. [Dissecting vertebral aneurysm with subarachnoid hemorrhage after ischemic onset on the same day: a case report]. *No Shinkei Geka* 2004;32:723–728.
- Jeon P, Kim BM, Kim DI, Shin YS, Kim KH, Park SI, et al. Emergent self-expanding stent placement for acute intracranial or extracranial internal carotid artery dissection with significant

- hemodynamic insufficiency. *AJNR Am J Neuroradiol* 2010;31:1529–1532.
17. Kim BM, Suh SH, Park SI, Shin YS, Chung EC, Lee MH, et al. Management and clinical outcome of acute basilar artery dissection. *AJNR Am J Neuroradiol* 2008;29:1937–1941.
  18. Nakagawa K, Touho H, Morisako T, Osaka Y, Tatsuzawa K, Nakae H, et al. Long-term follow-up study of unruptured vertebral artery dissection: clinical outcomes and serial angiographic findings. *J Neurosurg* 2000;93:19–25.
  19. Yoshimoto Y, Wakai S. Unruptured intracranial vertebral artery dissection. Clinical course and serial radiographic imagings. *Stroke* 1997;28:370–374.
  20. Berkovic SF, Spokes RL, Anderson RM, Bladin PF. Basilar artery dissection. *J Neurol Neurosurg Psychiatry* 1983;46:126–129.
  21. Brihaye J, Retif J, Jeanmart L, Flament-Durand J. Occlusion of the basilar artery in young patients. *Acta Neurochir (Wien)* 1971;25:225–229.
  22. Bugiani O, Piola P, Tabaton M. Nontraumatic dissecting aneurysm of the basilar artery. *Eur Neurol* 1983;22:256–260.
  23. Ruecker M, Furtner M, Knoflach M, Werner P, Gotwald T, Chemelli A, et al. Basilar artery dissection: series of 12 consecutive cases and review of the literature. *Cerebrovasc Dis* 2010;30:267–276.
  24. Arnold M, Bousser MG, Fahrni G, Fischer U, Georgiadis D, Gandjour J, et al. Vertebral artery dissection: presenting findings and predictors of outcome. *Stroke* 2006;37:2499–2503.
  25. de Bray JM, Penisson-Besnier I, Dubas F, Emile J. Extracranial and intracranial vertebrobasilar dissections: diagnosis and prognosis. *J Neurol Neurosurg Psychiatry* 1997;63:46–51.
  26. Chung J, Lim YC, Suh SH, Shim YS, Kim YB, Joo JY, et al. Stent-assisted coil embolization of ruptured wide-necked aneurysms in the acute period: incidence of and risk factors for periprocedural complications. *J Neurosurg* 2014;121:4–11.
  27. Zhao KJ, Zhao R, Huang QH, Xu Y, Hong B, Fang YB, et al. The interaction between stent(s) implantation, PICA involvement, and immediate occlusion degree affect symptomatic intracranial spontaneous vertebral artery dissection aneurysm (sis-VADA) recurrence after reconstructive treatment with stent(s)-assisted coiling. *Eur Radiol* 2014;24:2088–2096.
  28. Chung J, Suh SH, Hong CK, Joo JY, Lim YC, Shin YS, et al. Preliminary experience with self-expanding closed-cell stent placement in small arteries less than 2 mm in diameter for the treatment of intracranial aneurysms. *J Neurosurg* 2015;122:1503–1510.
  29. Kim BM, Kim DJ, Kim DI. Stent application for the treatment of cerebral aneurysms. *Neurointervention* 2011;6:53–70.
  30. Chung J, Matsuda Y, Nelson J, Keigher K, Lopes DK. A new low-profile visualized intraluminal support (LVIS) device, LVIS Blue: laboratory comparison between old and new LVIS. *Neurol Res* 2018;40:78–85.
  31. Makoyeva A, Bing F, Darsaut TE, Salazkin I, Raymond J. The varying porosity of braided self-expanding stents and flow diverters: an experimental study. *AJNR Am J Neuroradiol* 2013;34:596–602.
  32. Shapiro M, Raz E, Becske T, Nelson PK. Building multidevice pipeline constructs of favorable metal coverage: a practical guide. *AJNR Am J Neuroradiol* 2014;25:1556–1561.
  33. Lim YC, Shin YS, Chung J. Flow diversion via LVIS blue stent within enterprise stent in patients with vertebral artery dissecting aneurysm. *World Neurosurg* 2018;117:203–207.
  34. Cebral JR, Raschi M, Mut F, Ding YH, Dai D, Kadirvel R, et al. Analysis of flow changes in side branches jailed by flow diverters in rabbit models. *Int J Numer Method Biomed Eng* 2014;30:988–999.
  35. Dai D, Ding YH, Kadirvel R, Rad AE, Lewis DA, Kallmes DF. Patency of branches after coverage with multiple telescoping flow-diverter devices: an in vivo study in rabbits. *AJNR Am J Neuroradiol* 2012;33:171–174.
  36. Kallmes DF, Ding YH, Dai D, Kadirvel R, Lewis DA, Cloft HJ. A new endoluminal, flow-disrupting device for treatment of saccular aneurysms. *Stroke* 2007;38:2346–2352.
  37. Kallmes DF, Ding YH, Dai D, Kadirvel R, Lewis DA, Cloft HJ. A second-generation, endoluminal, flow-disrupting device for treatment of saccular aneurysms. *AJNR Am J Neuroradiol* 2009;30:1153–1158.
  38. Mazur MD, Kilburg C, Wang V, Taussky P. Pipeline embolization device for the treatment of vertebral artery aneurysms: the fate of covered branch vessels. *J Neurointerv Surg* 2016;8:1041–1047.
  39. Brinjikji W, Murad MH, Lanzino G, Cloft HJ, Kallmes DF. Endovascular treatment of intracranial aneurysms with flow diverters: a meta-analysis. *Stroke* 2013;44:442–447.
  40. de Barros Faria M, Castro RN, Lundquist J, Scrivano E, Ceratto R, Ferrario A, et al. The role of the pipeline embolization device for the treatment of dissecting intracranial aneurysms. *AJNR Am J Neuroradiol* 2011;32:2192–2195.
  41. Ducruet AF, Crowley RW, Albuquerque FC, McDougall CG. Reconstructive endovascular treatment of a ruptured vertebral artery dissecting aneurysm using the Pipeline embolization device. *J Neurointerv Surg* 2013;5:e20.
  42. Narata AP, Yilmaz H, Schaller K, Lovblad KO, Pereira VM. Flow-diverting stent for ruptured intracranial dissecting aneurysm of vertebral artery. *Neurosurgery* 2012;70:982–988; dis-

- cussion 988-989.
43. Yeung TW, Lai V, Lau HY, Poon WL, Tan CB, Wong YC. Long-term outcome of endovascular reconstruction with the Pipeline embolization device in the management of unruptured dissecting aneurysms of the intracranial vertebral artery. *J Neurosurg* 2012;116:882–887.
  44. Sonmez O, Brinjikji W, Murad MH, Lanzino G. Deconstructive and reconstructive techniques in treatment of vertebrobasilar dissecting aneurysms: a systematic review and meta-analysis. *AJNR Am J Neuroradiol* 2015;36:1293–1298.
  45. Ahn SS, Kim BM, Suh SH, Kim DJ, Kim DI, Shin YS, et al. Spontaneous symptomatic intracranial vertebrobasilar dissection: initial and follow-up imaging findings. *Radiology* 2012; 264:196–202.

## Cardiac Arrest in Traumatic Brain Injury

Oday Atallah<sup>1</sup>, Md Moshiur Rahman<sup>2</sup>, Bipin Chaurasia<sup>3</sup>, Vishal Chavda<sup>4</sup>, Amit Agrawal<sup>5</sup>

<sup>1</sup>Department of Neurosurgery, Hannover Medical School, Hannover, Germany

<sup>2</sup>Department of Neurosurgery, Holy Family Red Crescent Medical College, Dhaka, Bangladesh

<sup>3</sup>Department of Neurosurgery, Neurosurgery Clinic, Birgunj, Nepal

<sup>4</sup>Department of Medicine, Multispeciality Trauma and ICCU Centre, Sardar Hospital, Ahmedabad, Gujarat, India

<sup>5</sup>Department of Neurosurgery, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

Received: January 24, 2024

Accepted: April 18, 2024

### Corresponding Author:

Bipin Chaurasia, MS  
Department of Neurosurgery,  
Neurosurgery Clinic, Madhesh  
pradesh, Birgunj 44300, Nepal  
Tel: +9779845454636  
E-mail: trozexa@gmail.com

Traumatic brain injury (TBI) is a significant global health concern with substantial contributions to illness and mortality rates. This study aims to scrutinize the intricate interplay between neurological and circulatory abnormalities post-TBI, particularly focusing on the challenge posed by cardiac arrest in TBI patients. The study employs a comprehensive approach, utilizing clinical assessments, electrocardiograms, intracranial pressure monitoring, brain imaging, and biomarker utilization. It explores the effectiveness of these methods in detecting cardiac arrest in TBI patients. Additionally, the research delves into resuscitation techniques, hemodynamic stabilization, intracranial pressure management, and neurological enhancement as potential therapeutic modalities. The results highlight the importance of prompt initiation of cardiopulmonary resuscitation and adherence to advanced cardiac life support protocols in TBI patients with cardiac arrest. Prognostic factors such as injury severity, response time, effectiveness of resuscitation interventions, and pre-existing medical conditions are identified as crucial elements in predicting cardiac arrest outcomes in TBI patients. The study concludes by emphasizing the critical necessity of a comprehensive approach to understand and manage the complex relationship between cardiac arrest and TBI. Incorporating scientific discoveries, clinical perspectives, and technological advancements, the review underscores the importance of addressing this multifaceted medical challenge through a thorough analysis and effective management strategies.

**Keywords:** Cardiac arrest; Traumatic brain injury; Resuscitation

## INTRODUCTION

Cardiac arrest in individuals with traumatic brain injury (TBI) presents a multidimensional and potentially fatal medical emergency, posing a unique challenge for healthcare personnel and physicians<sup>1</sup>. TBI is characterized by abrupt and substantial brain damage resulting from external forces, triggering a cascade of physiological events, including disturbances in cardiovascular function

that can culminate in cardiac arrest<sup>1</sup>. The intricate interplay between neurological and cardiovascular pathologies identified in these cases underscores the necessity for a multidisciplinary approach to accurately diagnose, manage, and treat these conditions<sup>1</sup>. The occurrence of cardiac arrest in TBI patients significantly impacts both survival rates and neurological outcomes, creating a considerable obstacle to effective resuscitation and rehabilitation<sup>2</sup>. The presence of concurrent injuries or complications fur-

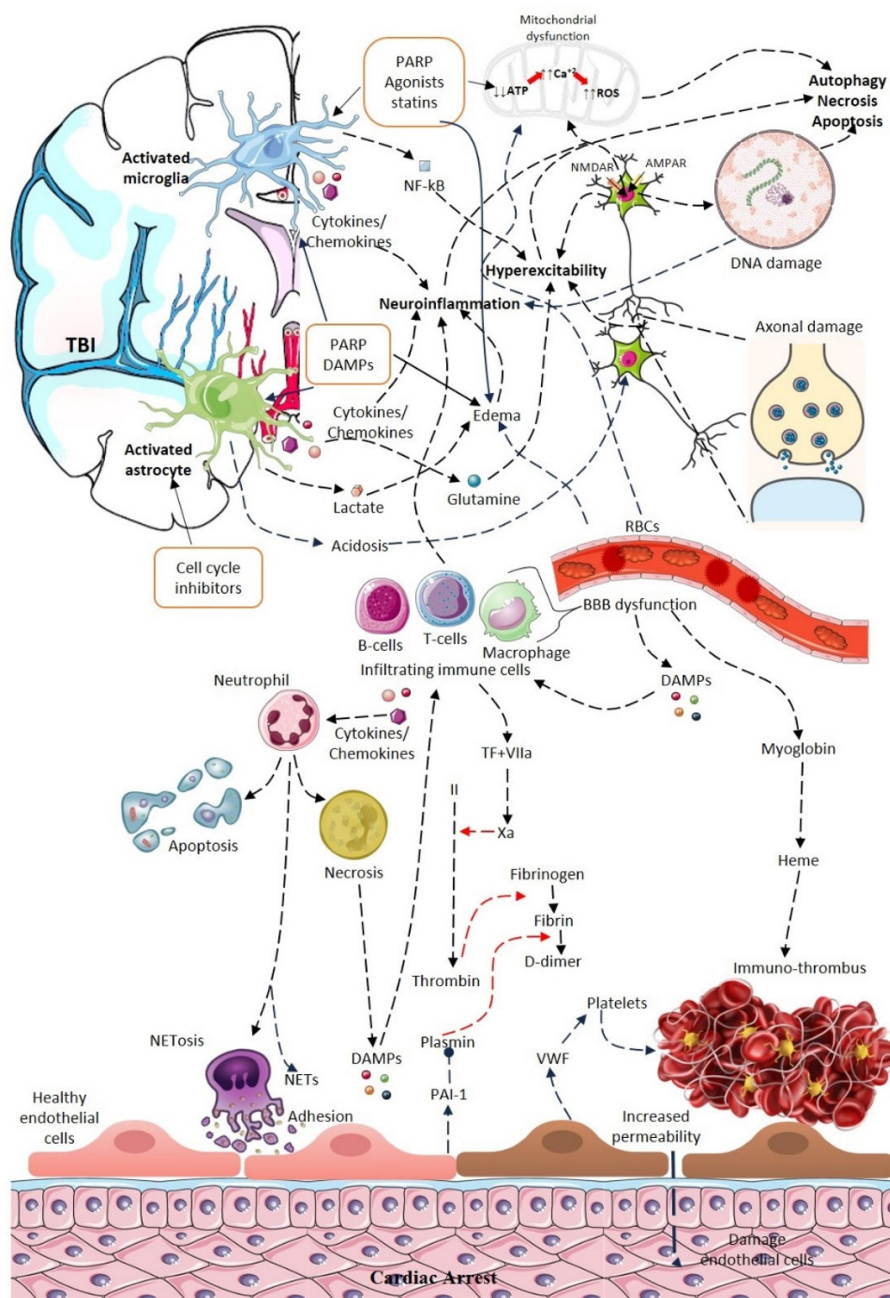


ther complicates this critical condition, making prompt recognition and treatment of cardiac arrest more challenging<sup>2</sup>). The pathophysiology of cardiac arrest in TBI involves a myriad of interacting factors. Elevated intracranial pressure, alterations in cerebral autoregulation, heightened sympathetic activity, and the incidence of secondary brain injuries are among the identified risk factors<sup>2-5</sup>). The objective of this study was to explore the intricate relationship between cardiac arrest and TBI, elucidating the underlying mechanisms, risk factors, and potential therapeutic options that may con-

tribute to overall outcomes (Fig. 1)<sup>2-5</sup>).

## METHODS

Cardiac arrest in TBI patients was the focus of this literature review, which aimed to synthesize and evaluate previous research on the subject. To gather up-to-date literature on this subject, electronic databases such as PubMed, Science Direct, and Web of Science were meticulously examined. Cardiopulmonary arrest, severe



**Fig. 1.** This figure delineates the pathophysiological and cell-molecular alterations occurring during cardiac arrest in traumatic brain injury. PARP: Poly-ADP ribose polymerase; NK-kb: Nuclear factor kappa B; DAMP: Danger-associated molecular patterns.

brain damage, and neurological-circulatory abnormalities were some of the MeSH keywords utilized. To expand the data set, we also looked through the reference lists of selected papers. Because it did not include any direct human participants, this study did not need permission from the institutional board's review for human research ethics.

Research with patients participating in either qualitative or quantitative investigations met the inclusion criteria. We only looked at items that were published in English. To guarantee a thorough examination of the results, only publications from peer-reviewed journals were considered. The abstracts and complete texts were evaluated by two authors who complied with the criteria for exclusion and inclusion, and a third author resolved any disagreements that arose to reduce the possibility of bias.

## OVERVIEW

Yang et al.<sup>6</sup> conducted a systematic review and meta-analysis comparing target temperature management (TTM) against normal temperature management (NTM) for cardiac arrest following TBI. In contrast to neurotherapeutic medicine, their meta-analysis revealed that TTM did not reduce mortality rates. However, it is noteworthy that for individuals with moderate or severe symptoms in the early stages, TTM might still hold potential in reducing death rates and improving prognosis. Specifically, TTM has demonstrated greater effectiveness in the early phases of moderate and severe conditions compared to NTM, leading to enhanced prognostic outcomes. Kochanek et al.<sup>7</sup> emphasized in their review that managing clinical outcomes for infants and children who have experienced severe TBI or asphyxia-induced cardiac arrest involves a series of therapies spanning various medical settings from the field to emergency rooms, intensive care units, rehabilitation centers, and potentially beyond. Despite the distinctions between these widely recognized pediatric traumas, prompt implementation of interventions aimed at preventing neuronal death in either scenario is likely crucial, possibly beginning at the injury site. According to Kochanek et al.<sup>7</sup>, managing cerebral edema, a pathophysiological condition often treated in pediatric intensive care units (PICUs), is more favorable as prevention rather than cure. Finally, this research delves into alternative therapies for individuals with severe brain injuries, exploring the potential for altering damaged neural networks and enhancing regenerative processes.

## PATHOPHYSIOLOGY

Individuals who have suffered TBI face an increased risk of car-

diac arrest due to a complex interplay of factors stemming from direct damage to the brain and the body's physiological responses to trauma. One primary etiology is the rise in intracranial pressure (ICP) resulting from a traumatic event. Elevated ICP can impact cerebral blood flow, escalating the risk of cardiovascular complications<sup>3</sup>. TBI is associated with abnormalities in autoregulation that impair the brain's ability to adequately control blood flow and perfusion, heightening the risk of cardiac arrest. The body's physiological response to trauma includes increased sympathetic activity, potentially leading to substantial increases in heart rate and blood pressure, thereby elevating the risk of cardiac arrest. Furthermore, the development of anoxia and reperfusion injury following trauma, signifying damage due to the restoration of blood flow, can adversely affect vital organs such as the heart. Additionally, the systemic inflammatory response commonly observed after TBI can trigger a chain of physiological events significantly impacting cardiovascular function and increasing the risk of cardiac arrest<sup>7</sup>. Individuals with TBI may experience issues with hypoxia and hypotension, further heightening the likelihood of cardiac arrest. TBIs can induce electrolyte imbalances, disrupting the heart's normal electrical activity, potentially resulting in arrhythmias and cardiac arrest. Brainstem involvement, brain herniation, contusions, or hemorrhages within the brainstem can profoundly affect the body's regulation of critical physiological functions, including heart activity.

## EXPLORING THE ROLE OF BIOMARKERS

Biomarkers have emerged as critical diagnostic, prognostic, and therapeutic tools in the complex domains of TBI and cardiac arrest. Various biomarkers, extensively researched in the context of brain injuries, provide insights into severity and prognosis (Table 1). Proteins such as S100B, neuron-specific enolase (NSE), and glial fibrillary acidic protein (GFAP) are among these indicators<sup>3</sup>. Inflammatory biomarkers like interleukin-8 (IL-8) and molecular elements such as microRNAs have shown promise in diagnosis and prognosis. Jarvis and Fink<sup>5</sup> note that these biomarkers can be detected in blood samples, cerebrospinal fluid, and through modern neuroimaging techniques, rendering them useful in clinical assessments. Identified biomarkers hold potential in tailoring treatment regimens for both TBI and cardiac arrest situations. However, to enhance diagnostic precision, discovering composite panels, developing consistent testing methodologies, and comprehensive evaluation of these biomarkers prior to clinical use are crucial<sup>8-11</sup>. Nonetheless, transitioning biomarkers from research investigations to clinical practice necessitates a rigorous vali-

**Table 1.** Synopsis of studies on cardiac arrest and traumatic brain injury

Study	Authors/year	Study Type	Population	Outcome Measures	Results
1	Kochanek et al. 2001 <sup>7)</sup>	Review	Pediatric TBI and Cardiac Arrest	Diagnosis, Prognostication	The importance of individualized treatments based on biomarkers is emphasized.
2	Jackson et al. 2022 <sup>4)</sup>	Experimental	Neuroprotection	Experimental PHLPP inhibitors	The compound NSC74429 has demonstrated neuroprotective effects against several modes of injury.
3	Mussack et al. 2002 <sup>10)</sup>	Prospective Cohort	Cardiac Arrest and TBI	S-100B and IL-8 serum levels	There is a positive correlation between elevated levels of S-100B and IL-8 and unfavorable outcomes.
4	Yang et al. 2022 <sup>6)</sup>	Meta-Analysis	Cardiac Arrest and TBI	Mortality, Prognosis	TTM has the ability to enhance the prognosis of individuals with moderate and severe conditions.
5	Prout et al. 2017 <sup>12)</sup>	Review	Pediatric TBI and Cardiac Arrest	Biomarker Investigation	The utilization of biomarkers has the potential to improve the processes of diagnosis, treatment, and prognosis.
6	Zhao et al. 2021 <sup>16)</sup>	Retrospective Review	Cardiac Arrest and TBI	Survival, Neurological Function	The survival rate is associated with the GCS score and pupil reactivity.

TBI: Traumatic brain injury; GCS: Glasgow-Coma-Scale; TTM: Target temperature management.

dition process<sup>12-15)</sup>. Thorough testing is imperative to ensure their clinical utility, accuracy, and reliability<sup>16)</sup>. Slovis<sup>17)</sup> emphasizes the necessity for substantial clinical investigations to validate the usefulness of biomarkers in improving patient outcomes and providing significant insights for medical decision-making. Mussack et al.<sup>10)</sup> investigated the blood levels of S-100B and Interleukin-8 in individuals experiencing cardiac arrest or traumatic brain injury. Their study evaluated levels upon admission and after 12 hours, followed by a 12-month assessment of long-term neurological implications. Results indicated higher levels of S-100B and Interleukin-8 at the scene of cardiac arrest, which increased after 12 hours. These findings demonstrate observable changes in S-100B and Interleukin-8 levels in individuals with both cardiac arrest and TBI. Zhao et al.<sup>16)</sup> selected 42 out of 402 TBI patients admitted to Stony Brook University Hospital with a Glasgow Coma Scale (GCS) score of 8. These patients experienced cardiac arrest during their stay. Seven of the eight patients involved in the accident displayed good neurological function and survived, leading to a discharge rate of 19.0%. The research identified GCS at admission and bilateral pupil responsiveness as significant predictive factors for survival. Surviving patients had an average GCS of 5.3, while non-survivors averaged 3.2 ( $p = 0.020$ ). Prout et al.<sup>12)</sup> examined biomarkers' potential value in diagnosing, assessing damage severity, and predicting outcomes in pediatric patients with TBI and cardiac arrest. Their work underscores the importance of supplementary prognostic indicators following TBI, specifically highlighting both the absolute rise in central nervous system-based macromolecules and the timing of their elevation. Post-TBI, pathophysiological pathways involve indicators linked to inflammatory mediators, oxidative stress response alterations, and energy metabolism abnormalities (Fig. 1).

## DIAGNOSTIC APPROACHES

Diagnostic approaches for identifying cardiac arrest episodes in individuals with TBI encompass various clinical tests and monitoring techniques. The clinical assessment, encompassing vital signs, neurological function, and overall clinical well-being, remains crucial. Electrocardiogram (ECG) monitoring is vital to detect arrhythmias and irregularities signaling cardiac arrest<sup>6)</sup>. Testing cardiac enzymes and troponin can also confirm heart involvement. Continuous electroencephalogram (EEG) monitoring aids in seizure detection and identifying changes in brain electrical activity suggesting cardiac issues. Sandroni et al. recognized somatosensory evoked potentials (SSEPs) and auditory evoked potentials (AEPs) as valuable in assessing sensory pathway integrity. These potentials can be used to evaluate the potential role of the brainstem in cardiac arrest occurrences. Monitoring ICP is crucial in managing TBI patients experiencing cardiac arrest as elevated ICP can restrict cerebral blood flow and worsen cardiac complications. Assessing brain structural integrity is pivotal to evaluating potential brainstem involvement and its impact on cardiac function. Reis et al.<sup>13)</sup> note that brain imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) provide valuable information. Laboratory tests, including blood analysis, can determine the body's physiological response to TBI and unveil metabolic anomalies affecting cardiovascular health. Echocardiography enables real-time monitoring of cardiac dynamics and identification of anomalies in heart anatomy and function. Combining these diagnostic techniques establishes a comprehensive framework for detecting cardiac arrest in TBI patients, facilitating prompt interventions and tailored treatment strategies based on individual patient conditions<sup>9,17-20)</sup>.

## THERAPEUTIC INTERVENTIONS

Given the intricate interplay between neurological and circulatory factors, an integrated therapeutic approach is essential in managing cardiac arrest in individuals with TBI. Therapeutic options encompass a spectrum of interventions targeting resuscitation, hemodynamic stabilization, intracranial pressure control, and neurological outcomes improvement<sup>13,21-23</sup>. Restoring circulation relies on the prompt initiation of cardiopulmonary resuscitation (CPR) and adherence to advanced cardiac life support (ACLS) guidelines. Ensuring proper airway management to guarantee adequate oxygenation and breathing is crucial to reduce the risk of further neurological damage in TBI patients experiencing cardiac arrest. Maintaining hemodynamic stability is essential to supply adequate blood flow to the brain. Cronberg et al.<sup>1</sup> highlight achieving optimal blood flow in the injured brain via techniques like fluid resuscitation and judicious use of vasoactive drugs. Therapeutic hypothermia emerges as a treatment option aimed at reducing secondary brain injury and improving neurological outcomes post-cardiac arrest. Precisely regulating body temperature is pivotal in this approach. Yang et al.<sup>6</sup> suggest that customized temperature management plays a significant role in neuroprotection by reducing oxidative stress and inflammation through precise temperature regulation. Additionally, interventions aimed at enhancing oxygen delivery and maintaining cerebral perfusion pressure should be considered to foster tissue recovery and maintain metabolic equilibrium within circulatory and cerebral systems. Managing ICP assumes importance in TBI patients experiencing cardiac arrest. Strategies like head-of-bed elevation, osmotic agent administration, and adjustments to respiratory parameters aim to prevent ICP elevation. Neuroprotective strategies, such as vigilant avoidance of hypotension and hyperthermia, safeguard the vulnerable brain from further injury. Continuous monitoring is indispensable in treating cardiac arrest in TBI patients. Continuous monitoring of neurological status, hemodynamic parameters, and vital signs informs treatment decisions and evaluates intervention efficacy. Leveraging modern monitoring technologies, including cerebral oxygenation measures and intracranial pressure monitoring, has the potential to significantly enhance therapeutic precision and efficacy for patients.

## ANIMAL MODEL EVIDENCE

Jackson et al.<sup>4</sup> evaluated compounds NSC13378, NSC25247, and NSC74429 in animal models, highlighting promising chemical characteristics for potential CNS targeting. Before this study, no research on neuroprotection using PHLPP inhibitors had been conducted. Neuronal culture tests indicated that NSC74429 dis-

played the highest level of neuroprotection at micromolar concentrations. NSC74429 demonstrated neuroprotective effects against staurosporine-induced apoptosis, glutamate-induced excitotoxicity, and hydrogen peroxide-induced necrosis/oxidative stress. Subsequent testing revealed that administering NSC74429 at a dose of 1 mg/kg for three days enhanced hippocampal survival in both rat models of suffocating cardiac arrest and mouse models of severe traumatic brain injury.

## CONCLUSION

Understanding the pathophysiological intricacies and reasons behind cardiac arrest in individuals with TBI holds paramount importance for medical practitioners. This comprehension is pivotal in enhancing the standard of patient care, elevating survival rates, and ultimately improving long-term neurological outcomes. The pursuit of novel therapies and advancements in multidisciplinary healthcare represents an ongoing endeavor aimed at mitigating the severe implications of cardiac arrest in TBI patients. Through this analysis of the intricate clinical scenario under consideration, our aim is to provide a comprehensive examination of current knowledge, underscore key areas necessitating further investigation, and foster continuous efforts to refine the treatment and enhance outcomes for individuals experiencing cardiac arrest in the context of TBI.

## NOTES

### ORCID

Oday Atallah, <https://orcid.org/0000-0002-3131-4104>

Bipin Chaurasia, <https://orcid.org/0000-0002-8392-2072>

### Ethics statement

This study was a literature review of previously published studies and was therefore exempt from institutional review board approval.

### Author contributions

Conceptualization: OA, BC. Data curation: OA, VC. Formal analysis: OA, MMR, VC, AA. Methodology: OA, MMR, BC. Visualization: MMR, BC, VC. Project administration: OA. Writing - original draft: OA, Writing - review & editing: MMR, BC, AA.

### Conflict of interest

There is no conflict of interest to disclose.

**Funding**

None.

**Data availability**

None.

**Acknowledgements**

None.

**REFERENCES**

- Cronberg T, Greer DM, Lilja G, Moulart V, Swindell P, Rossetti AO. Brain injury after cardiac arrest: from prognostication of comatose patients to rehabilitation. *Lancet Neurol* 2020;19:611–622.
- Dash PK, Zhao J, Hergenroeder G, Moore AN. Biomarkers for the diagnosis, prognosis, and evaluation of treatment efficacy for traumatic brain injury. *Neurotherapeutics* 2010;7:100–114.
- Esdaille CJ, Coppler PJ, Faro JW, Weisner ZM, Condle JP, Elmer J, et al, Pittsburgh Post Cardiac Arrest Service. Duration and clinical features of cardiac arrest predict early severe cerebral edema. *Resuscitation* 2020;153:111–118.
- Jackson TC, Dezfulian C, Vagni VA, Stezoski J, Janesko-Feldman K, Kochanek PM. PHLPP inhibitor NSC74429 is neuroprotective in rodent models of cardiac arrest and traumatic brain injury. *Biomolecules* 2022;12:1352.
- Jarvis JM, Fink EL. Neurofilament light chain-it is not just about concussions. *Pediatr Crit Care Med* 2020;21:685–686.
- Yang Z, Song Z, Hou M. Target temperature management versus normal temperature management for cardiac arrest after traumatic brain injury patient: a meta-analysis and systemic review. *Ther Hypothermia Temp Manag* 2022;12:139–145.
- Kochanek PM, Clark RS, Ruppel RA, Dixon CE. Cerebral resuscitation after traumatic brain injury and cardiopulmonary arrest in infants and children in the new millennium. *Pediatr Clin North Am* 2001;48:661–681.
- Lim HB, Smith M. Systemic complications after head injury: a clinical review. *Anaesthesia* 2007;62:474–482.
- Lemiale V, Dumas F, Mongardon N, Giovanetti O, Charpentier J, Chiche JD, et al. Intensive care unit mortality after cardiac arrest: the relative contribution of shock and brain injury in a large cohort. *Intensive Care Med* 2013;39:1972–1980.
- Mussack T, Biberthaler P, Kanz KG, Wiedemann E, Gippner-Steppert C, Mutschler W, et al. Serum S-100B and interleukin-8 as predictive markers for comparative neurologic outcome analysis of patients after cardiac arrest and severe traumatic brain injury. *Crit Care Med* 2002;30:2669–2674.
- Meaney DF, Morrison B, Dale Bass C. The mechanics of traumatic brain injury: a review of what we know and what we need to know for reducing its societal burden. *J Biomech Eng* 2014;136:021008.
- Prout AJ, Wolf MS, Fink EL. Translating biomarkers from research to clinical use in pediatric neurocritical care: focus on traumatic brain injury and cardiac arrest. *Curr Opin Pediatr* 2017;29:272–279.
- Reis C, Akyol O, Araujo C, Huang L, Enkhjargal B, Malaguit J, et al. Pathophysiology and the monitoring methods for cardiac arrest associated brain injury. *Int J Mol Sci* 2017;18:129.
- Ramiro JJ, Kumar A. Updates on management of anoxic brain injury after cardiac arrest. *Mo Med* 2015;112:136–141.
- Sekhon MS, Ainslie PN, Griesdale DE. Clinical pathophysiology of hypoxic ischemic brain injury after cardiac arrest: a "two-hit" model. *Crit Care* 2017;21:90.
- Zhao Z, Liang JJ, Wang Z, Winans NJ, Morris M, Doyle S, et al. Cardiac arrest after severe traumatic brain injury can be survivable with good outcomes. *Trauma Surg Acute Care Open* 2021;6:e000638.
- Slovis JC, Bach A, Beaulieu F, Zuckerberg G, Topjian A, Kirschen MP. Neuromonitoring after pediatric cardiac arrest: cerebral physiology and injury stratification. *Neurocrit Care* 2024;40:99–115.
- Saraceno G, Servadei F, Di Bergamo LT, Iaccarino C, Rubiano AM, Zoia C, et al. Do neurosurgeons follow the guidelines? A world-based survey on severe traumatic brain injury. *J Neurosurg Sci* 2021;65:465–473.
- Stocchetti N, Carbonara M, Citerio G, Ercole A, Skrifvars MB, Smielewski P, et al. Severe traumatic brain injury: targeted management in the intensive care unit. *Lancet Neurol* 2017;16:452–464.
- Sandroni C, Cronberg T, Sekhon M. Brain injury after cardiac arrest: pathophysiology, treatment, and prognosis. *Intensive Care Med* 2021;47:1393–1414.
- Kirschen MP, Yehya N, Graham K, Kilbaugh T, Berg RA, Topjian A, et al. Circulating neurofilament light chain is associated with survival after pediatric cardiac arrest. *Pediatr Crit Care Med* 2020;21:656–661.
- Saraceno G, Servadei F, Terzi Di Bergamo L, Iaccarino C, Rubiano AM, Zoia C, et al. Do neurosurgeons follow the guidelines? A world-based survey on severe traumatic brain injury. *J Neurosurg Sci* 2021;65:465–73.
- Bozkurt I, Umana GE, Deora H, Wellington J, Karakoc E, Chaurasia B. Factors affecting neurosurgeons' decisions to forgo life-sustaining treatments after traumatic brain injury. *World neurosurgery* 2022;159:e311–e323.

# Intracranial Pressure Monitoring in Patients With Traumatic Brain Injury: An Umbrella Review of Systematic Review and Meta-Analysis

William A Florez-Perdomo<sup>1</sup>, Rakesh Mishra<sup>2</sup>, Luis Rafael Moscote-Salar<sup>1</sup>, Rafael Cincu<sup>3</sup>, Ved Prakash Maurya<sup>4</sup>, Amit Agrawal<sup>5</sup>

<sup>1</sup>Colombian Clinical Research Group in Neurocritical Care, Bogota, Colombia

<sup>2</sup>Department of Neurosurgery, Bhopal Memorial Hospital and Research Centre, Bhopal, India

<sup>3</sup>Department of Neurosurgery, General University Hospital, Valencia, Spain

<sup>4</sup>Department of Neurosurgery, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

<sup>5</sup>Department of Neurosurgery, All India Institute of Medical Sciences, Saket Nagar, Bhopal, Madhya Pradesh, India

Received: October 27, 2023

Accepted: December 6, 2023

## Corresponding Author:

Amit Agrawal, MCh

Department of Neurosurgery, All India Institute of Medical

Sciences, Saket Nagar, Bhopal

462020, Madhya Pradesh, India

Tel: +91-8096410032

E-mail: [dramitagrawal@gmail.com](mailto:dramitagrawal@gmail.com),

[dramitagrawal@hotmail.com](mailto:dramitagrawal@hotmail.com)

## Background

The objective of this study is to summarize the evidence in Cochrane and non-Cochrane systematic reviews, the effects, and the benefits of monitoring intracranial pressure (ICP) in patients with head trauma with an indication of ICP monitoring.

## Methods

The process of preparing this overview followed the guidelines established by the Joanna Briggs Institute (JBI) for umbrella reviews. Two independent reviewers evaluated the quality of reporting, bias risk, methodologies, and evidence using three different tools: the Risk of Bias in Systematic Reviews (ROBIS) instrument, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), and A Measurement Tool to Assess Systematic Reviews (AMSTAR 2).

## Results

A total of five papers met the criteria for inclusion in the study. These papers consisted of 49 primary research studies and 19 unique primary research studies. One of the SRs indicated that using intracranial pressure (ICP) monitoring led to a reduction in mortality. Two of the SRs had mixed results with temporal variation, while two found no significant difference in mortality with ICP monitoring. It is important to note that the quality of the SRs varied, with some being of higher quality than others.

## Conclusion

There was no conclusive evidence that ICP monitoring reduces mortality in traumatic brain injury patients. There was high heterogeneity in included primary research studies. Future research should aim to address the limitations of these studies and provide more conclusive evidence regarding the effectiveness of ICP monitoring in reducing mortality in patients with traumatic brain injury.

**Keywords:** Intracranial pressure monitoring; Traumatic brain injury; Outcomes; Mortality; Length of hospital stay; Umbrella reviews

## INTRODUCTION

Traumatic brain injury (TBI) is a significant contributor to mortality and morbidity at a global level, disproportionately affecting individuals in their prime working years. This multifaceted health condition has far-reaching economic and social consequences, rendering it a significant public health concern, particularly in developing nations<sup>1</sup>. The gravity of the situation demands swift, concerted efforts to mitigate its impact and improve outcomes for those affected.

The most reliable method for monitoring intracranial pressure (ICP) in cases of traumatic brain injury involves the surgical placement of an intracranial sensor, which allows for direct measurement of pressure within the skull<sup>2</sup>. Three primary locations are utilized for sensor placement: intraventricular, intraparenchymal, and subdural. While this approach is highly effective for tracking patients with severe head trauma, it is also associated with a number of complications, including hemorrhage, obstruction, mispositioning, infection, and reduced accuracy in cases of asymmetric hemispheric lesions<sup>2</sup>. Furthermore, the invasive nature of this technique requires a neurosurgical procedure, which carries its own set of risks and considerations. Therefore, while intracranial sensor insertion may be the gold standard for ICP monitoring in TBI, it is important to carefully weigh the risks and benefits of this approach before proceeding with treatment.

The concept of intracranial pressure monitoring gained its popularity after the publication of brain trauma foundation (BTF) guidelines on the multimodal management of the traumatic brain injury. The multimodal monitoring suggest for the escalation of therapy in a tiered manner<sup>3</sup>. The approach for enhancing treatment for herniation syndromes is carried out in a tiered manner and ought to be executed without postponing invasive intracranial monitoring, also known as multimodal monitoring. The initial options that may be considered are placing the patient in an upright position, avoiding neck manipulation, addressing agitation and fever, attempting hyperosmolar therapy, and finally deciding whether urgent surgery is necessary. If there is clinical improvement, such as in pupil dilation or examination, these maneuvers may indicate that the patient is approaching the end of the intracranial volume-pressure curve. These crucial measures must be taken to ensure that the patient's health is preserved and that their herniation syndrome is managed effectively.

Since the start of ICP monitoring in TBI patients, there have been several studies that produce conflicting and mixed results on the outcome in TBI patients with ICP monitoring primarily

mortality and length of hospital stay. Using ICP monitoring to guide the patient management has its own limitations. ICP monitoring is resource intensive and time consuming and depends on the both the modality used for measurement and location of the probe. Therefore the monitoring may mislead when there is focal point of herniation. This is one of the reason why BTF guidelines recommends on ICP monitoring diffuse pathologies. It is noteworthy that in a study involving malignant stroke, a considerable number of patients exhibited a midline shift and pupillary changes despite ICP monitoring revealing an ICP < 22 mm Hg, thereby indicating that ICP values may not always reflect a concerning clinical picture<sup>4</sup>. One of the study found that the ICP monitoring is as good as the clinical examination on the outcomes following TBI<sup>5</sup>.

In severe traumatic brain injury (sTBI), Intracranial pressure monitoring is the preferred method of monitoring. However, the criteria for its insertion remains unclear. The brain trauma foundation Guidelines Edition 3 provided recommendations for ICP monitoring, and in the absence of new evidence, the latest revision defaulted to those recommendations<sup>6,7</sup>. Despite this, practice surveys have shown significant variation in the use of monitoring on both individual and institutional levels, with poor adherence to BTF recommendations<sup>8,9</sup>. This implies that the decision-making process is inconsistent and poorly understood, a critical issue when assessing the efficacy of ICP monitor-based care in non-controlled studies. Furthermore, some providers may view ICP monitoring data as having little additional clinical value in uncertain situations. Therefore, there is a pressing need for a more comprehensive understanding of the criteria for ICP monitoring insertion and improved adherence to guidelines to enhance the efficacy of ICP monitoring in the management of sTBI.

The precise indications for ICP monitoring in TBI patients are unknown and guidelines making recommendations have low penetrance and evidence for the same. Alali et al. published the predictors and clinical decision making rule for selecting the ICP monitoring in TBI patients based on the clinical and radiological parameters<sup>10</sup>. However there is significant variability on the method of ICP monitoring and frequency. As the ICP monitoring is resource intensive, its use is often limited to high resource settings and lower resource settings use alternative methods of ICP management. Therefore there is no confirming evidence that ICP monitoring reduces mortality in TBI patients.

This overview aims to summarize the evidence in Cochrane and non-Cochrane systematic reviews, the effects, and the benefits of monitoring intracranial pressure in patients with head trauma with an indication of ICP monitoring.

## METHODS

### Overview of reviews

We conducted an Umbrella Review to summarize the possible benefits and usefulness of monitoring intracranial pressure in patients with head trauma. This overview of reviews follows the guidelines and methodology laid down in the Joanna Briggs Institute manual for evidence synthesis in its Umbrella Review chapter<sup>11</sup>.

### Inclusion criteria

#### Participants

All patients with severe closed head trauma with an indication of intracranial pressure monitoring according to the Colombian Guidelines and the Brain trauma foundation guidelines

#### Intervention

Invasive monitoring of intracranial pressure by its different methods (external ventricular drainage, catheter with intraparenchymal sensors, or epidural catheters)

#### Comparison

No use of intracranial pressure monitoring.

### Outcomes

#### Primary

Mortality was defined as one point on the Glasgow Outcome Scale (GOS), or the mRS score of six, in patients with TBI at follow-up.

#### Secondary

ICU stay was defined by median days of ICU stay and complications (cardiovascular, infectious, thromboembolic, ischemic)

### Type of studies

This review considered systematic reviews of prospective, retrospective, or cross-sectional experimental and observational studies. Systematic reviews that include reports or case series were excluded. No ongoing systematic review was considered. Systematic reviews evaluating non-invasive measurements of intracranial pressure as diameter of the optic nerve sheath were excluded.

### Search

Five electronic databases were searched systematically and iteratively by two authors independently per the defined search strategy mentioned in [Supplementary Material](#). The following databases were searched for Systematic reviews: Cochrane Injuries Group

Specialized Register (up to February 2021); The Cochrane Library (until February 2021); MEDLINE (Ovid) February 2021; EMBASE (Ovid); PubMed [<http://www.ncbi.nlm.nih.gov/sites/entrez>] (February 2021); LILACS (February 2021). The search was constructed using terms and descriptors from the Medical Subject Heading (MeSH) and descriptors in health sciences (DeCs) for the ILACS search and was combined with Boolean operators. The keywords for systematic reviews and meta-analysis were incorporated into the search strategy enabling it to be more sensitive and specific. In addition, the reference list of the potentially eligible studies was searched to identify more citations. The search was not limited by date or by language.

### Selection of studies

After the search, the citations found in each database were entered into the Mendeley reference manager version 1.19.4 (George Mason University, Fairfax, Virginia, USA). Two reviewers independently examined the titles and abstracts to assess eligibility. Full texts were extracted, inclusion criteria were applied, and consensus resolved disagreements. The results of the search process are shown in a PRISMA flow chart (Preferred Reporting Items for Systematic Reviews and Meta-analysis) in [Fig. 1](#)<sup>12</sup>. Systematic review and meta-analysis were included in the present overview if: 1) All the original studies included in the SR-MA assessed the role of ICP monitoring in head injury patients and conformed to the PICO eligibility criteria laid out a priori; 2) If at least one of the outcomes were measured in the studies included in the SR-MA.

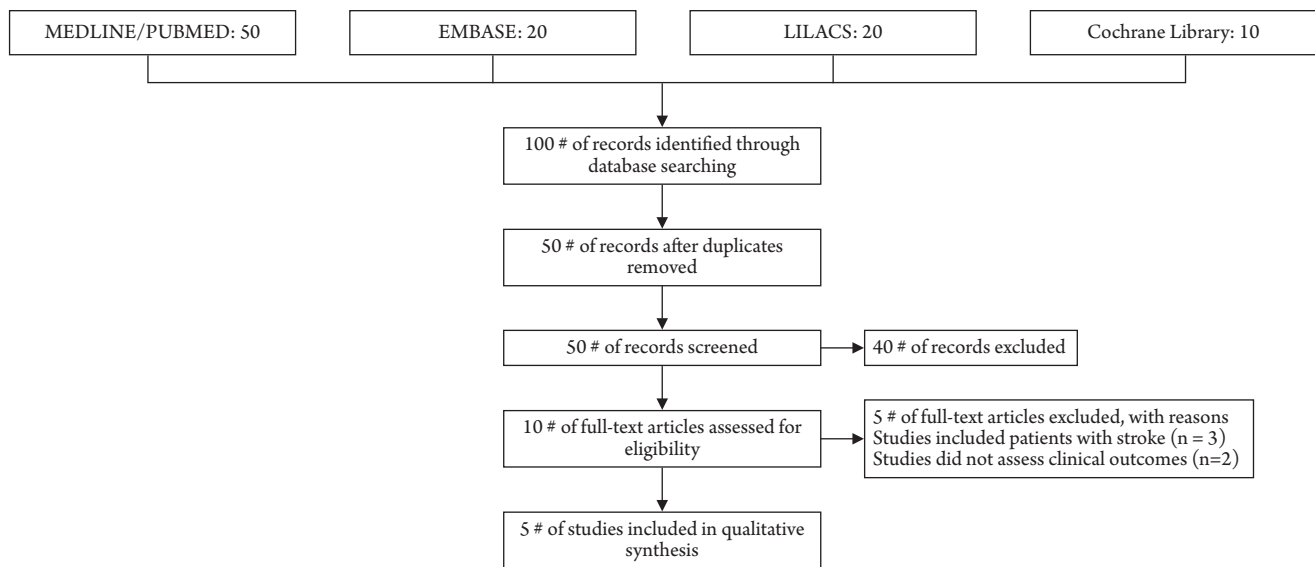
### Assessment of the quality of the included systematic reviews

The methodological quality of the systematic reviews of included randomized clinical trials was analyzed with the AMSTAR tool. AMSTAR is a valid, reliable, and easy-to-use tool<sup>13</sup>. It consists of 11 items and has content validity to measure methodological quality, in addition to the reliability of systematic reviews; Each of the 11 items is assigned a score of 1 if it meets the specific criteria or a score of 0 if it does not meet the criteria, is not clear, or is not applicable. The interpretation of critical appraisal is divided into three levels: 8 to 11 points are of high quality, 4 to 7 points are of moderate quality, and 0 to 3 points are of low quality. Study quality was assessed using this standardized tool by one of the reviewers and then checked by the second author. Any reviewer discrepancy was settled by mutual discussion or discussion with a third reviewer.

### Bias risk of included studies

The risk of bias in the included studies is made through the Risk of Bias in Systematic Reviews tool<sup>14</sup>. This tool is completed in





**Fig. 1.** PRISMA flow diagram of the study selection, screening, and inclusion process.

three phases: (1) assess relevance (optional), (2) identify concerns with the review process, and (3) judge the risk of bias in the review. Signalling questions are included to help assess specific concerns about potential biases with the review. We omit phase 1 because not relevant to result in the risk of bias assessment.

## RESULTS

### Overview of reviews

The database search yielded 100 studies, of which fifty were removed as duplicates in the citation manager software. Fifty articles were screened for eligibility as per the title and the abstract. The full text of ten articles was retrieved for final inclusion, and five SR-MA were found eligible for inclusion in the present overview per the eligibility criteria. From the pool of reviews, a grand total of 49 distinctive and individual original articles were identified as meeting our inclusion criteria. Further analysis revealed that out of these articles, a substantial number of 43 were deemed to be appropriate for inclusion in the comprehensive meta-analyses. Among these all the SR-MA's reported on mortality outcome in ICP monitoring group Vs non monitoring group. A total of 49 studies reported on the mortality outcome and 11 studies reported on the functional outcome and length of hospital stay. Total number of patients studies in the present overview from pool of systematic reviews were 73,085 and 61,714 patients were included in the meta-analysis.

### SR-MA characteristics

The characteristics of the included SR-Mas are presented in [Table 1](#). One study was published in 2012, 2014, and 2015, while two

were published in 2016. Among the five SR-MA included in the present overview, one presented data from observational studies only<sup>15</sup>), one from RCTs only<sup>5</sup>) and three from a combination of observational and RCT studies<sup>16-18</sup>). From all the SR-MAs seven were RCT and rest (n = 42) were observational studies. The median number of original studies included were nine with range of 2-18. Most SR-Mas included patients of both gender and all the SR-MAs included adult patients.

### Quality of SR-MAs and original studies

There was no tool for the assessment of quality mentioned in one of the SR-MA<sup>15</sup>). Cochrane risk of bias tool for the assessment of RCT and Newcastle Ottawa scale to assess the quality of observational studies was used in three SR-MAs<sup>5,16,17</sup>). One SR-MA used STROBE and Centre for Evidence Based Medicine (CBEM) criteria checklist to assess the quality of the included studies. All systematic reviews with meta-analysis (SR-MAs) included in the study demonstrated appropriate formulation of research inquiries, establishment of pre-defined and specified eligibility criteria, implementation of a systematic search methodology, and detailed reporting of primary study features and outcomes. The majority of SR-MAs conducted dual screening, evaluated for publication bias and heterogeneity. These findings suggest that while most SR-MAs adhere to standard procedures, there is still room for improvement in certain aspects of the review process, such as dual quality assessment. The authors of systematic reviews and meta-analyses employed a variety of instruments to evaluate the quality of the primary research studies. Because of the wide variety of tools used for quality assessment the quality of included studies

**Table 1.** Characteristic of included systematic reviews and meta-analysis

Study (Author, year)	Meta-analysis? Yes/No	Data base Search	PICO question	Outcome assessed	Risk of bias and quality assessment tool	Main Conclusion
Mendelson et al 2012 <sup>15)</sup>	No	MEDLINE (1966-October 2011) EMBASE (1977-October 2011)	Use ICP monitors and mortality in TBI patients comparison not monitoring	Mortality	Not reported	The isolated benefit of ICP monitoring in severe TBI is not clearly established. Clinical evidence is lacking as to the efficacy of ICP monitoring mostly attributed to the heterogeneous nature of the studies available on this topic. The significant modification of signal effect by confounding variables suggests that outcomes in severe TBI relate to both the presentation of the patient and the overall delivery of care rather than specific elements within the system.
Su et al 2014 <sup>17)</sup>	Yes	PUBMED Wan fang database VIP data base	P: patients with TBI I: ICP monitoring C: No ICP monitoring O: Mortality, Unfavorable outcome, events adverse, stay ICU	Mortality to 6 Months Unfavorable outcome GOSE 1 to 4 points in Score Events adverse Length Stay ICU	Cochrane Rias of bias assessment tool And New Castle-Ottawa Scale (NOS)	No benefit was found in patients with TBI who underwent ICP monitoring. Considering substantial clinical heterogeneity
Yuan et al 2015 <sup>18)</sup>	Yes	MEDLINE,EMBASE, Cochrane Central Register of Controlled Trials (Central) October 2013	Monitoring ICP vs No monitoring for TBI		STROBE and Centre for Evidence Based Medicine (CBEM) criteria	The current clinical evidence does not indicate that ICP monitoring overall is significantly superior to no ICP monitoring in terms of the mortality of TBI patients
Quesada et al 2016 <sup>5)</sup>	Yes	MEDLINE, HINARI EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL)	Monitoring ICP vs No monitoring for TBI	Mortality to 6 months Good Prognosis (GOSE better than 4) Poor Prognosis (GOSE 4 or less) Length of Stay ICU Stay ICU with specific cerebra support	Cochrane risk of bias tool and GRADE Scale	The monitoring of intracranial pressure no had an impact in terms of mortality. It also showed benefits in reducing polypharmacy and the number of interventions.
Shen et al 2016 <sup>16)</sup>	Yes	EMBASE, PUBMED, and the Cochrane Library	P: patients with TBI  I: ICP monitoring C: No ICP monitoring O: Mortality	Mortality in sub-groups  Overall mortality Mortality in ICU Mortality in 2 to 6 weeks	Cochrane risk of bias tool and New Castle-Ottawa Scale (NOS)	Superior survival was observed in severe TBI patients with ICP monitoring, yet the role of ICP monitoring in severe TBI patients remain to be further elucidated, more rigorously designed studies with long-term follow-up on the effects of ICP monitoring are needed

TBI: Traumatic brain injury, PICO: Patient/population, intervention, comparison and outcomes, ICP: Intracranial pressure, ICU: Intensive care unit.

could not be pooled together. These studies ranged from weakest evidence to strongest evidence but on a majority the included studies were of good quality. The quality assessment of included SR-

MAs using AMSTAR tool showed that one of the SR-MA was of moderate quality while four included SR-MA were of high quality (Table 2). Risk of Bias Assessment with Bristol's University ROBIS

**Table 2.** AMSTAR tool: assessment to methodological quality on systematic review included

Study	AMSTAR Questions											Total	Quality of Systematic Review
	1	2	3	4	5	6	7	8	9	10	11		
Mendelson et al 2012 <sup>15)</sup>	Yes	Yes	Yes	No	No	Yes	Yes	No	NA	No	Yes	6/11	Moderate
Su et al 2014 <sup>17)</sup>	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	9/11	High
Yuan et al 2015 <sup>18)</sup>	Yes	Yes	Yes	NR	No	No	Yes	Yes	Yes	Yes	Yes	9/11	High
Quesada et al 2016 <sup>5)</sup>	Yes	Yes	Yes	NR	No	Yes	Yes	Yes	Yes	No	Yes	8/11	High
Shen et al 2016 <sup>16)</sup>	Yes	NR	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9/11	High

NA: Not apply, NR: Not reported.

tool showed that study by Mendelson et al. was at moderate risk of bias in most of the domains of the tool, unclear in study by Quesada et al. and of low risk of bias in the rest of the SR-MAs. The risk of bias by the Bristol University ROBIS tool assessment is shown in Figs. 2 and 3.

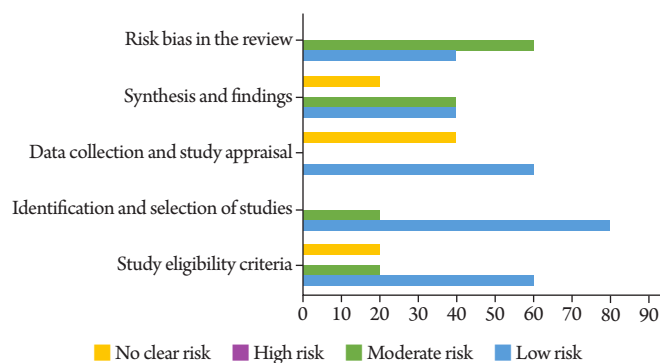
### Summary of the included SR-MAs

The five included SR-MAs presented comparison of 19,402 patients with ICP monitoring from a control of 53,825 patients without ICP monitoring. The types of ICP monitoring analysed in the included reviews were intraparenchymal (n = 935, 4.8%), external ventricular drainage (n = 620, 3.2%), epidural (n = 16), combined (n = 42), and not reported (n = 17804, 91.7%). The summary of the included SR-MAs are shown in Table 3.

The SR-MA included studies with adult patients<sup>15)</sup>. The included studies were six observational retrospective and non-randomized studies with 11,371 patients. Meta-analysis was not done due to marked heterogeneity in the included studies. The main concerns in the review were non-homogeneous inclusion and exclusion criteria. Individual studies did multivariate analysis but the number of variables in each varied. Quality assessment was not done but indicated the intrastudy differences due to several confounders like some of the included studies did the analysis without adjusting for the parameters of age, GCS etc.

This SR-MA included presented both systematic review and meta-analysis of the included studies from the studies including adult > 12 years including 385 patients<sup>5)</sup>. Only two RCTs were included. Cochrane risk of bias and grade tool was used to assess the quality of included studies and grade strength of evidence. Monitoring had no difference from clinical examination in prognosis but the length of stay and use of hypertonic saline was less in the monitoring group. Out of the two RCTs included one had unknown risk of bias in the random sequence generation, allocation concealment, reporting bias and other biases.

The SR-MA included 18 studies, 2 RCT rest observational, including 7,637 patients with ICP monitoring and 17,862 with no ICP monitoring<sup>16)</sup>. Cochrane risk of bias tool and Newcastle-Ottawa scale was included for the quality assessment. Included RCTs had



**Fig. 2.** Risk of bias graph. Review authors' judgements about each risk of bias item presented as percentages across all included studies.

unclear risk of selection bias, detection bias, reporting bias and other biases. The results obtained were mixed results. The outcomes of the study demonstrated no significant decline in mortality rates among the ICP monitored group for those who were hospitalized before 2007, hospital mortality for the same group, and mortality in randomized controlled trials. Despite this, the overall mortality rate, mortality rate for those hospitalized after 2007, hospital mortality rate for those hospitalized after 2007, and mortality rate in observational studies for those hospitalized after 2007, along with the 2-week mortality rate and 6-month mortality rate, were reduced in the ICP monitored group. It was discovered that patients with an elevated ICP were more likely to necessitate ICP monitoring. The findings indicate that the implementation of ICP monitoring can be beneficial for certain patient groups.

The SR-MA included two RCT and seven cohort with a total of 11,038 patients<sup>17)</sup>. There was no significant effect on the mortality, adverse events but the hospital stay was longer in the patients with ICP monitoring. There was considerable heterogeneity in the included studies. Cochrane risk of bias tool and Newcastle-Ottawa scale was used to assess the quality assessment of the included studies.

A comprehensive analysis of 14 studies<sup>18)</sup> comprising of 24,792 patients was conducted, and it was found that there was no significant evidence to suggest that ICP monitoring was associated with a reduction in the risk of death (pooled OR 0.93 [95% CI, 0.77–

Study	PHASE 2				PHASE 3
	Study eligibility Criteria	Identification and selection of studies	Data collection and Study appraisal	Synthesis and findings	Risk Bias in the Review
Mendelson et al 2012 <sup>15</sup>					
Su et al 2014 <sup>17</sup>					
Yuan et al 2015 <sup>18</sup>					
Quesada et al 2016 <sup>5</sup>					
Shen et al 2016 <sup>16</sup>					
High Risk					
Moderate Risk					
Low Risk					
No Clear Risk					

Fig. 3. Risk of bias assessment with Bristol’s University ROBIS tool: review authors’ judgements about each risk of bias item for each included systematic review.

Table 3. Summary of systematic reviews included in this Umbrella review

Study	N	Type of included Studies	Type of ICP monitor	Quality of included studies	Results of Outcome with heterogeneity
Mendelson et al 2012 <sup>15)</sup>	11,434 ICP monitoring: 2,717 Control: 8,717	Retrospective observational studies: 8 Total: 8	Intracerebral: 203 (8.46%) EVD: 124 (4.56%) Epidural: 8 (0.29%) Combined: 21 (0.77%) Not reported: 2,361 (86.9%)	Not Reported	Mortality OR 0.77, p=0.015 28-day Mortality OR 2.1 [95% CI, 0.80–5.6] p=0.13 Heterogeneity: Not Applicable
Su et al 2014 <sup>17)</sup>	11,143 ICP monitoring: 3,282 Control: 7,861	RCT: 2 Retrospective Observational Studies: 7 Total: 9	Not Reported	NOS score High (8–9): 4 (44.44%) Moderate (5–7): 3 (33.33%) Low (0–4): 0 (0%) Not Reported: 2 (22.22%)	Mortality OR 1.16 [95% CI, 0.87–1.54] p=0.31 I2=80% Heterogeneity: High Unfavorable Outcome: OR 1.40 [95% CI, 0.99–1.98] p=0.06 I2=4% Heterogeneity: Low Adverse events: OR 1.04 [95% CI, 0.64–1.70] p=0.87 I2=78% Heterogeneity: High Length of hospital stay Mean differences 6.32 [95% CI, 4.9–7.75] p<0.0001 I2=99% Heterogeneity: Very High
Yuan et al 2015 <sup>18)</sup>	24,792 ICP monitoring: 6,744 Control: 18,048	RCT: 1 Retrospective Observational Studies: 9 Prospective Observational Studies: 4 Total: 14	Intracerebral: 732 (10.81%) EVD: 339 (5.02%) Epidural: 8 (0.12%) Combined: 21 (0.31%) Not reported: 5644 (83.69%)	STROBE Check list High: 16–20: 10 (71.43%) Moderate 11–15: 2 (14.28%) Low: ≤ 10: 1 (0.714%) Not Reported: 1 (0.714%) CEBM strength of evidence 4: n=6 2b: n=4 3b: n=3 1b: n=1	Mortality In ICU: OR 0.92 [95% CI, 0.79–1.06] p=0.26 I2=41% Heterogeneity: Low In Hospital OR 1.06 [95% CI, 0.8–1.42] p=0.68 I2=84% Heterogeneity: High Length ICU stay Mean differences 0.29 [95% CI, 0.3–0.32] p<0.0001 I2=93% Heterogeneity: Very High Length Hospital stay Mean differences 0.21 [95% CI, 0.04–0.37] p=0.01 I2=100% Heterogeneity: High

(Continued to the next page)

Table 3. Continued

Study	N	Type of included Studies	Type of ICP monitor	Quality of included studies	Results of Outcome with heterogeneity
Quesada et al 2016 <sup>5)</sup>	358 ICP monitoring: 176 Control: 182	RCT: 2	EVD: 157 (89.2%) Not Reported: 34 (19.32%)	GRADE Scale High Quality: 2 (100%)	Mortality RR 0.85 [95% CI, 0.67–1.07] p=0.17 I <sup>2</sup> =0% Heterogeneity: Low Outcomes Good RR 1.05 [95% CI, 0.84–1.31] p=0.69 I <sup>2</sup> =20% Heterogeneity: Low Poor RR 0.95 [95% CI, 0.79–1.15] p=0.60 I <sup>2</sup> =0% ICU Stay Overall Mean differences 3 [95% CI, 2–4] p<0.0001 Heterogeneity: Not applicable With Specific support for brain injuries Mean differences –1.4 [95% CI, –2.37 to –0.43] p<0.0001 Heterogeneity: Not applicable
Shen et al 2016 <sup>16)</sup>	25500 ICP monitoring: 6,483 Control: 19,017	RCT: 2 Retrospective Observational Studies: 16 Total: 18	Not reported	NOS score High (8–9): 14 (77.77%) Moderate (5–7): 2 (11.11%) Low (0–4): 0 (0%) Not Reported: 2 (11.11%)	Mortality: Overall Risk Ratio 0.85 [95% CI, 0.73–0.98] p=0.02 I <sup>2</sup> =84% Heterogeneity: High In Hospital: Before 2007: Risk Ratio 1.18 [95% CI, 0.89–1.56] p=0.25 I <sup>2</sup> =86% Heterogeneity: High After 2007: Risk Ratio 0.72 [95% CI, 0.63–0.83] p<0.00001 I <sup>2</sup> =68% Heterogeneity: High ICU mortality: Risk Ratio 1.01 [95% CI, 0.9–1.13] p=0.85 I <sup>2</sup> =0% Heterogeneity: Low

ICP: Intracranial pressure, EVD: External ventricular drainage, RCT: randomized controlled trial, NOS: New Castle-Ottawa Scale, STROBE: STrengthening the Reporting of OBServational studies in Epidemiology, ICU: Intensive care unit, CEBM: The Centre for Evidence-Based Medicine, GRADE: The Grading of Recommendations Assessment, Development and Evaluation.

1.11], p = 0.40). However, the results of the meta-analysis revealed that 7 out of the 14 studies, which included 12,944 patients, and were published between January 2012 and October 2013, indicated that ICP monitoring was significantly linked with a greater reduction in mortality compared to no ICP monitoring (pooled OR 0.56 [95% CI, 0.41–0.78], p = 0.0006). These findings highlight the importance of keeping up-to-date with the latest research, as newer studies may provide more accurate and reliable results. Interestingly, the 7 studies conducted in North America showed no significant evidence to suggest that ICP monitoring lowered the risk of death, which was similar to the studies conducted in other regions. Furthermore, it was found that the group subjected to ICP monitoring had significantly longer ICU LOSs (mean difference [MD] 0.29 [95% CI, 0.21–0.37]; p < 0.00001). These results sug-

gest that ICP monitoring may not always be beneficial, and further research is needed to explore its effectiveness and potential drawbacks. In conclusion, the results of the meta-analysis provide valuable insights into the effectiveness of ICP monitoring and highlight the need for continued research in this area. The pooled analysis showed that the length of hospital stay was longer in the ICP monitoring group.

### Effectiveness of ICP monitoring on mortality

There was no conclusive evidence arising from the pooling of SR-MA that the ICP has efficacy in reducing the mortality. The study by Mendelson et al.<sup>15)</sup> found that the positive effect of ICP monitoring on reducing mortality, while rest of the SR-MA found no significant difference in the mortality among the two groups.

Interestingly in the study by Yuan et al.<sup>18)</sup> and Shen et al.<sup>16)</sup> the authors found that there is temporal discrepancy in the mortality outcome with the ICP monitoring. They found that there was no significant difference among the groups on pooling the results from studies done prior to 2007 and 2012 respectively, while the later studies suggested that the ICP monitoring had beneficial effect on the mortality outcome.

## DISCUSSION

This comprehensive review provides a summary of the published evidence on the impact of ICP monitoring on the duration of hospital stays, mortality rates, and procedure-related adverse events in adult patients suffering from traumatic brain injury. This review is based on a total of 49 primary research studies and 19 unique primary studies, as analyzed by the five SR-MAs. Mortality was reported as outcome in majority of the primary studies. Only one SR-MA found that the use of ICP monitoring lowered the mortality in the TBI patients<sup>15)</sup>. SR-MAs found that there was no significant effect on the reduction of mortality with ICP monitoring<sup>5,17)</sup>. In two SR-MAs the results varied according to the time of publication of primary studies with later studies having a positive effect of ICP monitoring on reducing the mortality while earlier studies did not find any significant effect<sup>16,18)</sup>. One of the SR-MA found that the resources used in the ICU were less with the use of ICP monitoring group due to better targeted therapy<sup>5)</sup>. The effect of ICP monitoring on the length of hospital stay was reduced in the ICP monitoring group in one of the SR-MA<sup>5,18)</sup> while it was prolonged in the other<sup>15)</sup>. There was high heterogeneity in the SR-MAs<sup>5,15-18)</sup>. The high heterogeneity in the included primary research studies could be due to the combination of different study types in the systematic reviews, heterogenous population and mode of ICP monitoring. The variables studied in each of the primary research studies were varying and that could add to the heterogeneity. Though most of the primary research studies focused on adult patients with both genders and severe traumatic brain injury, the classification of severity of the brain in jury was not uniform in all of the studies. The study by Quesda et al. was the only SR-MA that assessed the neuropsychological function as the outcome and found that there was no significant impact of ICP monitoring on the neuropsychological function of TBI patients<sup>5)</sup>. The study included two RCTs and was rated as high quality of evidence; however among the two studies the study by Chestnut et al. was at low risk of bias while there was unclear risk of bias in the study by Kostic et al. domains of random sequence generation, allocation concealment, reporting bias and other biases of the Cochrane risk of bias tool. Three SR-MAs have combined the obser-

vatational studies with RCTs and performed the subgroup analysis and found that though there was no significant decrease in mortality with the ICP monitoring in the RCTs, observational studies tend to show more effect of reduced mortality. These results were extracted from a pool of five SR-MAs of which one was rated of moderate quality and rest four as high quality by the AMSTAR tool. Because of high heterogeneity in the included studies included in the present overview and inclusion of RCTs and observational studies, we have high degree of certainty in the conclusions from the present overview. The findings from the present overview align with the RCTs and most of the recent systematic reviews that there is no significant effect of ICP monitoring on reducing the mortality. The studies on the procedure related events, neuropsychological outcomes and length of hospital stay are limited in number to make any meaningful conclusions and more primary research studies are required to find the association.

Shibahashi et al. have published the results of the real world experience in a propensity score matched analysis of 31,660 patients from 765 hospitals from the Japanese inpatient nationwide database and found that there was significantly reduced mortality in ICP monitoring group (31.9% vs. 39.1 %) and a longer duration of hospital stay (35 vs. 28 days)<sup>19)</sup>. The gaps in the evidence is likely to filled by more studies on the topic gathering real world experience and avoiding the potential confounders.

One of the reasons for conflicting evidence could also be due to the fact that it is not known from the primary research studies as to what was the objective of the placement of the ICP monitoring devices. As found in the several studies, the focus has been on utilizing the values obtained from the ICP monitoring in guiding the management, while the ICP monitoring device itself can be used to lower the ICP when placed inside the ventricles with intermittent CSF release<sup>20-22)</sup>. In one of the retrospective study with different protocols of ICP monitoring from two different trauma centres, authors reported that there was no significant difference in mortality and the complications varied according to the device used for ICP monitoring<sup>23)</sup>. According to a study conducted by the National Trauma Databank, the monitoring of ICP demonstrated an association with a notable 45% rise in mortality rates. This correlation remained significant even after accounting for head Abbreviated Injury Scale (AIS) and Injury Severity Score (ISS)<sup>24)</sup>. The difference in outcomes with ICP monitoring in individual studies could also be due to difference in adherence to the management guidelines and delay in insertion of the ICP monitoring. As found in the study by shafi et al. The adherence and compliance was only 45%<sup>24)</sup>. The strict adherence to a protocol-driven management strategy for TBI, which involves the placement of an ICP monitor for all sTBI patients, resulted in a noteworthy reduction in mortality.

ty rates that, while not statistically significant, is nevertheless noteworthy<sup>25</sup>). Furthermore, this approach also led to a marked reduction in overall costs, as well as a significant decrease in both ICU and hospital stay durations<sup>25</sup>).

### Limitations

This overview of reviews synthesizes the literature on the effect of ICP monitoring in traumatic brain injury patients. One of the limitation of the present study is that we have not addressed some important research questions as no systematic reviews addressed them. One of the important research question not addressed is the relationship of ICP monitoring with the radiological extent or the severity of head injury patients. Though some of the included SR-MAs did the analysis stratified on the severity of the head injury the included studies and variables studied were quite heterogeneous. Though most of the included SR-MAs were of high quality, still the strength of evidence is not very strong owing to inherent limitations of the observational studies and combining RCT with observational studies in a SR-MA also leads to conflicting evidence. The technique of ICP monitoring, and method varied extensively in the included studies and more than 90% of the included primary research studies did not report on the method of ICP monitoring and this is a significant limitation. The adverse events and mortality might also get influence by the mode of ICP monitoring. One of the limitation we have found is that the results were different based on timeline and this could be due to better techniques and equipments available for ICP monitoring evolving over time. Further with time, there has been an overall improvement in the management of traumatic brain injuries across the ICUs globally and therefore a time series evaluation of effect of ICP monitoring on outcomes following TBI would yield more uniform results. The results from the present overview are conflicting from some of the larger and more recent studies published; however the aims of the present reviews was to synthesize the evidence from the existing literature of systematic reviews, these have not been accounted for.

### CONCLUSION

Notwithstanding the limitations, in the present literature synthesis we have found that the studies showed mixed results on the effect of ICP monitoring in outcomes following traumatic brain injury and there is no compelling evidence that ICP monitoring reduces the mortality. We have found high heterogeneity in the studies and future studies addressing the mentioned limitations might help us to answer the question and increase the strength of evidence on use of ICP monitoring. Due to lack of evidence on the role of ICP monitoring in reducing the mortality in TBI patients,

and increased use of ICP monitoring post brain trauma foundation guidelines, it has been found that more ICP targeted therapies are used in the patients undergoing ICP monitoring. Therefore, the present overview suggest that the outcomes of ICP monitoring has been continuously evolving with time and therefore there is no compelling evidence to recommend its universal use or to remove it from use till stronger evidence is found either in support or against ICP monitoring. ICP monitoring should be used as stated in the brain trauma foundation guidelines in an level one traumacentre facility with the availability of targeted ICP management therapies.

### NOTES

#### ORCID

William A Florez-Perdomo, <https://orcid.org/0000-0001-5065-7711>  
Luis Rafael Moscote-Salar, <https://orcid.org/0000-0002-4180-6962>  
Ved Prakash Maurya, <https://orcid.org/0000-0001-7570-1176>  
Amit Agrawal, <https://orcid.org/0000-0002-3287-5448>

#### Author contributions

Conceptualization: All authors, Data curation: WAFP, VPM, AA. Formal analysis: WAFP, LRMS, AA. Methodology: All authors. Visualization: WAFP. Writing - original draft: All authors. Writing - review & editing: All authors.

#### Conflict of interest

There is no conflict of interest to disclose.

#### Funding

None.

#### Data availability

None.

#### Acknowledgments

None.

### SUPPLEMENTARY MATERIALS

Further details on supplementary materials are presented online (available at <https://doi.org/10.32587/jnic.2023.00731>).

### REFERENCES

1. Carteri RB, Silva RA. Traumatic brain injury hospital incidence in Brazil: an analysis of the past 10 years. *Rev Bras Ter Intensiva* 2021;33:282–289.

2. Nag DS, Sahu S, Swain A, Kant S. Intracranial pressure monitoring: Gold standard and recent innovations. *World J Clin Cases* 2019;7:1535–1553.
3. Chesnut R, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, et al. A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med* 2020;46:919–929.
4. Poca MA, Benejam B, Sahuquillo J, Riveiro M, Frascheri L, Merino MA, et al. Monitoring intracranial pressure in patients with malignant middle cerebral artery infarction: is it useful? *J Neurosurg* 2010;112:648–57.
5. Quesada MF, Duran MA, Laiseca EF, Flórez WA. Una revisión sistemática del monitoreo de la presión intracraneana en adultos con trauma craneoencefálico severo. *Revista Chilena de Neurocirugía* 2019;42:160–167.
6. Brain Trauma Foundation; American Association of Neurological Surgeons; Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. *J Neurotrauma* 2007;24 Suppl 1:S1–106.
7. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery* 2017;80:6–15.
8. Bulger EM, Nathens AB, Rivara FP, Moore M, MacKenzie EJ, Jurkovich GJ, Brain Trauma Foundation. Management of severe head injury: institutional variations in care and effect on outcome. *Crit Care Med* 2002;30:1870–1876.
9. Sivakumar S, Taccone FS, Rehman M, Hinson H, Naval N, Lazaridis C. Hemodynamic and neuro-monitoring for neurocritically ill patients: An international survey of intensivists. *J Crit Care* 2017;39:40–47.
10. Alali AS, Temkin N, Barber J, Pridgeon J, Chaddock K, Dikmen S, et al. A clinical decision rule to predict intracranial hypertension in severe traumatic brain injury. *J Neurosurg* 2018;131:612–619.
11. Aromataris E, Munn Z. *JBIC Manual for Evidence Synthesis*. 2020. <https://jbi-global-wiki.refined.site/space/MANUAL>. [Accessed Apr 8 2022].
12. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
13. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of health-care interventions, or both. *BMJ* 2017;358:j4008.
14. Whiting P, Savović J, Higgins JP, Caldwell DM, Reeves BC, Shea B, et al, ROBIS group. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol* 2016;69:225–234.
15. Mendelson AA, Gillis C, Henderson WR, Ronco JJ, Dhingra V, Griesdale DE. Intracranial pressure monitors in traumatic brain injury: a systematic review. *Can J Neurol Sci* 2012;39:571–576.
16. Shen L, Wang Z, Su Z, Qiu S, Xu J, Zhou Y, et al. Effects of intracranial pressure monitoring on mortality in patients with severe traumatic brain injury: a meta-analysis. *PLoS One* 2016;11:e0168901.
17. Su SH, Wang F, Hai J, Liu NT, Yu F, Wu YF, et al. The effects of intracranial pressure monitoring in patients with traumatic brain injury. *PLoS One* 2014;9:e87432.
18. Yuan Q, Wu X, Sun Y, Yu J, Li Z, Du Z, et al. Impact of intracranial pressure monitoring on mortality in patients with traumatic brain injury: a systematic review and meta-analysis. *J Neurosurg* 2015;122:574–587.
19. Shibahashi K, Ohbe H, Matsui H, Yasunaga H. Real-world benefit of intracranial pressure monitoring in the management of severe traumatic brain injury: a propensity score matching analysis using a nationwide inpatient database. *J Neurosurg* 2023;139:1514–1522.
20. Chesnut RM, Aguilera S, Buki A, Bulger EM, Citerio G, Cooper DJ, et al. Perceived utility of intracranial pressure monitoring in traumatic brain injury: a seattle international brain injury consensus conference consensus-based analysis and recommendations. *Neurosurgery* 2023;93:399–408.
21. Chesnut RM, Temkin N, Carney N, Dikmen S, Rondina C, Videtta W, et al, Global Neurotrauma Research Group. A trial of intracranial-pressure monitoring in traumatic brain injury. *N Engl J Med* 2012;367:2471–2481.
22. Chesnut RM, Bleck TP, Citerio G, Classen J, Cooper DJ, Coplin WM, et al. A consensus-based interpretation of the benchmark evidence from South American Trials: treatment of intracranial pressure trial. *J Neurotrauma* 2015;32:1722–1724.
23. Guyot LL, Dowling C, Diaz FG, Michael DB. Cerebral monitoring devices: analysis of complications. *Acta Neurochir Suppl* 1998;71:47–49.
24. Shafi S, Diaz-Arrastia R, Madden C, Gentilello L. Intracranial pressure monitoring in brain-injured patients is associated with worsening of survival. *J Trauma* 2008;64:335–340.
25. Fakhry SM, Trask AL, Waller MA, Watts DD; IRTC Neurotrauma Task Force. Management of brain-injured patients by an evidence-based medicine protocol improves outcomes and decreases hospital charges. *J Trauma* 2004;56:492–499; discussion 499–500.



# Comparison the Perfusion/Diffusion Mismatching Judging From CT-Based and MR-Based Study

Jae-Yong Shim, Do-Sung Yoo, Kwang-Wook Jo, Hae-Kwan Park

Department of Neurosurgery, The Catholic University of Korea, Eunpyeong St. Mary's Hospital, Seoul, Korea

Received: December 1, 2023

Accepted: April 18, 2024

## Corresponding Author:

Jae-Yong Shim, MD

Department of Neurosurgery,  
The Catholic University of Korea,  
Eunpyeong St. Mary's Hospital,  
327, Sosa-ro, Bucheon 14647,  
Korea

Tel: +82-32-345-3425

E-mail: [impr0326@naver.com](mailto:impr0326@naver.com)

## Background

The development of endovascular devices and clinical experience, recanalization rate after intraarterial thrombectomy (IA-Tx) has increased. Recent papers reported that the amount of perfusion/diffusion (P/D)-mismatching in digital analysis from computer tomography perfusion (CTP) image is well correlated well with P/D-mismatching from magnetic resonance image. The purpose of this study is compare the patient clinical outcomes after IA-Tx, judging from CTP based and magnetic resonance imaging (MRI) based study.

## Methods

218 patients with anterior circulation large vessel occlusion (LVO) treated by IA-Tx were included in this analysis. In the MRI group (n=80), P/D-mismatching from MRI based image analysis by visual method and in the CTP group (n=138), and recently, P/D-mismatching was decided by automatized computer programmatic analyzed from CTP based image (Syngo.via program).

## Results

Favorable outcome (modified Rankin Score: 0–2), mortality, recanalization, and clinically significant hemorrhage was 56.3% (45/80), 6.25% (5/80), 81.3% (65/80) and 25% (20/80) in MRI group and 4.9% (62/138), 8.9% (18/138), 91.3% (126/138) and 40.6% (56/138) in CTP group (p=0.000, 0.235, 0.007 and 0.013). Reperfusion injury (27.5% vs. 15.0%, p=0.018) but favorable outcome was high 55.0% vs. 44.9%, p=0.00) in the MRI study group.

## Conclusion

In our study, patient selection according to the P/D-mismatching from MR-based imaging and CTP-based image was not different in final clinical outcome. Recent IA-Tx, showed high recanalization rate but it also cause high incidence of reperfusion injury.

**Keywords:** Computer tomography perfusion; Intraarterial thrombectomy; Hemorrhagic complication; Perfusion-diffusion; Recanalization rate; Reperfusion injury

## INTRODUCTION

The aim of ischemic stroke therapy is reperfusion of the ischemic penumbra tissue in order to salvage threatened but potential-

ly viable brain tissues<sup>1,2</sup>. To improve clinical outcomes of stroke patients, various treatment methods have been developed, with each having its advantages and limitations<sup>3-8</sup>.

Since the MR CLEAN study<sup>3</sup>, the first report showing that in-

traarterial thrombectomy (IA-Tx) is more favorable for improve clinical outcomes than intravenous tissue plasminogen activator (IV-tPA) in large vessel occlusion (LVO) patients. Recently, thanks to the development of endovascular devices and clinical experience, the percentage of recanalization rate has increased from about 70–80% to over 95%<sup>9)</sup>.

Although successful recanalization rate is increasing, but in some cases, reperfusion treatment can result unfavorable outcomes. In this futile recanalization patients, there is no clinical benefit for a successful recanalization that may sometimes cause an unexpected brain injuries. To avoid the reperfusion injury and to obtain the patient safety and treatment effectiveness of IA-Tx, proper patient selection for IA-Tx is increasingly important<sup>10-13)</sup>.

Many papers have reported that perfusion/diffusion (P/D)-mismatch on brain magnetic resonance imaging (MRI) image might be the best method for selecting IA-Tx patients<sup>2,8,9,13-15)</sup>. Nonetheless, MRI evaluation of acute ischemic patients has several limitations, including a relative long time required to acquire image, high cost, equipment limitations, and patient related reasons<sup>9,13,16)</sup>. Recent several years, papers have reported that brain computed tomography (CT) image is as informative as P/D-mismatch on magnetic resonance (MR) but clinical application of these CT image instead of MRI image was questionable<sup>2,4,9,14,11,16-19)</sup>.

From the three or four years ago, we are facing an additional challenge that we have never experienced before, namely the coronavirus disease 2019 (COVID-19) pandemic. Owing to the additional risk caused by the pandemic, we are unable to evaluate MRI images of stroke patients, especially if the patient shows fever or chest problems on chest X-ray. Serologic diagnostic testing for COVID-19 requires at least 6 hours.

For these several reasons, a CT-perfusion (CTP) with and digitalized computerized program (Syngo.via, Siemens Healthcare GmbH, Erlangen, Germany) was used instead of MR-based P/D-mismatching, to select infarction patients for IA-Tx. In this study, although we could not checked CTP and MRI on the same patient, compared clinical outcome between the 80 patient data treated with IA-Tx who was selected by the MR-based image study before the pandemic period and the 138 patient data who was selected by CTP based image after the pandemic season.

## METHODS

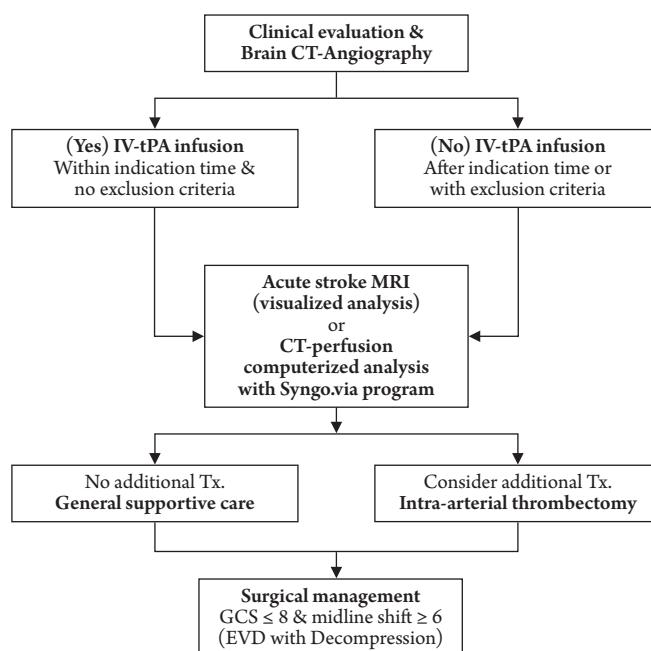
This retrospective, observational study was approved by our Institutional Ethics Committee. The treatment protocol was approved by our Institutional Review Board (approval number: PC17RESI0028). All patients or their representatives provided

written consent for treatment.

## Patient characteristics

From Mar. 2015 to Nov. 2022, a total of 218 patients diagnosed with anterior circulation LVO and treated with IA-Tx were included in this study. In the MRI group, from Mar. 2015 to May 2018, 80 patients underwent CT-angiography (CTA) as an initial image study and checked stroke MRI (Magnetom Vida, Siemens Medical System, Nucich, Germany) about 1 hours after IV-tPA administration and before the IA-Tx. MRI study was taken. And in CTP group, 63 patients admitted between Jun. 2019 and Nov. 2022 underwent a CTA as an initial image study and decide the IV-tPA administration or not. Than a CTP (Somatom Definition Edge, Siemens Medical Systems, Forchheim, Germany) was checked before the IA-Tx. If the neurologic status (evaluated by NIHSS or motor grade) of the patient was not improved after IV-tPA, the patient was brought to an angiography suite for additional IA-Tx therapy (Fig. 1).

The mean age of patients was  $69.8 \pm 12.6$  years (range, 20 to 98 years, median: 70 years). There were 124 (56.9%) male patients. Eighty (36.7%) patients was MRI group and 138 (63.3%) patients was CTP group. There was no significant difference in a ge ( $p = 0.795$ ), initial NIHSS score ( $p = 0.529$ ), or gender ( $p = 0.499$ ) between the two groups (MRI and CTP groups) (Table 1). How-



**Fig. 1.** Flow diagram of magnetic resonance based treatment protocol. CT: Computer tomography; IV-tPA: Intravenous tissue plasminogen activator; MRI: Magnetic resonance imaging; GCS: Glasgow Coma scale; EVD: Extraventricular drainage.

**Table 1.** Characteristics and clinical outcomes of the 143 patients treated with IA-Tx

	Magnetic resonance base group	Computer tomography base group	Significance statistical
Patients no.	80	138	
Age (years)			
Mean $\pm$ SD (median)	64.2 $\pm$ 12.1 (70)	73.0 $\pm$ 11.8 (73)	
Male sex (%)	45 (56.3)	79 (57.2)	0.499
NIHSS score (Median)	13.2 $\pm$ 6.3 (12)	12.4 $\pm$ 6.8 (13)	
Occlusion vessel site			
MCA Lt. (%)	19 (23.8)	48 (34.8)	
Rt. (%)	30 (37.5)	54 (39.1)	
ICA Lt. (%)	16 (20.0)	17 (12.3)	
Rt. (%)	15 (18.8)	19 (13.8)	
Time to femoral puncture	5.9 $\pm$ 2.6 (6.0)	6.8 $\pm$ 5.0 (5.5)	
Clinical outcomes (mRS)			
0	20	5	
1	12	38	
2	12	22	
Favorable (%)	44 (55.0)	62 (44.9)	0.000
3	12	19	
4	16	55	
5	3	46	
6 (Mortality)	5 (6.3)	18 (8.9)	0.235
Recanalization (%)	65 (81.3)	126 (91.3)	0.007
sICH (%)	20 (25.0)	56 (40.6)	0.013
Reperfusion Injury	12 (15.0)	38 (27.5)	0.018
P/D-mismatching (%)	59/80 (73.8)	116 (84.1)	0.049

NIHSS: National Institute of Health Stroke Score; P/D: Perfusion weighted image/diffusion weighted image; IA-Tx: Intra-arterial thrombolysis; mRS; Modified Rankin Scale; OP: Operation; SD: Standard deviation; sICH: Significant intracerebral hemorrhage.

ever, analysis for in IV-tPA treated before the IA-Tx, revealed that the IV-tPA administration (42/80 in MRI group vs. 44/138 in CTP group,  $p=0.002$ ) faster in CT group and femoral artery puncture time (5.9 hours in MRI group vs. 6.9 hours in CTP group,  $p=0.000$ ) was faster in MR group.

### Radiologic analysis

Each patient's radiological results were analyzed (visual analysis of MR perfusion-diffusion mismatching) by radiologists after an acute treatment was completed. If radiologists' conclusions regarding a patient's images were not in agreement, another radiologist was consulted. For CTP group, ischemic core and penumbra area were calculated using a Syngo.via program (Siemens Healthcare GmbH, Erlangen, Germany).

All scans were done with 40 cc of nonionic iodinated contrast (Isovue-370, iopamidol, 370 mg iodine/mL; Bracco Diagnostics, Princeton, NJ, USA). In the digitalized automatic program (Syngo.via CT Neuro Perfusion VB40), recently defined thresholds for infarcted and hypoperfused tissues (relative cerebral blood flow (rCBF)  $< 30\%$  and  $T_{max} > 6$  s, respectively) were

used<sup>2,4,9-11,14,16-19</sup>.

Targeted mismatching ratio was defined to be more than 1.8. It was calculated from the ischemic penumbra area divided the ischemic core area. Acute stroke MRI studies have described diffusion weighted image (DWI) and perfusion weighted image (PWI) techniques elsewhere<sup>2,20</sup>. A P/D-mismatching profile was defined as a PWI lesion  $> 180\%$  or more of the DWI lesion<sup>21</sup>. Recanalization was measured using the thrombolysis in cerebral infarction (TICI) score. Successful recanalization was defined as TICI grade 2b/3<sup>3</sup>.

In patients treated with IA-Tx, a follow-up plain CT image was obtained immediately after IA-Tx. Clinically significant ICH was defined as a hemorrhage identified on the follow-up CT scan associated with a 4 point or greater increase in National Institute of Health Stroke Score (NIHSS) score, consistent with the European Cooperative Acute Stroke Study (ECASS) I & II criteria<sup>13,31</sup>. Reperfusion injury was defined as a disastrous outcome in the form of fatal edema or intracranial hemorrhage that concomitantly reversed benefits of re-establishing CBF following mechanical or chemical therapies for acute ischemic stroke<sup>10,22</sup>.

### Intraarterial thrombectomy

Angiographic images (Artis Q biplane; Siemens Medical Systems, Nucich, Germany) were obtained using standard techniques. Usually, the right-side groin was prepped and draped in a sterile fashion. The femoral artery was catheterized with an 8-French sheath and 7-F Terumo guidewire (Terumo Inc., Somerset, NJ, USA) and a 6-French Cello balloon guide catheter (ev3, Irvine, CA, USA) or a Sofia intermediate catheter (MicroVention, Aliso Viejo, CA, USA) in some cases were inserted through the guiding catheter. Multiple runs in multiple views were obtained to identify the site of occlusion. The diseased segment was catheterized highly selectively with a Marksman (ev3, Irvine, CA, USA) and Synchro 2 (Boston Scientific, Natick, MA, USA). Mechanical thrombectomy was performed using a Solitaire FR device (ev3, Irvine, CA, USA), a Trevo 18 microcatheter (Stryker, Kalamazoo, MI, USA), and Penumbra suction devices combining an outer Penumbra catheter and an inner Rebar 18 microcatheter (ev3, Irvine, CA, USA). The stent was usually deployed and kept in place about five minutes. It was then retrieved with aspiration through the balloon guide device. This procedure was repeated until the occlusion site opened. However, in some patients, recanalization efforts failed or the stent device became detached at the occluded site. After IA-Tx procedure, all patients were transferred to the neurosurgical intensive care unit for several days.

### Surgery indications for decompressive craniectomy and postoperative management

DC indications were the followings : (1) the appearance of massive unilateral brain swelling on computed tomography (CT) scans with correlating clinical deterioration, (2) worsening of Glasgow Coma scale (GCS) score  $\leq 8$  and/or dilated pupils that were unresponsive to light, (3) midline shift of more than 6 mm, and/or (4) obliteration of cistern structures on CT scans.<sup>23,24</sup> Patients with primary fatal brainstem failure, indicated by an initial and persisting GCS score of 3 and/or bilaterally fixed and dilated pupils, were excluded from the surgical decompression. After the decompressive surgery, conventional medical managements, including hyperosmotic agents, hyperventilation, and extraventricular drainage (EVD), were initiated if the ventricular pressure exceeded 20 mmHg.

### Variables assessed

Factors included age, sex, NIHSS score on admission, IV-tPA administration or not, P/D-mismatch on visual analysis on stroke MRI image and digitalized computerized analysis on CTP image, and time from the onset of symptoms to IA-Tx intervention, recanalization rate, complications, and clinical outcomes were analyzed.

Clinical results were analyzed according to the MRI based analysis and digital analysis (Syngovia program) in CTP group. A favorable or good outcome was defined as a mRS score of 0 to 2. Complications including postoperative clinical significant ICH, massive brain edema and reperfusion injury<sup>14,25</sup>.

### Statistical analyses

All data are presented as a mean  $\pm$  standard deviation and/or a median. A Wilcoxon signed-rank test was used to analyze NIHSS score and mRS. Unpaired t-test and Fisher's exact test were used to analyze results between groups. Statistical analyses for each outcome were analyzed using SPSS<sup>®</sup> software version 20 (IBM, Armonk, NY, USA). For all statistical analyses, significance level was defined at  $p$ -value  $\leq 0.05$ .

## RESULTS

### Clinical outcomes according to the MRI group and CTP group

Patient demographic and clinical results between the MRI group and the CTP group were compared in [Table 1](#). The mean initial neurologic status (evaluated with NIHSS) was  $13.2 \pm 6.3$  (median: 12) for the MRI group and  $12.6 \pm 6.8$  (median: 13) for the CTP group, showing no significant difference between the two groups ( $p = 0.520$ ) ([Table 1](#)).

Favorable outcome (modified Rankin Score: 0–2), mortality, recanalization, and clinically significant hemorrhage was 56.3% (45/80), 6.25% (5/80), 81.3% (65/80) and 25% (20/80) in MRI group and 4.9% (62/138), 8.9% (18/138), 91.3% (126/138) and 40.6% (56/138) in CTP group ( $p = 0.000, 0.235, 0.007$  and  $0.013$ ).

Recanalization rate was 81.3% (65/80) in the MRI study group and 91.3% (126/138) in the CT study group ( $p = 0.007$ ) ([Table 1](#)). Reperfusion injury (27.5% in CT group vs, 15.0% in MR group,  $p = 0.018$ ) but favorable outcome was high 55.0% vs. 44.9%,  $p = 0.00$ ) in the MRI study group.

### Compare the clinical outcomes according to IV-tPA or not

Administration of IV-tPA before IA-Tx did not influence patient outcomes or complications (data not shown). The percentages of patients with successful recanalization, favorable outcomes, or those who died or had hemorrhagic complications after receiving IV-tPA was (90.5%, 49.2%, 4.8%, and 31.7%, respectively) did not differ significantly from those in patients who did not receive IV-tPA (86.3%, 50.0%, 6.3%, and 37.5%,  $p = 0.306, p = 0.530, p = 0.498$ , and  $p = 0.295$ , respectively).

## Complications according to the MRI group and CTP group

Compare the MRI group and CTP group showed that clinical significant ICH was identified in 25.0% (20/80) of patients in the MRI study group and in 40.6% (56/138) of patients in the CTP study group ( $p = 0.004$ ). After the successful recanalization by IA-Tx, reperfusion injury developed in 40.0% (32/80) of patients in the MRI-based group and in 50.9% (32/63) in the CTP-based group ( $p = 0.013$ ). In this analysis, mortality did not differ significantly between the both groups 6.3% in the CT group vs. 8.9% in the MR group,  $p = 0.235$  (Table 1).

## DISCUSSION

Reopening of the occluded vessels before critical cell damage occurs is main principal of cerebral ischemic stroke treatment. During the last several decades, various methods to treat stroke have been developed, with each having its treatment successes and limitations<sup>1-8,12,14,15,26</sup>. After the NINDS study, IV-tPA administration within 3 hours from symptom onset without contraindication has become the standard treatment for ischemic stroke patients<sup>5</sup>. Since the ECASS III study, the critical therapeutic window was extended to up to 4.5 hours after ischemic symptom onset<sup>7</sup>. IV-tPA therapy has the merit of early beginning of treatment and limitations of poor recanalization rate and various contraindication for administration. And bridging therapy, in which IV-tPA and IA-Tx are combined, has been reported to result in high successful recanalization rate over 80-90% of patients with acceptable safety<sup>4,13-15,23,27,28</sup>.

More recently, recanalization and favorable clinical outcomes after IA-Tx with or without IV-tPA in major LVO have been reported to be better than those of IV-tPA only<sup>3,4</sup>. But in some instance, even after a successful reperfusion by the IA-Tx, the treatment result is ultimately futile because the patient's neurologic status shows no improvement<sup>12</sup>. While in some instance, patient outcomes are favorable although reperfusion treatment is initiated after what would normally be considered the therapeutic window has passed<sup>14,15</sup>.

The success of recanalization of LVO, is increasing thanks to the development of new thrombolysis devices and greater interventional experience. However, without proper patient selection protocols, reperfusion therapy may cause unexpected complications and lead to worse clinical outcomes<sup>12</sup>. Brain imaging technique getting more and more important to select patients, fit for the reperfusion therapy. To find the ischemic penumbra on brain image had tried over the last several decades<sup>2,8-11,13-16</sup>.

At the beginning of IV-tPA treatment, non-contrast CT scan was

employed as the standard diagnostic image to exclude ICH. Nowadays, advanced dynamic imaging techniques such as CTA, CTP, and acute stroke MRI have become important<sup>9-11,13-16,25,27,28</sup>. It is becoming increasingly important to evaluate the viability of ischemic tissues to improve therapeutic results because the physiologic state is unique for each patient<sup>9,13-15</sup>. Until now, an MRI based P/D-mismatching is thought to be the best approach for proper patient selection. Many studies have assessed the merit and definition of MRI based P/D-mismatching for patient selection in IV-tPA or IA-Tx treatment<sup>2,4,9,13,14,23,28</sup>. The specified criteria for the target mismatch profile on several diagnostic image technique were summarized on previous studies. These criteria were: 1) ratio between volumes of critically hypoperfused tissue and the ischemic core of 1.8 or more, 2) an absolute difference between the infarction core and the penumbra area of 15 mL or more; 3) ischemic core volume of less than 70 mL; and 4) less than 100 mL of tissue with a severe delay in bolus arrival ( $T_{max} > 6$  s)<sup>2,9,11,13-15,17,19,24,29,30</sup>.

Quantitative CTP based, P/D-mismatch classification using CBF and  $T_{max}$  is similar to perfusion-diffusion MRI. The greater accessibility of CTP may facilitate the generalizability of P/D-mismatch based selection in clinical practice and trials<sup>11,17-19</sup>.

Although P/D-mismatching identified in an MRI study is the best tool for selecting acute ischemic stroke patients, this method has some practical drawbacks. To obtain an MRI image, a quite long extra time is required. If the patient with metallic implants in the body is a contraindication, some patients with neurologic or respiratory problems may find it impossible to tolerate the MRI process long enough to produce a diagnostic image. In addition, it is impossible on MRI based image study to calculate the mismatching amount in a digitalized program<sup>9,10,14-16,24</sup>. During the COVID-19 pandemic season, MRI studies to evaluate the infarction core or P/D-mismatch are practically problematic for those with suspected COVID-19 infection or febrile patients. Many papers already reported that CTP based computerized digital analysis for patient selection for P/D-mismatching is as effective as MRI based method<sup>11,17-19</sup>.

From this study, P/D-mismatching patients in visual analysis showed favorable outcome (modified Rankin Score: 0-2) was 55.0% (44/80) in MRI group and 44.9% (62/138) at digitalized computerized analysis in CTP group ( $p = 0.000$ ).

Recanalization rate, mortality, clinical significant ICH, and reperfusion injury were variables according to patients and managed interventionalists not by treatment methods. Many previous studies have reported that IV-tPA administration before IA-Tx does not influence clinical outcomes<sup>23,24,26</sup>.

Massive brain edema and clinical significant ICH after IV-tPA or

IA-Tx are defined as reperfusion injuries<sup>22)</sup>. In some patients, fail to improve clinical results despite evident recanalization. This might occur due to incomplete tissue reperfusion, injury of the neurovascular unit, and/or distal microthrombosis, which has been termed a “no-reflow phenomenon.” On the other end, there is unregulated reperfusion with hemorrhagic transformation. This process occurs due to activation of inflammatory mediators along with an impaired autoregulatory of the brain vasculature. These factors can predispose blood extravasation when the ischemic brain tissue is ultimately reperfused<sup>10,22,25)</sup>.

Decompressive craniectomy (DC) to treat massive brain edema caused by major infarction patients is regarded as effective treatment option for patient survival<sup>13,31)</sup>. However, in this study, we did not evaluate the clinical significance of DC treatment because surgical intervention was entirely decided by the neurosurgeon who was in charge of each patient, various surgical indication and surgical method were applied.

In order to improve clinical outcomes and lessen the complications in acute stroke patients, identifying the ischemic core and the penumbra area from the brain image is the most important for patient selection. From this study, MRI based mismatching analysis showed similar clinical outcomes as CTP base mismatching patients selection method, Author would like to emphasize that for image analysis P/D-mismatching from MRI and CTP was similar but for improve the clinical outcome after treatment, proper patient selection and gentle manage the IA-Tx devices is important.

### Limitations

Several limitations in our study, this study was not randomized control study. Both image study was not taken at same patients. And according to neurosurgeon, IA-Tx technique and decision make is somewhat different. Except for the P/D-mismatching analysis image technique, other treatments applied as same as possible.

### CONCLUSION

In order to improve clinical outcomes and lessen the complications in acute stroke patients, identifying the ischemic core and the penumbra area, P/D-mismatching, is the most important for patient selection. From this study, the CT based P/D-mismatching analysis showed same clinical outcomes as the MR base P/D-mismatching analysis, and gently management of the IA-Tx devices is important, avoid to make a complications.

## NOTES

### Ethics statement

This retrospective, observational study was approved by our Institutional Ethics Committee. The treatment protocol was approved by our Institutional Review Board (approval number: PC17RESI0028). All patients or their representatives provided written consent for treatment.

### Author contributions

Writing - review & editing: All authors.

### Conflict of interest

There is no conflict of interest to disclose.

### Funding

None.

### Data availability

None.

### Acknowledgements

None.

## REFERENCES

1. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015;372:1009–1018.
2. Al-Mufti F, Amuluru K, Roth W, Nuoman R, El-Ghanem M, Meyers PM. Cerebral Ischemic Reperfusion Injury Following Recanalization of Large Vessel Occlusions. *Neurosurgery* 2018; 82:781–789.
3. Hacke W, Kaste M, Bluhmki E, Brozman M, Dávalos A, Guidetti D, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008;359:1317–1329.
4. Disorders NIO, Group Sr-PSS. Tissue plasminogen activator for acute ischemic stroke. *New England Journal of Medicine* 1995;333:1581–1588.
5. Bathla G, Ortega-Gutierrez S, Klotz E, Juergens M, Zevallos CB, Ansari S, et al. Comparing the outcomes of two independent computed tomography perfusion softwares and their impact on therapeutic decisions in acute ischemic stroke. *J Neurointerv Surg* 2020;12:1028–1032.
6. Hussein HM, Georgiadis AL, Vazquez G, Miley JT, Memon

- MZ, Mohammad YM, et al. Occurrence and predictors of futile recanalization following endovascular treatment among patients with acute ischemic stroke: a multicenter study. *AJNR Am J Neuroradiol* 2010;31:454–458.
7. Lansberg MG, Straka M, Kemp S, Mlynash M, Wechsler LR, Jovin TG, et al. MRI profile and response to endovascular reperfusion after stroke (DEFUSE 2): a prospective cohort study. *Lancet Neurol* 2012;11:860–867.
  8. Investigators IS. Combined intravenous and intra-arterial recanalization for acute ischemic stroke: the Interventional Management of Stroke Study. *Stroke* 2004;35:904–911.
  9. Davis S, Donnan GA. Time is Penumbra: imaging, selection and outcome. The Johann jacob wepfer award 2014. *Cerebrovasc Dis* 2014;38:59–72.
  10. Astrup J, Siesjo BK, Symon L. Thresholds in cerebral ischemia: the ischemic penumbra. *Stroke* 1981;12:723–725.
  11. Furlan A, Higashida R, Wechsler L, Gent M, Rowley H, Kase C, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. *Prolyse in Acute Cerebral Thromboembolism*. *Jama* 1999;282:2003–2011.
  12. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018; 378:11–21.
  13. Labeyrie MA, Turc G, Hess A, Hervo P, Mas JL, Meder JF, et al. Diffusion lesion reversal after thrombolysis: a MR correlate of early neurological improvement. *Stroke* 2012;43:2986–2991.
  14. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Ling-sma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015;372:11–20.
  15. Pan J, Konstas AA, Bateman B, Ortolano GA, Pile-Spellman J. Reperfusion injury following cerebral ischemia: pathophysiology, MR imaging, and potential therapies. *Neuroradiology* 2007;49:93–102.
  16. Albers GW, Goyal M, Jahan R, Bonafe A, Diener HC, Levy EI, et al. Ischemic core and hypoperfusion volumes predict infarct size in SWIFT PRIME. *Ann Neurol* 2016;79:76–89.
  17. Lees KR, Bluhmki E, von Kummer R, Brott TG, Toni D, Grotta JC, et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet* 2010;375: 1695–1703.
  18. Campbell BC, Christensen S, Levi CR, Desmond PM, Donnan GA, Davis SM, et al. Comparison of computed tomography perfusion and magnetic resonance imaging perfusion-diffusion mismatch in ischemic stroke. *Stroke* 2012;43:2648–2653.
  19. Kidwell CS, Jahan R, Gornbein J, Alger JR, Nenov V, Ajani Z, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. *N Engl J Med* 2013;368:914–923.
  20. Schaefer PW, Barak ER, Kamalian S, Gharai LR, Schwamm L, Gonzalez RG, et al. Quantitative assessment of core/penumbra mismatch in acute stroke: CT and MR perfusion imaging are strongly correlated when sufficient brain volume is imaged. *Stroke* 2008;39:2986–2992.
  21. Investigators IIT. The Interventional Management of Stroke (IMS) II Study. *Stroke* 2007;38:2127–2135.
  22. Yoo DS, Won YD, Huh PW, Shin HE, Kim KT, Kang SG, et al. Therapeutic results of intra-arterial thrombolysis after full-dose intravenous tissue plasminogen activator administration. *AJNR Am J Neuroradiol* 2010;31:1536–1540.
  23. Yoon W, Seo JJ, Kim JK, Cho KH, Park JG, Kang HK. Contrast enhancement and contrast extravasation on computed tomography after intra-arterial thrombolysis in patients with acute ischemic stroke. *Stroke* 2004;35:876–881.
  24. Olivot JM, Albuher JF, Guenego A, Thalamas C, Mlynash M, Rousseau V, et al. Mismatch profile influences outcome after mechanical thrombectomy. *Stroke* 2021;52:232–240.
  25. Hofmeijer J, Kappelle LJ, Algra A, Amelink GJ, van Gijn J, van der Worp HB. Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAM-LET]): a multicentre, open, randomised trial. *Lancet Neurol* 2009;8:326–333.
  26. Rosso C, Samson Y. The ischemic penumbra: the location rather than the volume of recovery determines outcome. *Curr Opin Neurol* 2014;27:35–41.
  27. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med* 2015;372:2285–2295.
  28. Cereda CW, Christensen S, Campbell BC, Mishra NK, Mlynash M, Levi C, Straka M, et al. A benchmarking tool to evaluate computer tomography perfusion infarct core predictions against a DWI standard. *J Cereb Blood Flow Metab* 2016; 36:1780–1789.
  29. Khoury N, Dargazanli C, Guenego A, Zuber K, Ekmen A, Charbonnier G, et al. Visual assessment of diffusion weighted imaging infarct volume lacks accuracy and reliability. *J Neurointerv Surg* 2019;11:947–954.
  30. Mazighi M, Serfaty JM, Labreuche J, Laissy JP, Meseguer E, Lavallée PC, Cabrejo L, et al. Comparison of intravenous alteplase with a combined intravenous-endovascular approach in pa-

- tients with stroke and confirmed arterial occlusion (RECANALISE study): a prospective cohort study. *Lancet Neurol* 2009;8:802–809.
31. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med* 2018;378:708–718.



## Virtual Neurosurgery Education Conferences on Social Medi: A Perspective

Minaam Farooq<sup>1</sup>, Noor Atiq<sup>2</sup>, Amr Badary<sup>3</sup>, Bipin Chaurasia<sup>4</sup>

<sup>1</sup>Department of Neurological Surgery, King Edward Medical University, Mayo Hospital Lahore, Pakistan

<sup>2</sup>Department of Neurosurgery, King Edward Medical University, Mayo Hospital Lahore, Pakistan

<sup>3</sup>Department of Neurosurgery, Dessau Clinical Center, Dessau-Rosslau, Brandenburg University, Germany

<sup>4</sup>Department of Neurosurgery, Neurosurgery clinic, Jaypoly Clinic, Birgunj, Nepal

Received: December 15, 2023

Accepted: January 27, 2024

### Corresponding Author:

Bipin Chaurasia, MS

Department of Neurosurgery,  
Neurosurgery Clinic, Jaypoly  
Clinic, Madhesh Pradesh, Birgunj  
44300, Nepal

Tel: +9779845454636

E-mail: trozexa@gmail.com

Over the recent years, the field of Neurosurgery has witnessed a major transformation in the dissemination of knowledge and professional development using virtual webinars. This change has primarily been accelerated after the COVID-19 pandemic and the associated 'social distancing'<sup>1)</sup>. As the health-care system was faced with unprecedented changes, the utilization of online platforms for neurosurgical education emerged pivotal in bridging the gap created by restricted in person interactions<sup>2)</sup>. Groups such as the Society for Neuro-Oncology (SNO), World Federation of Neurosurgical Societies (WFNS), Neurosurgery Cocktail, American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) committees have transformed their annual meetings and conferences into an online format<sup>3)</sup>. Neurotrauma webinars have been held with societies in Latin America (La Federación Latinoamericana de Sociedades de Neurocirugía [FLANC]), Asia (Asian Australasian Society of Neurological Surgeons [AASNS]), Africa (Continental Association of African Neurological Surgeons [CAANS]), and the Asian Congress of Neurological Surgeons (ACNS)<sup>4)</sup>. All the above mentioned associations as well as European Association of Neurosurgical Societies (EANS) are effectively taking forward this dynamic approach of virtual education, not only for the neurosurgery residents and physicians but for the medical students in their academic years as well, aiding them in making better career choices<sup>5)</sup>.

Hence, this practice is on the rise and rightly so. These advancements in online neurosurgical education have dismantled the geographical barriers allowing neurosurgeons from all over the world direct access to knowledge and expertise. This makes the whole platform extremely inclusive<sup>6)</sup>. This inclusivity is further complemented by the live Q/A sessions, fostering the idea of better engagement and immediate feedback. Financially, it provides a cost effective alternative to the in person conferences by reducing expenses associated with travel and accommodation, something that significantly benefits doctors in low income areas and underdeveloped countries<sup>6)</sup>. Another great benefit in learning that virtual webinars provide is in the opportunity to review the recorded lectures at a later time. This reinforces the learning and enables better grasp on the knowledge at the ease of the learner. In a research conducted with neurosurgery residents, it showed that they demonstrated a keen interest and increasing appreciation for this medium of learning and as this new generation is the developer of the future curriculum, it speaks significantly of how the approach to medical education is rapidly becoming digitalized<sup>7)</sup>.

However, at the same time where online webinars provide easy accessibility to medical information they do reduce the avenues of professional networking. The sheer importance of face to face interaction for personal learning and professional skill building is something that is undeniable. Professional code of conduct and interaction is rarely something that can be efficiently learnt while being in the confines of one's room, alone. Online webinars thus, can hamper the culture of team building that eventually might have an impact on the overall work place dynamic in the longer run<sup>8)</sup>. Moreover, with the passage of time, various studies and interviews with the neurosurgery residents and physicians have demonstrated that despite advances in technology and virtual learning, it still is unable to mimic the in depth experience of learning and attainment of practical skills that the hands-on, in-person learning has to offer. This does mean that virtual learning platform cannot be relied upon as a sole means of education and that it still significantly requires improvements by the use of artificial intelligence technologies and new software facilities, something that is underway<sup>9)</sup>. However, the technical difficulties related to the availability of stable internet connectivity and high quality 3D simulators to perform and practice procedures on continues to be an affordability issue for a major chunk of the under privileged nations. This creates a discrepancy in the quality of learning and medical practice demonstrated by the neurosurgical community as a whole<sup>2,8)</sup>. In addition to that, viewer attention span and concentration during online seminars has also been noticed to have an impact on the outcome. Studies demonstrate that the maximum attention span of an adult is no more than 20 minutes and so a need to make the webinars more viewer- friendly exists<sup>10)</sup>. This can be done by making webinars more interactive allowing active engagement of its viewers, reducing the duration of the webinar, and allowing break rooms something that EANS and AANS virtual webinars currently do incorporate. With this growing advancement in the technological field it is unfair to ignore the difficulty that the older generation of neurosurgeons and attending find in getting comfortable with this up rise of virtual education and demonstrated here<sup>7)</sup> and so due attention should be paid to this aspect as well.

Looking ahead, balancing the convenience of online webinars with irreplaceable value of hands on experiences and in person interactions remains crucial for the holistic development of neurosurgery as a field. The importance of in person learning for skill development cannot be denied and thus online education avenues can only be used as adjuncts to the traditional ways. Furthermore, improving the existing quality of virtual webinars is paramount as well. Webinar based neurosurgery can evolve by better incorporating specialized, hands-on virtual training modules, enabling surgeons to practice procedures in a simulated environment. Integrat-

ing advanced technologies like 3D modeling, augmented reality, or surgical simulations within these webinars can and will enhance the understanding and skill development<sup>8)</sup>. Online medical education in neurosurgery should continue to be a collaborative platform where global neurosurgeons share experiences and innovative techniques to enrich the learning experience and advance the field collectively. With the world becoming so rapidly digitalized, it is only appropriate that medical field makes use of it in the most diligent way possible. However, avenues to make this virtual platform best suited to the demands of the field of neurosurgery is going to be an uphill continuous effort.

## NOTES

### Author contributions

Conceptualization: MF, NA, BC. Data curation: MF. Formal analysis: MF, NA, AB. Project administration: BC, Visualization: NA, AB, BC. Writing - original draft: MF. Writing - review & editing: BC.

### Conflict of interest

There is no conflict of interest to disclose.

### Funding

None.

### Data availability

None.

### Acknowledgements

None.

## REFERENCES

1. Sharif S, Hafiz M. Virtual world spine 2020: the first online conference during the COVID pandemic. *World Neurosurg* 2021;150:256–258.
2. El-Ghandour NM, Ezzat AA, Zaazoue MA, Gonzalez-Lopez P, Jhavar BS, Soliman MA. Virtual learning during the COVID-19 pandemic: a turning point in neurosurgical education. *Neurosurg Focus* 2020;49:E18.
3. Patel NV, D'Amico R, Ivan ME, Komotar RJ, Sheehan JP. Spotlight on Education: Neuro-oncology Webinars - Tumor News [Internet]. AANS/CNS Section on Tumors Newsletter. Available from: <https://newsletters.aans.org/tumor/tumor-news-fall-winter-2020/spotlight-on-education-neuro-oncology-webinars/>.

4. WFNS. WFNS 100 Webinar Series\_br\_#74 Neurotraumatology. WFNS [Internet]. 2023 [2023 Jun 16]. Available from: <https://wfns.org/newsletter/361>.
5. Shlobin NA, Radwanski RE, Kortz MW, Rasouli JJ, Gibbs WN, Than KD, et al. Utility of virtual spine neurosurgery education for medical students. *World Neurosurg* 2022;163:179–186.
6. Conti A, Magnani M, Zoli M, Kockro RA, Tuleasca C, Peschillo S, et al. Social media for global neurosurgery. Benefits and limitations of a groundbreaking approach to communication and education. *Brain & spine* 2023;3:101728.
7. Al-Ahmari AN, Ajlan AM, Bajunaid K, Alotaibi NM, Al-Habib H, Sabbagh AJ, et al. Perception of neurosurgery residents and attendings on online webinars during COVID-19 pandemic and implications on future education. *World Neurosurg* 2021;146:e811–e816.
8. Bongetta D, Zoia C. Editorial: training and education in neurosurgery: challenges and strategies for the next ten years. *Front Surg* 2022;9:984208.
9. Odayappan A, Venkatesh R, Tammineni R, Nachiappan S, Iswarya M. Perspectives of physicians regarding the role of webinars on medical education during the COVID-19 pandemic. *Indian J Ophthalmol* 2021;69:1251–1256.
10. Bradbury NA. Attention span during lectures: 8 seconds, 10 minutes, or more? *Adv Physiol Educ* 2016;40:509–513.

### General Information

1. Journal of Neurointensive Care (JNIC) is the official journal of the Korean Neurointensive Care Society and published biannually ((the last day of April and October). This Journal publishes important papers covering the whole field of neurosurgical intensive care unit, including studies in neuroscience, neurology, and molecular biology. Studies on rare cases and technical notes of special instruments or equipment that might be useful to the field of neurosurgical intensive care are also acceptable. Drawing upon the expertise of an interdisciplinary team of physicians from neurosurgery, neurology, anesthesiology, critical care, and nursing backgrounds, (JNIC) covers all aspects neurosurgical intensivists need to be aware of in order to provide optimal patient care.
2. It should be assured that authors must not simultaneously submit an identical or similar paper for publication elsewhere. Multiple publication is acceptable only in the case of meeting the criteria of Uniform Requirements for Manuscripts Submitted to Biomedical Journals (Ann Intern Med 108: 258-265, 1988). Manuscripts must be prepared in accordance with Uniform requirements for Manuscripts submitted to Biomedical Journal developed by International Committee of Medical Journal Editors (February 2006).
3. All manuscripts must be written in English. Authors should minimize the use of English abbreviations. Spell out all abbreviations at first occurrence, and then introduce them by placing the abbreviation in parenthesis after the term being abbreviated. Abbreviation should be avoided as possible as one can. When it is used, full expression of the abbreviation following abbreviated word in parentheses should be given at first use. All units should be given in metric system (The International System of Units: SI units).

### Submission of Manuscript

1. Authors are requested to submit their papers electronically by using online manuscript submission system(<http://submit.e-jnic.org>). This site will guide authors stepwise through the submission process.
2. Upon submission of a manuscript, authors should upload author checklist and copyright transfer agreement form

(<http://e-jnic.org/authors/authors.php>).

3. The list of the authors in the manuscript should include only those who were directly involved in the process of the work. Authors can refer to the guideline by Harvard University in 1999 to find details on authorship(<http://www.hms.harvard.edu/integrity/authorship.html>).
4. The editorial board will make a decision on the approval for publication of the submitted manuscripts, and can request any further corrections, revisions, and deletions to the article text if necessary.
5. The price for all work requiring review, publishing, and re-printing of the paper will be determined by the editorial board.

### Manuscript Preparation

All manuscripts should be written in English using in 11 points Arial font and double-spaced.

#### 1. Publication type

JNIC publishes editorials, reviews, original articles including clinical and laboratory research, case reports, letters to the editor and etc. Please review the below article type specifications including the required article lengths, illustrations, table limits and reference counts. The word count excludes the title page, abstract, tables, acknowledgements, contributions and references. Manuscripts should be as succinct as possible. Any article longer than these limits should be discussed with the editor.

#### a) Editorials

Editorials are invited perspectives dealing with very active fields of research, hot interest, fresh insights, and debates.

**Word count:** up to 1,000 words

**Tables and figures:** at editorial discretion

**References:** up to 10, ideally 5

#### b) Review articles

The authors and topics for review articles will be selected by the editorial board and review articles should also undergo the review process. Manuscripts include titlepage, unstructured

abstract and keyword, main text (introduction, manuscript body, conclusion), conflict of interest, acknowledgements (if necessary), references, tables, figure legends, and figures.

**Abstract:** 200 words

**Word count:** up to 3,000 words

**Tables and figures:** up to 7

**References:** 40

### c) Original articles

Original articles should contain the results of clinical or basic research and should be sufficiently well documented to be acceptable to critical readers. The manuscript for an original article should be organized in the following sequence: title page, structured abstract and keywords, main text (introduction, methods, results, discussion, conclusion), conflict of interest, acknowledgements (if necessary), references, tables, figure legends, figures, and supplementary data.

**Abstract:** Structured, 250 words

**Word count:** up to 3,500 words

**Tables and figures:** up to 7

**References:** 30

### d) Case reports

Case reports will be published only in exceptional circumstances, when they illustrate a rare occurrence of clinical importance. These manuscripts should be organized in the following sequence: title page, unstructured abstract and keywords, introduction, case report(s), discussion, conclusion, acknowledgements, references, tables, figure legends, and figures.

**Abstract:** 150 words

**Word count:** 1,500 words

**Tables and figures:** up to 5

**References:** 10

### e) Letters to the editor

Authors can submit a sound critic or opinion for the specific article published in the journal, topic of general interest regarding neurosurgical intensive care, personal view on a specific scientific issue, departmental announcements or changes, or other information of the clinical fields.

**Word count:** 1,000 words

**Tables and figures:** up to 2

**References:** 10

### f) Special article

Special articles are devoted to providing updated reports by specialists in various fields or significant issues (e.g., history of the field) for the members of the society. The authors and topics of special drafts will be assigned and specially requested by the editorial board. The authors' views in special drafts will be respected as much as possible.

### g) Other Publication Types

Other publication types may be accepted. The recommended format should be discussed with the Editorial Board.

## 2. Manuscript format

Authors should refer to "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (<http://www.icmje.org/about-icmje/faqs/icmje-recommendations/>). The article should be organized in the order of title, abstract (Objective, Methods, Results, and Conclusion sections should be included in laboratory investigation or clinical article but are not necessary in other types of studies), key words, introduction, materials and methods, results, discussion, conclusions, references, tables, and figures or illustrations. In case reports, materials and methods and results can be replaced with cases.

### 1) Title page

The title page should be composed of external and internal title pages.

- a) The external title page should contain the article title, and full names of all authors with their institutional affiliations in English. The type of manuscript (Original Article, Case Report or Case series, Technical report, Letter to editor, etc.) should be also addressed. When the work includes multiple authors with different affiliations, the institution where the research was mainly conducted should be spelled out first, then be followed by foot notes in superscript Arabic numerals beside the authors' names to describe their affiliation in a consecutive order of the numbers. Then, mark the running head as not to exceed 50 characters in English. The external title page should also contain the address, TEL. and FAX. numbers, and e-mail address of the corresponding author at the bottom of the page, as well as information on the previous presentation of the manuscript in conferences and funding resources, if necessary.
- b) The internal title page should only contain the article title in English. The internal title page must not contain any information on the names and affiliations of the authors.

### 2) Abstract and Keywords

All manuscripts must contain an abstract. A list of Key Words,

with a maximum of six items, should be included at the end of the abstract. The selection of Key Words should be based on Medical Subject Heading (MeSH) of Index Medicus and the Web site (<http://www.nlm.nih.gov/mesh/MBrowser.html>). The abstract should include brief descriptions on the objective, methods, results, and conclusion as well as a detailed description of the data. An abstract containing 250 words or less is required for original articles, 200 words for review articles and 150 words for case. Abstracts for Laboratory Investigation and Clinical Article should begin with the statement of the paper's purpose and end with conclusions. Abstracts for other types of papers should begin with a brief and clear statement of the paper's purpose and be followed by appropriate details that support the conclusions of the paper.

### **3) Introduction**

The introduction should address the purpose of the article concisely and include background reports mainly relevant to the purpose of the paper (detailed review of the literature should be addressed in the discussion section).

### **4) Materials and Methods**

Materials and Methods section should include sufficient details of the design, objects, and methods of the article in order, as well as the data analysis strategies and control of bias in the study. Enough details need to be addressed in the methodology section of an experimental study so that it can be further replicated by others. When reporting experiments with human subjects, the authors should indicate whether they received an approval from the Institutional Review Board for the study. When reporting experiments with animal subjects, the authors should indicate whether the handling of the animals was supervised by the research board of the affiliated institution or a similar one. Photographs disclosing patients must be accompanied by a signed release form from the patient or family permitting publication. We endorse the principles embodied in the 'Declaration of Helsinki' and expect that all investigations involving human materials have been performed in accordance with these principles. For animal experiment, 'the Guiding Principles in the Care and Use of Animals' approved by the American Physiological Society must be observed. Explanation of the experimental methods should be concise and sufficient for repetition by other qualified investigators. Procedures that have been published previously should not be described in detail. However, new or significant modifications of previously published procedures need full descriptions. The sources of special chemicals or preparations should be given along with their location (name of company, city and state, and country).

Method of statistical analyses and criteria of significance level should be described. In Case Reports, case history or case description replace the Materials and Methods section as well as Results section.

Please inform us the approved number of IRB when you submit the manuscript.

### **5) Results**

The authors should describe logically their results of observations and analyses performed using methodology given in the previous section and provide actual data. For biometric measurements in which considerable amount of stochastic variation exists a statistical treatment should be used in principle. The result section should include solely the findings of the current study, and not refer to previous reports. While an effort should be made to avoid overlapping descriptions by Tables and by main text, important trends and points in the Table should be described in the text. Experimental results should be described using Arabic numbers and the SI unit system.

### **6) Discussion**

Discussions about the findings of the research and interpretations in relation to other studies are made. It is necessary to emphasize the new and critical findings of the study, not to repeat the results of the study presented in the previous sections. The meaning and limitation of observed facts should be described, and the conclusion should be related to the objective of the study only when it is supported by the results of the research. It is encouraged for the authors to use subheadings in the discussion section so that the readers can follow the logical flow of the authors' thought.

### **7) Conclusion**

The conclusion section should include a concise statement of the major findings of the study in accordance with the study purpose.

### **8) References**

- a) Only references cited in text must appear in the reference list and marked in the form of superscript at the end of the sentences they were used in text (example: reference<sup>11,15,18</sup>).
- b) All references should be alphabetized by the first author's last name.
- c) When a work has six or less authors, cite the names of all authors. When a work has over six authors, cite the first six authors' name followed by "et al." Abbreviations for journal titles should be congruent with the style of Index Medicus. A journal title with one word does not need to be written out in abbreviation. The

styles of references are as follows:

### Journal

1. Dávalos A, Pereira VM, Chapot R, BonaféA, Andersson T, Gralla J, et al. Retrospective multicenter study of solitaire FR for revascularization in the treatment of acute ischemic stroke. *Stroke* 2012;43:2699–2705.

### Website

1. World Health Organization, The International Spinal Cord Society. International perspectives on spinal cord injury. Geneva, CH: World Health Organization, 2013([http://apps.who.int/iris/bitstream/10665/94192/1/WHO\\_NMH\\_VIP\\_13.03\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/94192/1/WHO_NMH_VIP_13.03_eng.pdf?ua=1)) [Accessed October 1, 2018]

### Book

1. Conover WJ: Practical Nonparametric Statistics, ed 2. New York: Jon Wiley & Sons; 1971. p. 216-218.

### Article in a Book

1. Ojemann RG: Surgical management of bacterial intracranial aneurysms in Schmideck HH, Sweet HH (eds): Operative Neurosurgical Techniques. Indications, Methods and Results, ed 2. Orlando: Grune& Stratton; 1988. p. 997-1001

## 9) Tables, figures, and illustrations

Tables and figure legends should be included below the references pages at the end of the paper, but figures should be submitted separately from the text of paper. Table should be simple and should not duplicate information in figures. Title all tables and number them with Arabic numerals in the order of their citation. Type each table on a separate sheet. Describe all abbreviations. Each column should have an appropriate heading, and if numerical measurements are given, the unit should be added to column heading. The significance of results should be indicated by appropriate statistical analysis. Table footnotes should be indicated with superscript markings. When remarks are used to explain items of the table, the markers should be given in the order of \*, †, ‡, §, ||.

Each figure should be submitted as a separate file, with the

figure number as the file name (i.e. Fig1.jpg). When a figure is composed of more than 2 parts, authors should combine the figure in the correct orientation. Separate files without embedded labels should be submitted only if the Editorial board requests them after the peer review. Authors should submit figures in black and white if they want them to be printed in black and white. Authors are responsible for any additional costs of producing color figures.

The files should have following resolutions for printing: line art at 300 dpi, combination half-tones at 300 dpi, and half-tones (gray scale or color without type or lettering) at 300 dpi. If the quality of the photographs is considered as inappropriate for printing, re-submission of them can be requested by the journal. Tables, graphs, figures, and photographs should be used only when necessary.

## Publication

Once a manuscript is accepted for publication by the journal, it will be sent to the press, and page proofs will be sent to authors. Authors must respond to the page proofs as soon as possible after making necessary corrections of misspellings, and the location of the photographs, figures or tables. Authors can make corrections for only typing errors and are not allowed to make any author alteration or substantive changes of the text. Proofs must be returned to the press within 72 hours of receipt. No response from the authors within this time frame will lead the publication of the proof read without corrections, and the editorial board is not responsible for any mistakes or errors occurring in this process.

## Post-Publication Discussion and Corrections

The post-publication discussion is available through letter to the editor. If any readers have a concern on any articles published, they can submit letter to the editor on the articles. If there founds any errors or mistakes in the article, it can be corrected through errata, corrigenda, or retraction.

Title of article: \_\_\_\_\_

Author(s): \_\_\_\_\_

Author(s) should check the following items under the heading of 'Authors'. The spaces under the heading of 'Editorial Staff' are reserved for editorial office. Please leave no marking at the spaces under the heading of 'Editorial Staff'.

### 1. Mandatory components of a manuscript

- 1) Manuscript layouts  Yes /  No
  - 2) Manuscript should be prepared in following sequences;
    - a) Original Article: title page, inner title page, abstract and keywords, introduction, materials and methods, results, discussion, conclusion, conflicts of interest\*, acknowledgment, references, tables, figure legends, figures and supplementary data.  Yes /  No
    - b) Case Report: title page, inner title page, abstract and keywords, introduction, case report, discussion, conclusion, references, tables, figure legends and figures.  Yes /  No
    - c) Review Article: title page, inner title page, abstract and key words, introduction, manuscript body, conclusion, conflict of interest\*, acknowledgment, references, tables, figure legends and figures.  Yes /  No
- \*If applicable

### 2. Word count

- 1) The word count of abstract and manuscript are within limits for the publication type.  Yes /  No
- 2) Please indicate the total word number at the title page.  Yes /  No
- 3) All pages are numbered in sequence, starting with the title page.  Yes /  No

### 3. Title page

The title page must contain all of the followings; clear title, name and affiliation of all authors, information of the corresponding author (address, telephone number, fax number, and e-mail address), type of article and running head.  Yes /  No

### 4. Inner title page

Only title of the manuscript is listed. Any information on the authors and corresponding author is not shown on the inner title page  Yes /  No

### 5. Abstract

- 1) Abstract should have four parts, which are objective, methods, results, and conclusion. Please indicate the word number after Key words.  Yes /  No
- 2) Recommended words from Medical Subject Heading Terms database at <http://www.ncbi.nlm.nih.gov/mesh/MBrowser.html> are used for Key word and the words are written within a maximum of six.  Yes /  No

### 6. Text

- 1) Text is written in 11 points Arial fonts with double line spacing and 3 cm as bottom and left and right margins on A4 paper  Yes /  No
- 2) Every word except name of a place, a personal name, and a proper noun is written in lower case. Also, some words such as names of virus, Latin and p values are written in italics. Comma as thousand separators must be placed for indicating numbers.  Yes /  No



**7. Figures and tables**

Cite in numerical order as they are first mentioned in the text

**Yes** /  **No**

**8. References**

1) References are described followed by the rules of the Journal of JNIC

**Yes** /  **No**

2) It is recommended that references may contain at least one of the articles of JNIC. If it may not, please specify the reason in the cover letter.

**Yes** /  **No**

**9. Tables**

1) Table style should follow the conventional rules as suggested in Instructions to Authors.

**Yes** /  **No**

2) Tables should be self-explanatory, and the data must not be duplicated in the text or figures

**Yes** /  **No**

**10. Figures and Figure legends**

Each figure should be submitted as a separate file, with the figure number as the file name (i.e. Fig1.jpg). When a figure is composed of more than 2 parts, authors should combine the figure in the correct orientation. Separate files without embedded labels should be submitted only if the Editorial board requests them after the peer review. Authors should submit figures in black and white if they want them to be printed in black and white. Authors are responsible for any additional costs of producing color figures.

**Yes** /  **No**

**11. Figure resolution**

Author must guarantee the quality of figures. It should be noted that the manuscript could be rejected if print-suitable high-quality figures are not provided at the initial phase of submission.

**Yes** /  **No**

**12. Figure legend**

Figure legend should be self-explanatory. Abbreviations should not be used, and the present tense must be used for the description. Appropriate description of dyeing method and magnification for histological figure should be provided

**Yes** /  **No**

**13. Submission**

All authors should sign on the transfer of copyright and agreement and corresponding author should indicate that he (she) takes full responsibility of authorship from all authors.

**Yes** /  **No**

**Date:** \_\_\_\_\_

Editorial office use only

suitable for review process     a qualified consent for submission acceptance     needs author's correction

**Date:** \_\_\_\_\_

The author(s) submit my/our manuscript with the following title

---

---

in consideration of the Editorial Board of the Journal of Neurointensive Care reviewing, editing and publishing. This manuscript contains

\_\_\_\_\_ page(s), \_\_\_\_\_ Figure(s), \_\_\_\_\_ Picture(s), \_\_\_\_\_ Table(s).

I/we hereby transfer, assign and otherwise convey to the Korean Neurointensive Care Society upon acceptance of the manuscript for publication by the Journal of Neurointensive Care all copyright. I/we have all rights except copyright. I/we can use part or all of the contents of the manuscript under written agreement of the Korean Neurointensive Care Society. In case that I/we use materials from the manuscript I/we will clarify the reference.

I/we certify that the contents of the manuscript, in all or in part, has not been published and is not being considered for publication elsewhere, unless otherwise specified herein.

I certify that I have made a substantial contribution to the medical/scientific/intellectual content of the manuscript and on that basis agree to be named as an author.

I approve the manuscript for publication and will take public responsibility for its content.

Each of the undersigned is an author of the manuscript and all authors are named on this document.

**Author's name**

**Author's signature**

**Date**

_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____