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Review Article

Unruptured Intracranial Aneurysms: To Treat or Observe? Risk-benefit Analysis in Surgical versus Conservative Management

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Abstract

Aneurysmal subarachnoid haemorrhage is catastrophic neurological event with the primary neuroparenchymal insult and raised intracranial pressure as well rebleeding, vasospasm, cerebral ischaemia, hydrocephalus and other complications leading to high mortality and morbidity. The overall incidence of unruptured intracranial aneurysm (IA) is estimated to be about 3%. The risk of rupture, despite various predictive scales, cannot be accurately defined. Moreover, almost 5% of patients undergoing preventive intervention face severe morbidity and even death. In such a delicate situation, the decision to treat must be individualised and needs to achieve a fine balance between the estimated rupture risk and the procedural complication risk, specifically accounting for long term functional disabilities and loss of quality of life related to such an adverse event. In this review, we discuss the challenges in the decision-making process of management of unruptured IA.

Keywords: *Cerebral aneurysm, endovascular treatment, microsurgery, observation, prognosis, unruptured*

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Introduction

The rate of incidental diagnosis of unruptured intracranial aneurysm (UIA) is increasing globally with the easy availability of imaging facilities. Since 2005, the IA detection rate has increased from 1.7% to 3.4%. Between 2% and 4% of the population may potentially be diagnosed with an UIA and between 3 and 15 of 100,000 persons per year suffer a subarachnoid haemorrhage (SAH).[1]

Their management constitutes a great challenge for cerebrovascular specialists. The average 5-year risk of rupture is estimated between 0.4% and 17.8%, based on various features and factors. The overall rupture rate is low with only 1 rupture per 200–400 patients per year.[2] However, mortality and morbidity in aneurysmal SAH is substantial; 12% die immediately, more than 30% die within 1 month, 25%–50% die within 6 months, and 30% of survivors remain dependent.[3] Most intracranial aneurysms (IAs) do not bleed, and the best treatment approach is debatable. Untreated UIAs can also induce psychological stress, leading to anxiety, depression and impaired quality of life.[4] On the other hand, preventive treatment exposes patients to an overall risk of 1% mortality and 5% morbidity (<0.1% and <3%, respectively, for small lesions).[5] The thin line of balance between risks and benefits of different management options needs to be individualised.

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Factors Predicting Rupture

Patient factors

- Patient's age below 50 years
- Female sex
- Hypertension
- Smoking
- First-degree relatives with IAs or previous SAH
- Connective tissue disorders such as Marfan syndrome, polycystic kidney disease.[6,7]

Aneurysm factors

- IA dome size ≥5 mm
- Irregular aneurysm contour – three times risk
- Daughter sac (irregular outpouching less than half the size of the parent aneurysm) – 5.5 times risk

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- Multilobulated IAs – 7.3 times risk
- Multiple aneurysms
- ACommA and PcommA complex, posterior circulation
- Aneurysms associated with arteriovenous malformations. (especially feeding artery and intranidal aneurysms)
- Perpendicular height and size ratio (maximum diameter to parent vessel diameter) and the dome-neck aspect ratio (lower ratio, lower risk)
- Growth of aneurysm on follow-up (defined as size increase ≥1 mm in any direction) – is a strong factor associated with an increased risk of rupture, with a 1-year risk ranging from 2% to 10% according to the size, site, and shape of the aneurysm[8,9] [Figure 1].

Growth of Intracranial Aneurysms

Cerebral aneurysm growth can occur in two ways: an increase in the size of an existing aneurysm (*in situ*), or formation of a de novo aneurysm at a different location. Like the risk of development and rupture, the growth of IAs has been associated with female sex, smoking, uncontrolled blood pressure, excessive alcohol consumption and multiplicity of aneurysms. The growth trajectory is often non-linear. For growing aneurysm, the reported annualised rupture rate is as high as 18.5% and is a strong indication for intervention.[10]

Assessment of Risk of Bleeding of Unruptured Intracranial Aneurysm

The International Study of Unruptured IAs (ISUIA) study is the largest observational study on the natural history of UIAs, providing the foundation to the current guidelines for the management. It is estimated that the haemorrhage risk for <10 mm size UIA was 0.05% while with previous SAH from another aneurysm was 0.5%–1%. The haemorrhage risk for ≥25 mm UIA was 6%. Location and age were the independent predictors. Treatment-related morbidity and mortality ranged from 13% to 17%, thus exceeding the natural risk for those <10 mm with no previous bleed.[11]

The size dependent correlation to bleed was highlighted in the Unruptured Cerebral Aneurysm Study (UCAS) study in the Japanese cohort of 6697 aneurysms. The annual rate of rupture on follow-up was 0.95%. With aneurysms that were 3–4 mm in size as the reference, the hazard ratios for size categories were as follows: 5–6 mm, 1.13 (95% confidence interval [CI], 0.58–2.22); 7–9 mm, 3.35 (95% CI, 1.87–6.00); 10–24 mm, 9.09 (95% CI, 5.25–15.74); and 25 mm or larger, 76.26 (95% CI, 32.76–177.54). AcommA and PcommA aneurysms and those with daughter sacs were more likely to rupture.[12]

The Small Unruptured IA Verification study (SUAVe study) prospectively followed aneurysms <5 mm in size for a mean of 41.0 months and noted a quite low annual

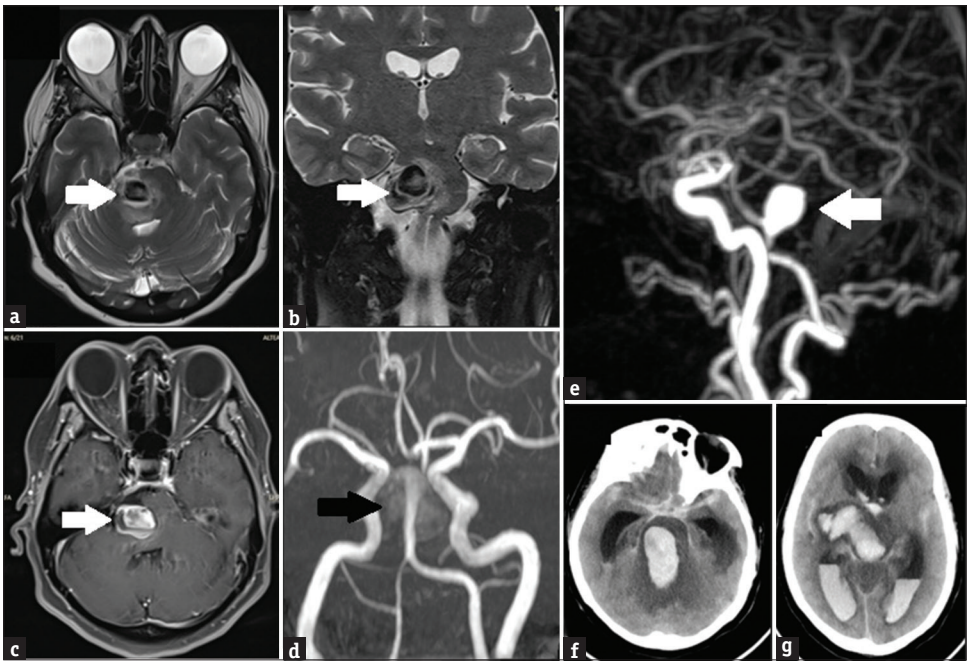

Figure 1: A 56 year old lady presented with diplopia and facial weakness from 10 days. Magnetic resonance imaging (MRI) brain – T2 axial (a), T2 coronal (b), T1 contrast axial (c), and two-dimensional time-of-flight MRI (d and e) showed a partially thrombosed vertebrobasilar segment aneurysm. She was admitted and planned for DSA next morning. However, she suffered a massive fatal subarachnoid intraparenchymal and intraventricular hemorrhage on the same night (f and g) before any intervention

rupture rate of 0.54%. Based on their observations, they suggested that patient <50 years of age, presence of hypertension, and multiple aneurysms with diameters of > or = 4 mm, were the predictive factors for rupture and this subset should be considered for treatment to prevent future aneurysmal rupture.[13]

Treatment scoring systems enhance the assessment of risk factors related to aneurysm rupture. The scores provide a number on a scale that facilitates a decision of intervention or follow up. The population, hypertension, age, size of aneurysm, earlier SAH and site of aneurysm (PHASES score) was developed with pooled data from a meta-analysis of six prospective cohort studies (including ISUIA and UCAS) to construct a risk prediction chart to estimate 5-year aneurysm rupture risk by risk factor status.[14] The predictability using PHASES score is compromised by omission of known risk factors like smoking, familial history and aneurysm shape. The PHASES score did evoke criticism and could not be generalized to the Asian population. The score can underpredict rupture risk of smaller aneurysms.[15] A PHASES score of 3 is associated with a low (<0.7%), but not negligible likelihood of aneurysm rupture, despite the low specificity while the odds are high (1.3% or more) if >4. Patients with a score of 3 or 4 are at an equipoise.[16] Patients with PHASES scores ≥6 had significantly higher rates bleed (1.7% or more) and poor neurologic outcome.[17]

The Unruptured IA Treatment Score (UIATS) incorporates treatment-related risk factors to personalise aneurysm management.[18] Developed by Delphi consensus method among a multidisciplinary group of 69 specialists, it incorporated patient specific factors (age, risk factors, clinical symptoms and quality of life), aneurysm risk factors (size, morphology, location and growth) and treatment risks (age, size, complexity and a constant intervention-related risk). A retrospective sensitivity analysis applying UIATS score to ruptured aneurysms to determine predictability of outcomes suggests a sensitivity of only 44%, suggesting a low capability of prediction of risk of rupture.[19]

THE ELAPSS score (Earlier SAH, Location, Age, Population, Size and Shape of aneurysm) also incorporates aneurysm morphology in the predicting the growth rate as a surrogate measure of rupture risk at 3- and 5-year periods and determining follow-up and imaging intervals. The score ranges from 0 to 40 with higher score indicating higher growth rate.[20]

A retrospective comparison between the UIATS and PHASES scores has suggested that the PHASES score has been much better at discriminating between ruptured IAs and unruptured IAs, possibly due to high weightage of aneurysm independent factors.[21] Another retrospective application of PHASES or ELAPPS score to ruptured aneurysms, categorised 45% UIAs to low-or very low-risk class by the PHASES risk calculator and 45.5% of the patients to lower intermediate-risk class via ELAPPS calculator. Thus, not all IA ruptures can be predicted. However, the scorings systems allow us to get reasonably close to estimating the potential risks and require additional insight from an experienced team to choose a proper treatment modality.[22]

Newer Imaging Assessment of Rupture Risk

In addition to aneurysm size, aneurysm morphology is a significant determinant of rupture risk. This includes pathoanatomical features and dynamic flow-related stresses.

Computational Fluid Dynamics (CFD) and Fluid-structure Interaction (FSI): CFD analyses patient-specific vascular anatomy and tortuosity, simulation of blood flow and its dynamics, and its interaction with the aneurysm wall. Thus, the study offers a method of understanding the blood flow patterns. CFD and FSI studies are not used routinely due to diverse methodologies and variable patient specific inputs. They are still used as an investigational and research tool and may be employed for special cases.[23]

High-resolution Vessel Wall Imaging (HR-VWI): factors such as wall thickness, haemodynamics and flow related stress are crucial in generating local shear forces leading to degeneration, wall thinning and ultimate rupture. This degeneration can be picked up as wall enhancement on magnetic resonance imaging (MRI). HR-VWI has gained attention as a modality for identifying unstable aneurysms at high risk for potential rupture, although it has not yet been validated for clinical use. However, current evidence suggests that HR-VWI could potentially provide new insights and may become an important non-invasive biomarker of aneurysm instability and risk of rupture, as imaging techniques continue to improve. Data suggest that the lack of aneurysm wall enhancement has a strong negative predictive value.[24]

Small Unruptured Intracranial Aneurysm

The uncertainty of invasive versus conservative approach is even higher with small UIA.[25] The rupture rates of small UIAs remain questionable, especially in the 3–5 mm size group. Retrospective studies show significantly higher frequency of small, ruptured IAs than

anticipated. On the other hand, natural history studies suggest a very low risk of rupture. The population wide Tromsø study, utilising 3-Tesla magnetic resonance angiography (MRA), identified a 6.6% incidence of aneurysms ≥2 mm size. This number reaches 8.3% if ≥1 mm and extradural aneurysms are included.[26] 79.4% of UIA in the study were <5 mm. Both ISUIA and UCAS have defined cutoff points for low risk of rupture as 7 mm. As mentioned earlier, the SUAVe study focused on UIAs smaller than 5 mm showing annual rupture risk of 0.54% per year and growth in 6.7% cases. This is associated with an elevated risk of rupture that can reach 2%–10% per year.[27] Rutledge *et al*. also showed that 75% of aneurysmal SAH in their study were caused by aneurysms ≤7 mm in size, with 48% being smaller than 5 mm. Their median PHASES score was 5, corresponding to a 5-year rupture risk of 1.3%.[28]

Microsurgery for Unruptured Aneurysm – Safety and Advantages

Certain factors contribute to lesser procedural complications in surgery for UIAs:

1. Unlike ruptured aneurysm with SAH, the brain is not edematous and swollen making identification of important surgical landmarks easy. The need for brain retraction is minimal[29]
2. Defined anatomy enables the surgeon to perform more tailored, minimally invasive craniotomies, relying mainly on meticulous arachnoid dissection to widen exposure corridors and ease manipulation and handling, despite less cortical exposure[30]
3. Intra-procedural rupture of aneurysms is less frequent during clipping of unruptured aneurysms compared to ruptured cases, in contrary to coiling, where the risk is unchanged.[31]

Treatment of Unruptured Intracranial Aneurysm

No large volume randomised control trials have been successfully conducted till recently to address the issue on the management of UIA. An randomised controlled trial (RCT) comparing endovascular treatment (EVT) versus observation was stopped because of poor recruitment when 80 patients of the planned 2000 patients had been enrolled.[32] Individual prognostication and prediction are difficult due to limited data from longitudinal and observational studies, case series or device specific registries of patients and inability to precisely define the natural history. All recommendations are based on very low quality of evidence.

The Canadian Unruptured Endovascular versus Surgery study is the only RCT that compared clipping and EVT for the treatment of UIAs. It included 290 unruptured aneurysms, eligible for both clipping and EVT. The primary outcome was 'treatment failure' at 1 year, defined as a composite endpoint comprising either initial failure of aneurysm treatment, occurrence of an intracranial haemorrhage during follow-up or evidence of a residual or recurrent aneurysm. Secondary outcomes included neurological deficits and overall morbidity/mortality according to the modified Rankin Scale (mRS). Treatment failure was seen in 19% of EVT and 9% of surgical patients. The difference was mainly due to the superior occlusion achieved in the surgical group (93% vs. 85% at 1 year). Clipping resulted in higher complications (22% vs. 12%), but this did not result in worse functional outcomes after 1 year. A longer average hospital stay was also seen in clipped patients (6.7 vs. 3.8 days). The limitations to this study include the relatively small number of patients, slowly accrued during >10 years. Techniques and treatments have substantially changed over this time. Relatively few patients were treated with newer stents, flow diverters, or intrasaccular flow disruptors. Posterior circulation aneurysm formed a minority, there was lack of blinding of outcome assessors, and the follow-up period of 1 year is insufficient to capture all recurrences.[33]

Hence, the best available evidence on general principles of UIA treatment suggests that clipping is more effective at occluding aneurysms, with similar functional outcomes compared to EVT. This does come at the expense of a higher complication rate and extended hospital stay. While complete obliteration of aneurysms is noted in >96% surgical clipping in most series, the reported failure of EVT ranges from 5% to 30%. The choice of intervention must be wisely made as the risk of rupture may be less than that of the risk of unfavourable outcomes with endovascular or surgical treatment (3.2%–4.8% and 4.2%–6.7%, respectively).[34,35] Hence, adult patients whose 5-year risk of rupture is more than the risk of morbidity related to the preventive modality deemed best suited and safest to treat that aneurysm, are considered for preventive intervention. Treatment should be preferably planned at high-volume centres (>100 cases/year) to minimise the complications. A team approach with shared decision-making process with the patient involvement is recommended[36] [Figure 2a].

Treatment of Symptomatic Unruptured Intracranial Aneurysm

The two commonest clinical scenarios of UIA with mass effect include:

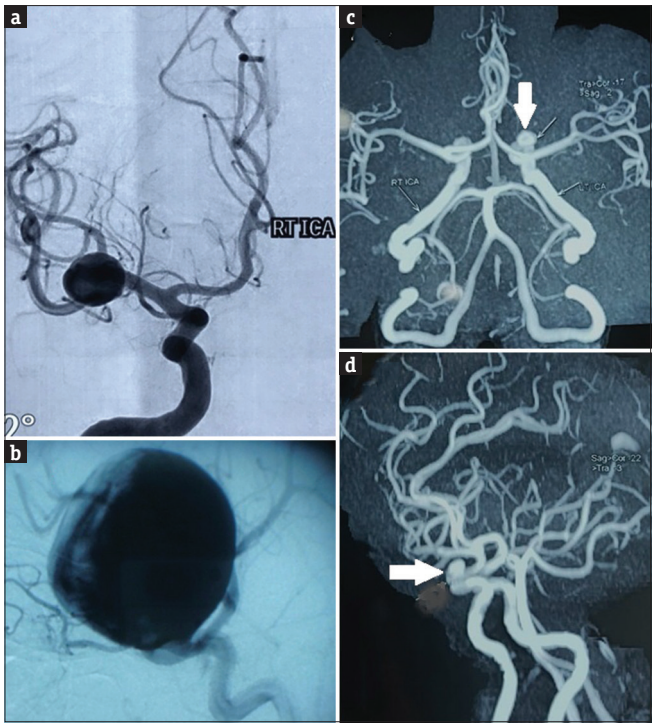

Figure 2: (a) Shows a large middle cerebral artery bifurcation unruptured aneurysm which was managed with surgical clipping. (b) Shows a giant ophthalmic segment aneurysm presenting with visual compromise, managed successfully with surgical clipping. (c and d) Shows an incidentally detected small 4 mm left ophthalmic internal carotid artery aneurysm adviced clinical monitoring and follow-up imaging

1. PcommA UIA with occulomotor nerve palsy – A sudden onset of (partial) occulomotor nerve palsy (ONP) is regarded as a warning sign for impeding rupture and should be treated emergently. Improvement in oculomotor functions was seen more frequently in clipped patients. Preoperative lower severity and intervention with 7 days resulted in favourable outcomes[37,38]
2. ICA – Paraclinoid aneurysm with vision impairment [Figure 2b] – A meta-analysis of 39 studies that included a total of 2458 patients showed vision improvement in 58% after clipping, 49% after coiling and 71% after FD. Vision worsened in 11% of patients after clipping, 9% after coiling and 5% after FD. There was no significant difference in the rate of worsened vision or iatrogenic visual impairment across either modality. Occlusion rates were higher with surgery (98% vs. 73%), although there was a higher surgical morbidity. These findings suggest that while surgical clipping is a more effective was to relieve mass effect and improve visual outcomes compared to coiling, FD is an effective option for treatment of visually symptomatic paraclinoid aneurysms, with progessive reduction of mass effect at a lower morbidity risk, with good safety and efficacy.[39]

Another analysis of studies of use of flow diverters for neuro-opthalmic symptoms showed complete recovery or improvement in patients with isolated visual symptoms in 30.6% and 56.6% cases. Similarly, isolated oculomotor symptoms recovered completely in 47.8% and improved in 78%. An increased likelihood of symptom improvement was observed when treatment was performed early (<1 month) after symptom onset. Morbidity was 5% and mortality was 3.9%. Thus, flow diversion promotes recovery or improvement of compressive symptoms in a large proportion of patients but is associated with significant rates of morbidity and mortality.[40] Transient and permanent worsening of the symptoms can.[41,42]

Role of Inflammation in the Formation and Rupture of Aneurysms – The Emerging Role of Medical Management

Vascular smooth muscle cells and lymphocytes are the key cellular components in IA development and rupture risk. Excessive wall shear stress causes blood flow conditions that activate pro-inflammatory signalling in endothelial cells. These subsequently recruit macrophages. The inflammatory transformation of vascular smooth muscle cells, lymphocytic infiltration, and activity of interleukin 6 and tumor necrosis factor-alpha contributes to the pathogenesis. Inhibiting this inflammation process may be a crucial novel pharmacological therapy to halt the progression of IA.

The use of aspirin (COX-1 inhibition) and statins (HMG CoA reductase inhibition)-acting through their anti-inflammatory effect are known to reduce vessel wall macrophage infiltrate, mobilize of endothlial progenitors for vessel wall repair and inhibit MMP in smooth muscle. Their benefit is suggested in various studies and analysis, although large-scale randomised trials is awaited.[43]

Unruptured Intracranial Aneurysm in Patients on Antiplatelets or Anticoagulants

Patients on antiplatelet or anticoagulant medications can be planned for conservative treatment of low risk UIA as the risks of rupture and SAH are not increased by the administration of medications. The risk of an ischemic event due to the primary disease needing these mediations is generally higher than the risk of aneurysm rupture for an asymptomatic IA with low-risk features. However, in the event of rupture, these medications will impair coagulation mechanisms leading to increased severity of the bleed extent.[44]

Follow Up Imaging of Untreated Unruptured Intracranial Aneurysm

Follow-up in patients treated conservatively is essential and should be planned with periodic MRA or CTA. No optimal time frame is suggested but conventional dictum suggests an annual study for the first 3 years, and then at a reduced frequency if radiologically and clinically stable. For small, asymptomatic UIAs (<3 mm in diameter), less frequent imaging can be suggested if an aneurysm is stable in consecutive studies. TOF-MRA without contrast for surveillance imaging often provides sufficient information to detect the changes in aneurysm size or recurrence and reduces radiation exposure [Figure 2c and d]. Digital substraction angiography (DSA) may be utilised when patient or aneurysm specific factors need a detailed evaluation.[45]

Screening for Unruptured Intracranial Aneurysm – Recommendations

Screening for unruptured IA has been suggested in first degree relatives in families with > 1 affected person with an IA or aneurysmal SAH. Furthermore, patients with several diseases that increase IA development risk; autosomal dominant polycystic kidney disease, coarctation of the aorta, Ehlers-Danlos syndrome type IV, bicuspid aortic valve, microcephalic osteodysplastic, and primordial dwarfism are deemed candidates for regular screening.[45]

Artifical Intelligence in Prediction of Unruptured Intracranial Aneurysmrupture Risk

Artifical intelligence (AI) – Deep learning and Radiomics-based Machine learning models provide better accuracy when compared to commonly used statistical tools such as logistic regression. AI models that can analyse multiple parameters simultaneously and work with large volumes of data including imaging, objective data of flow and morphological characteristics. AI grants the computational power to explore complicated non-linear relationships in extensive amounts of data, and its predictive power increases with increasing datasets for training. Although we have not quite yet reached the threshold for routine clinical application, AI has great potential to solve IA management issues in a patient-centric manner.[46] The ARISE-1 consortium suggested the incorporation of artificial intelligence to capture sequential aneurysm growth, identify predictors of rupture, and predict the risk of rupture to guide treatment options.[47]

Conclusion – The Challenges in Preventive Interventions – A Dilemma

Decision-making for preventive interventions of UIA is difficult. The natural risk of the disease should be carefully weighed against the risk of intervention in each patient. This approach has recently been challenged by Raabe *et al*. as it may result in over-treatment of asymptomatic patients. They suggest that decision-making should be outcome-based with counting the cumulative loss of quality-adjusted life years related to a bleed event, rather than risk-based, comparing the interventional risk with the ongoing yearly risk of the natural course.[48] However, this approach still replaces real evidence with mathematical models and extrapolations. The unique challenge in unruptured aneurysm treatment lies in the potential emergence of new neurological deficits, especially considering the asymptomatic nature of most patients. These deficits, frequently overlooked by conventional grading systems like mRS and GOS, can lead to enduring daily challenge.[49]

Better outcomes should not be calculated but observed in reality. Hence, a nuanced, individualized and pragmatic approach is necessary, hinged upon a thorough evaluation of diverse patient and aneurysm-related factors.[50]

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Role of Minimally Invasive Techniques in Neurovascular Surgery: Supraorbital Keyhole, Mini-Pterional and Endoscopic Endonasal Approaches – Gimmick or Game-changer

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Abstract

The adoption of keyhole approaches for intracranial aneurysm clipping has increased in neurosurgery. Select anterior-circulation aneurysms are amenable to minimally invasive exposure via the supraorbital keyhole, lateral supraorbital and mini-pterional approaches. Choice of approach depends on aneurysm location and angioarchitecture. Although these cosmetically favourable techniques appeal to both patients and surgeons, many neurosurgeons remain apprehensive about managing intraoperative events through smaller corridors. This narrative review summarises the available literature on benefits and limitations of keyhole clipping for anterior circulation aneurysms, highlights technical pearls, and addresses the common concerns of young neurosurgeons to help guide safe adoption.

Keywords: *Aneurysm, endoscopic clipping, keyhole, mini-pterional, supraorbital keyhole approach*

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Introduction

Once the optimal surgical outcome is achieved, the patient's concern often shifts towards cosmetic results. The increasing trend towards laparoscopic procedures instead of open laparotomies reflects this preference, and neurosurgery is no exception. With recent technological advancements, surgical approaches have become more refined, supporting the benefits of minimally invasive techniques. The goals of minimally invasive neurosurgery are to obtain sufficient exposure without compromising safety, while achieving the outcomes comparable to those of larger craniotomies.

Keyhole craniotomy is a customised approach that provides a direct and shorter route to the target area and therefore must be selected cautiously and judiciously.[1] Dr. Axel Perneczky introduced and popularised the supraorbital keyhole approach (SOKHA) for addressing pathologies confined to the anterior cranial fossa, the anterior portion of the middle cranial fossa and the para-sellar region. This approach proved effective for small-to medium-sized tumours and demonstrated better patient satisfaction and cosmetic results.[2]

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Although keyhole techniques were initially used primarily for selected tumour cases, neurosurgeons were hesitant to apply similar approaches in neurovascular surgery. However, current literature suggests that, in carefully selected patients, miniature craniotomies can be effectively used for aneurysm clipping. When determining the appropriate surgical approach, the surgeon's experience, the aneurysm's angioarchitecture and patient safety remain the most important considerations. As keyhole surgeries have not yet been described for cerebral arteriovenous malformations (AVMs), this narrative review focuses on keyhole approaches for aneurysms.

Pterional versus Supra Orbital Key-Hole Approach

The pterional craniotomy is the most commonly performed approach worldwide for aneurysm clipping, offering a versatile surgical corridor to the circle of Willis. While the pterional approach provides transsylvian

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access to the anterior circulation, the SOKHA provides a direct subfrontal route. Certain aneurysm configurations are better suited to a direct subfrontal approach than to a lateral transsylvian one.[3] The pterional craniotomy is associated with a larger skin incision, risk of facial nerve injury, and post-operative temporalis muscle atrophy. In contrast, SOKHA utilises a smaller trans-ciliary or trans-palpebral incision and avoids temporalis muscle manipulation. In addition, SOKHA has been associated with shorter operative time (140 min vs. 184 min) and reduced blood loss (160 ml vs. 250 ml) compared to the standard pterional approach.[4] The *pros and cons* of keyhole approach is summarised in Table 1.

With any smaller craniotomy, neurosurgeon remains perplexed about the surgical exposure and ability to deal with the unwanted intraoperative events especially in clipping of aneurysms. There have been ample literatures comparing standard pterional craniotomy and SOKHA on these concerns. Multiple comparative studies have reported no significant differences between the pterional approach and SOKHA in terms of parent vessel exposure, temporary clipping or intraoperative rupture rates.[4-6] A recent meta-analysis similarly found no difference in intraoperative rupture rates and concluded that mini-craniotomy is a viable option for unruptured aneurysms.[5,7] Long-term outcomes in both ruptured and unruptured aneurysms have also been shown to be comparable between the two approaches.[5,8] Patient satisfaction scores tend to favour SOKHA due to improved cosmetic results.[2]

The surgeon well versed in pterional approach for aneurysm clipping can transition to keyhole techniques in appropriately selected cases. They can chose among SOKHA, lateral supraorbital or mini-pterional options based on the location and angioarchitecture of the aneurysm.[9] The frontal sinus violation during a supraorbital craniotomy can be managed in a standard manner.[9,10] For surgeons, it is just a transition from concern to confidence.[11] The likelihood of requiring a revision decompressive craniectomy for post-operative infarction is similar for both approaches.

Table 1: Pros and cons of keyhole approach

Pros
Smaller incision and bone flap - improved cosmesis and reduced soft-tissue trauma
Potentially less operative pain and faster recovery/shorter hospital stay
Focused corridor reduces unnecessary brain exposure
When combined with endoscopy, allows adequate visualization
Cons
Narrow working angle – limited instrument manoeuvrability for complex/large aneurysms
Reduced visualization of proximal and distal control in some situations
Greater technical demand and steeper learning curve
Higher likelihood of need to extend exposure or convert to standard craniotomy when complications occur

The main concern of a neurosurgeon during an aneurysm clipping is intraoperative rupture. Intraoperative ruptures can be divided into two categories. First, the controlled rupture, defined as the aneurysmal rupture during the final dissection or clip application once the proximal control has been achieved. This type of intraoperative rupture can be tackled with nearly equal efficiencies in both pterional or SOKHAs.[5,7] Elective temporary clip application is associated with better outcomes than emergency temporary clipping, and this principle applies equally in keyhole surgery.[12] The second type of intraoperative rupture is before gaining proximal control and is known as uncontrolled rupture. This uncontrolled rupture is devastating regardless of craniotomy size. Even with a larger craniotomy, proximal control can be difficult in the setting of brain swelling and neurological outcomes are generally poor in such circumstances. The rate of conversion to a larger craniotomy due to intraoperative events during keyhole aneurysm clipping is currently unknown. The common apprehensions among neurosurgeons in choosing a keyhole approach are summarised in Table 2.

Increasing Exposure in Supraorbital Keyhole Approach

To effectively manage unexpected intraoperative events, adequate operative space must be ensured. Several technical adjustments can enhance exposure in SOKHA, particularly when treating ruptured aneurysms. The most important factor is brain relaxation achieved through optimal anaesthesia and the use of brain decongestants. The operative window may be expanded by up to 60% by using the fronto-orbital variant of SOKHA.[13] In addition, the skin incision can be extended laterally along the natural crease to allow a slightly larger craniotomy when necessary.

Placement of an external ventricular drain through Kocher's point reduces intracranial pressure and decreases the need for frontal lobe retraction. Further brain relaxation can be achieved by early cerebrospinal fluid (CSF) drainage from the optico-carotid cisterns. In the pterional approach, CSF release through Sylvian fissure dissection precedes frontal lobe retraction, whereas in SOKHA this occurs through a subfrontal route. This difference can raise the concerns in cases of anteriorly or inferiorly directed Anterior Communicating Artery (ACOM) aneurysms. However, in both

Table 2: Common apprehensions about keyhole approach and their solutions

1. Patient selection feels uncertain
Tips: Start with straightforward, small, unruptured anterior circulation aneurysms with favourable projection; review 3D angiography carefully for trajectory planning. Plan site of proximal control and the clipping angle
2. Limited visualization will prevent safe clipping
Tips: Routinely use angled endoscopes or endoscopic-assisted inspection; neuronavigation and intraoperative Doppler/ICG angiography help confirm anatomy and clip position
3. The learning curve will risk patients
Tip: Build competency and confidence on cadavers, attend and practice in neurosurgical workshops, seek mentorship with an experienced keyhole operator, and assist several cases before taking primary responsibility
4. The operating space is narrow
Tips: Use adequate depth of anaesthesia and brain decongestants. Consider fronto-orbital variant of supraorbital keyhole approach, extend skin incision laterally for making larger bone flap, use external ventricular drain to relax the brain
5. What if there's uncontrolled intraoperative bleeding?
Tips: Adhere to the basic principle of aneurysm clipping – get proximal control before neck dissection, use elective temporary clip plan for proximal control before definitive dissection, do not panic, apply suction over rupture site and call for help

ICG: Indocyanine green, 3D: Three-dimensional

approaches, definitive clipping is typically performed via a subfrontal corridor once adequate brain relaxation has been achieved.

Microscope versus Endoscope

The operating microscope has traditionally been used for aneurysm clipping through SOKHA; however, the edges of the small craniotomy can limit visualisation angles. The microscope provides a narrowed visual field, and increasing magnification further reduces light intensity. To overcome this, an endoscope can be used as an adjunct, offering a 'reverse cone' view. Endoscopy provides superior illumination and a panoramic view of blind spots through variable viewing angles, facilitating aneurysm dissection without traction. It also allows clear visualisation of distal clip blades to assess clip placement adequacy. For surgeons who are not comfortable using the endoscope from the beginning, a hybrid technique can be adopted. In this approach, the initial dissection is performed under the microscope, and the endoscope is introduced later for final dissection and clip application.

Intraoperative endoscopic assistance is a valuable adjunct during microsurgical clipping. Multiple studies have demonstrated that the use of an endoscope improves aneurysm occlusion rates and facilitates preservation of perforating vessels. In a series by Chavan *et al*., 6 of 25 aneurysms required clip readjustment after appearing satisfactory under microscopic visualization alone.[14] Similarly, a systematic review and meta-analysis reported that endoscopic assistance resulted in an average 13% rate of clip repositioning following initial microscopic placement. Furthermore, 77% of aneurysms clipped with endoscopic assistance demonstrated improved outcomes compared to those treated solely under the microscope, without an increase in complication rates.[15] These findings indicate that when endoscopic equipment is available, it should be routinely used as an adjunct to the operating microscope during aneurysm clipping.

Endoscopic Supraorbital Keyhole Approach

The first description of endoscope-assisted clipping through the SOKHA approach is attributed to Dr. B. S. Sharma.[16] Subsequently, Kumar *et al*. demonstrated fully endoscopic clipping of ACOM aneurysms using SOKHA, including successful management of intraoperative rupture under endoscopic visualisation.[3,17] Once brain relaxation is achieved through CSF drainage, adequate working space becomes available for endoscope manoeuvrability. Placement of an external ventricular drain through Kocher's point can further facilitate operating conditions.

Although most surgeons currently use two-dimensional (2D) endoscopes, three-dimensional (3D) endoscopic systems are now available and can be supplemented with indocyanine green (ICG) fluorescence imaging. The limitations of traditional 2D endoscopy can be addressed using 3D endoscopy, which improves visualisation by providing enhanced depth perception and a clearer 3D view of complex aneurysmal anatomy.[18] A better understanding of the spatial relationships between the aneurysm and the surrounding vessels may facilitate more precise clipping and potentially reduce operative time. Although 3D endoscopy offers a more realistic and immersive view, the higher equipment cost remains a concern. Other researchers also have confirmed that fully endoscopic aneurysm clipping is feasible with favourable outcomes.[19,20] While standard microsurgical instruments may be used, customised tools such as single-shaft clip applicators provide greater advantage when working through the narrow corridor of the SOKHA approach.[17] The development and increasing use of exclusive endoscopic clipping techniques represent a step towards future robotic neurovascular surgery.[21]

The present-day 3D exoscopes represent a hybrid between the microscope and the endoscope, and this synergy provides a more ergonomic, real-time

3D display for the entire operating team.[22] Surgical outcomes of aneurysm clipping performed using exoscopes have been reported to be comparable to those achieved with the operating microscope.[22-24] Furthermore, ICG video-angiography can be effectively utilized with exoscopes.[25] However, current experience with exoscopic aneurysm clipping is largely restricted to traditional large craniotomies, and their applicability in keyhole surgery has yet to be established.

Mini Pterional Approach

MCA aneurysms can also be clipped using the mini-craniotomy concept, either through the lateral supraorbital or the mini-pterional approach. Esposito *et al*. recommended the lateral supraorbital approach for aneurysms located within 15 mm of the M1 origin, and the mini-pterional craniotomy for those located more than 15 mm distal to the M1 origin.[26] 3D computed tomography angiographic reconstructions are helpful in determining the most appropriate mini-craniotomy technique. In the lateral supraorbital approach, the mini-craniotomy is created approximately two-thirds above and one-third below the superior temporal line. This approach does not extensively expose the sylvian fissure; instead, gentle frontal lobe retraction permits limited proximal sylvian dissection sufficient for aneurysm clipping. In contrast, the mini-pterional craniotomy is performed entirely below the superior temporal line and is centered directly over the sylvian fissure.

The surgical exposure obtained with mini-pterional craniotomy is not significantly different from that of the standard pterional approach.[27] Occlusion rates, operative time, intraoperative rupture rates, post-operative hematoma, vasospasm and infection rates have been found comparable between pterional keyhole and supraorbital keyhole techniques.[5,28] The lateral supraorbital approach is also suitable for selected ICA aneurysms.

Keyhole Approach for Distal Anterior Cerebral Artery Aneurysms

The keyhole concept can also be applied to the clipping of distal anterior cerebral artery (DACA) aneurysms, which are approached interhemispherically.[29-31] A small parasagittal craniotomy flap can be created, and the scalp incision is selected based on the height and projection of the aneurysm. For low-lying aneurysms, an incision between the two supraorbital notches may be used, whereas high-lying aneurysms may be approached through a transverse incision placed behind the hairline.[29,30] Neuronavigation is valuable in planning a focused craniotomy.

The primary limitation of a smaller craniotomy in this setting is the potential obstruction from bridging veins. For this reason, keyhole approaches to DACA aneurysms have been infrequently reported in the literature. However, an operative corridor of approximately 2 cm is typically sufficient. CSF release from the interhemispheric fissure facilitates brain relaxation and creates working space. If the brain remains tense or bulging, placement of an external ventricular drain can help reduce frontal lobe pressure and improve exposure.

Endoscopic Endonasal Approach

With increasing experience and technological advancements in endoscopic endonasal surgery, some neurosurgeons have explored this route for aneurysm clipping. In a systematic review, Martinez-Perez *et al*. identified nine eligible studies comprising 27 patients with 35 aneurysms. Most aneurysms (26/35) were unruptured and all were located in a midline or paramedian position. The aneurysm obliteration rate achieved with the endonasal endoscopic approach was 86%, while complications occurred in 26% of cases, with CSF leak being the most common undesired complication.[32]

For midline anterior circulation aneurysms, such as ACOM aneurysms, an endonasal trans-tubercular approach may be utilised. This approach provides a direct frontal view of the para-ACOM region; however, lateral access is limited by the presence of the bilateral optic nerves. Although cadaveric studies have provided a good anatomical understanding, the technical challenges *in vivo* with a pulsatile brain make endonasal trans-tubercular clipping more difficult compared to the SOKHA.[33,34]

Anatomically, the endonasal trans-tubercular route is suitable mainly for aneurysms directed superiorly or inferiorly, where the clip can be applied with a relatively straightforward trajectory. Even in these cases, visualisation of the distal clip blades can be limited. For anteriorly directed aneurysms, the dome is encountered first, increasing the risk of premature rupture before proximal control is achieved. For posteriorly directed aneurysms, the aneurysm lies behind the ACOM complex, making neck dissection more demanding. In addition, when the proximal A1 segment is located deeper, securing proximal control becomes difficult.

In the restricted working corridor of the endonasal approach, placement of a temporary clip, if required, may interfere with the application of the definitive clip. Furthermore, in the event of intraoperative rupture, there is no effective rescue strategy. These limitations explain why only unruptured aneurysms have been clipped via

the endonasal route in reported series. Post-operative CSF rhinorrhoea remains another concern, and in some cases, the presence of clip shanks can hinder adequate dural reconstruction.

Traditional transcranial approaches to midline or paramedian posterior circulation aneurysms can be challenging. The endoscopic endonasal approach may offer a direct midline corridor in carefully selected cases. This approach is best suited for laterally directed aneurysms, while anteriorly directed aneurysms carry a higher risk of premature rupture during exposure. For basilar or para-basilar aneurysms, clival drilling is required depending on the aneurysm height. When the aneurysm is located above the level of the posterior clinoid process, pituitary transposition becomes necessary, which introduces the risk of post-operative pituitary dysfunction.[35] Due to these limitations and the narrow working corridor, transcranial approaches generally remain superior to the endoscopic endonasal route for most posterior circulation aneurysms.

Conclusions

The mini-craniotomy options can be used for anterior circulation aneurysm clipping provided surgical experience and angio-architecture is appropriate. The advantages of mini-craniotomy include a smaller incision, reduced muscle trauma, shorter hospital stay, and improved cosmetic outcome. However, the limitations include reduced surgical exposure, increased surgeon apprehension, and difficulty in handling intraoperative ruptures. It is therefore essential to adhere to fundamental aneurysm surgery principles, particularly obtaining proximal control before dissecting the aneurysm. Both the supraorbital keyhole and mini-pterional approaches allow effective use of the microscope as well as the endoscope. Endoscopic endonasal approaches remain mainly applicable to selected unruptured aneurysms, especially those in the posterior circulation.

Minimal invasive surgical options should be considered neither a game-changer nor a gimmick. Mini-pterional and supraorbital approaches yield equivalent safety and efficacy in selected anterior circulation aneurysms, while endonasal clipping remains investigational. The choice of approach must be determined by the surgeon's expertise, the aneurysm's morphology, and – above all – patient safety.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Global Cerebrovascular Surgery Training: A Comprehensive Analysis of Current State, Challenges and Future Directions

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Abstract

Cerebrovascular surgery training stands at a critical juncture, facing a dual challenge of profound global disparities and a fundamental paradigm shift from open microsurgical techniques to endovascular interventions. This review analyses the current global landscape of training programmes to identify gaps and propose strategic solutions. We synthesised data from recent global workforce mapping studies (2024), systematic reviews and fellowship outcome analyses across 192 countries. The dataset encompasses 1261 neurosurgery training programmes and 10,546 trainees worldwide, alongside specific case volume trends and equipment availability metrics. Analysis reveals a 20-fold disparity in neurosurgeon density between high-income countries (2.44 per 100,000) and low-income countries (0.12 per 100,000). While 91% of training programmes report endovascular exposure, only 26% of residents achieve core competency during residency, creating a critical skills gap. Over the past decade, open cerebrovascular case volumes have declined by 15%–20%, while endovascular procedures have risen by 25%–30%. Currently, there are only 12 active open cerebrovascular fellowships in the U. S., contrasted with a rapid 300% expansion in neuroendovascular fellowship programmes. The sustainability of comprehensive cerebrovascular care is threatened by widening global inequities and a training model that lags behind technological evolution. Urgent restructuring is required through the implementation of longitudinal dual-pathway curricula, widespread integration of simulation technology, expanded international fellowship collaborations and targeted infrastructure investment in low-resource settings.

Keywords: *Cerebrovascular surgery, competency-based education, endovascular training, fellowship programmes, global neurosurgery, neurosurgery training, simulation training*

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Introduction

Cerebrovascular surgery has undergone a transformative evolution over the last two decades. The rapid ascent of endovascular techniques has fundamentally altered the management of aneurysms, arteriovenous malformations and acute ischaemic stroke, creating a new standard of care that prioritises minimally invasive interventions.[1,2] While this shift has significantly improved patient outcomes, it has simultaneously disrupted traditional training models, creating a complex educational landscape where trainees must master two distinct and technically demanding skill sets amidst divergent case volume trends.

Concurrently, the global distribution of neurosurgical care remains profoundly unequal. Recent workforce mapping initiatives have illuminated staggering disparities in training capacity, with the vast majority of resources concentrated in high-income countries (HICs), while low- and middle-income countries (LMICs) face

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critical shortages.[3] The density of neurosurgeons varies by a factor of 20 between the wealthiest and poorest nations, a gap that perpetuates significant inequities in patient access and survival.

This comprehensive review aims to synthesise current data on the state of global cerebrovascular surgery training. By analysing workforce statistics, regional infrastructure gaps, evolving training paradigms and fellowship outcomes, we seek to provide a holistic view of the challenges facing the speciality. Furthermore, we evaluate emerging solutions, including simulation technologies and international collaborative models, to propose strategic recommendations for ensuring the future competency of the global cerebrovascular workforce.

Global Training Capacity and Workforce Statistics

The global neurosurgical landscape is defined by its uneven distribution. Analysis of data from 187 countries identifies 1261 training programmes worldwide, educating a total of 10,546 trainees.[4] However, the geographic allocation of these programmes is heavily skewed towards economic prosperity.

Programme distribution by income level

HICs host the majority of training infrastructure. Specifically, HICs account for 696 programmes (55.2%), while upper-middle income countries (UMICs) have 275 (21.8%), low- and middle-income countries (LMICs) have 156 (12.4%) and low-income countries (LICs) possess only 100 programmes (7.9%) [Figure 1]. This distribution leaves vast populations in the Global South with minimal access to specialised training.

Workforce density disparities

Current data indicate a global workforce of 72,967 neurosurgeons, yielding a pooled density of 0.93 per 100,000 population. However, this average masks severe regional deficits. In HICs, the density stands at 2.44 per 100,000, compared to 1.13 in UMICs, 0.37 in LMICs and a critical 0.12 in LICs [Figure 2]. This 20-fold disparity represents a humanitarian crisis in surgical access.

Training density analysis

Future workforce capacity is similarly constrained. Training density – defined as the number of trainees per 100,000 population – mirrors the consultant workforce gap. HICs maintain a training density of 0.48, roughly nearly eight times higher than that of LICs (0.07) [Figure 3]. Without

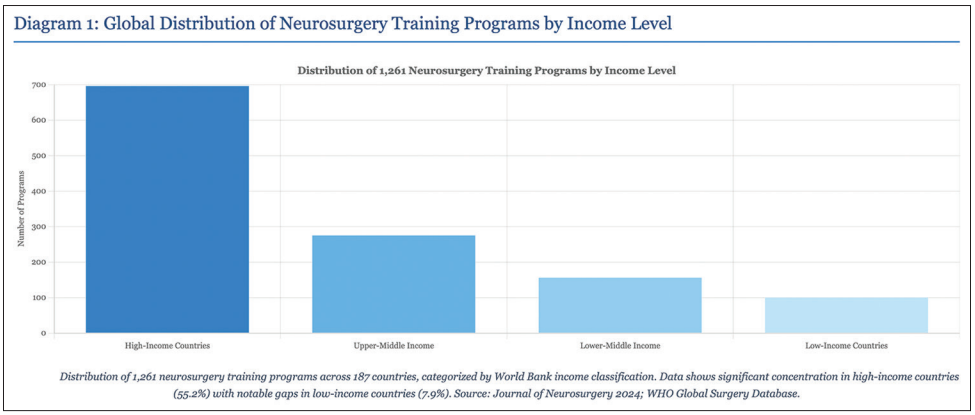

Figure 1: Global distribution of neurosurgery training programs by income level

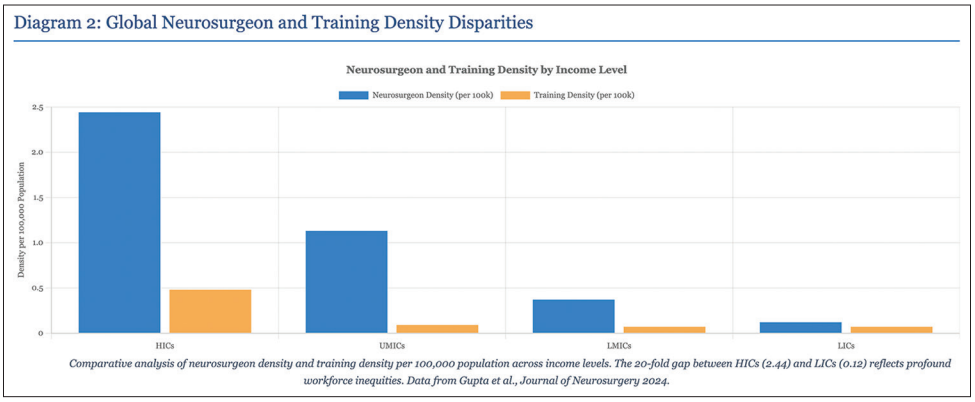

Figure 2: Global Neurosurgeon and Training density disparities

significant intervention, these training deficits guarantee the persistence of workforce shortages for decades to come.

Comprehensive data summary

Table 1 summarises the key metrics defining the global training landscape, highlighting the correlation between economic status and neurosurgical capacity.

Regional Disparities and Infrastructure Gaps

Effective cerebrovascular training requires more than personnel; it demands access to sophisticated technology. Disparities in equipment availability severely limit the scope of training in resource-poor settings.

Equipment access

Biplane angiography suites are essential for modern endovascular training. While 67.2% of programmes in HICs have access to this technology, only 4.5% of programmes in LICs do – a staggering 15-fold difference [Figure 4]. Similar gaps exist for intraoperative neuronavigation (63.9% HIC vs. 5.5% LIC) and operating microscopes (89.5% HIC vs. 34.2% LIC). These infrastructure deficits force trainees in LICs to learn on outdated equipment, potentially compromising their ability to perform modern standard-of-care procedures.

Subspeciality training exposure

The depth of training is also compromised. Trainees in HICs enjoy widespread access to subspeciality rotations, whereas those in LICs often lack exposure to critical fields [Figure 5]. Access to dedicated endovascular neurosurgery training is available in 54.9% of HIC programmes but only 6.4% of LIC programmes.

The Evolving Training Paradigm

The most significant pedagogical challenge in cerebrovascular surgery is the divergence of case volumes.

Case volume trends

Over the past decade (2015–2025), a clear inverse relationship has emerged. Open cerebrovascular surgical volume has declined by approximately 15%–20%, driven by the success of endovascular alternatives for aneurysms. Conversely, endovascular case volumes have risen by 25%–30% [Figure 6].[5] This shift threatens the acquisition of open surgical skills, as residents have fewer opportunities to perform craniotomies for vascular lesions.

Trainee participation evolution

Resident log data confirms this shift. Participation in endovascular procedures increased from 11.7% to 39.6% between 2015 and 2022. During the same period,

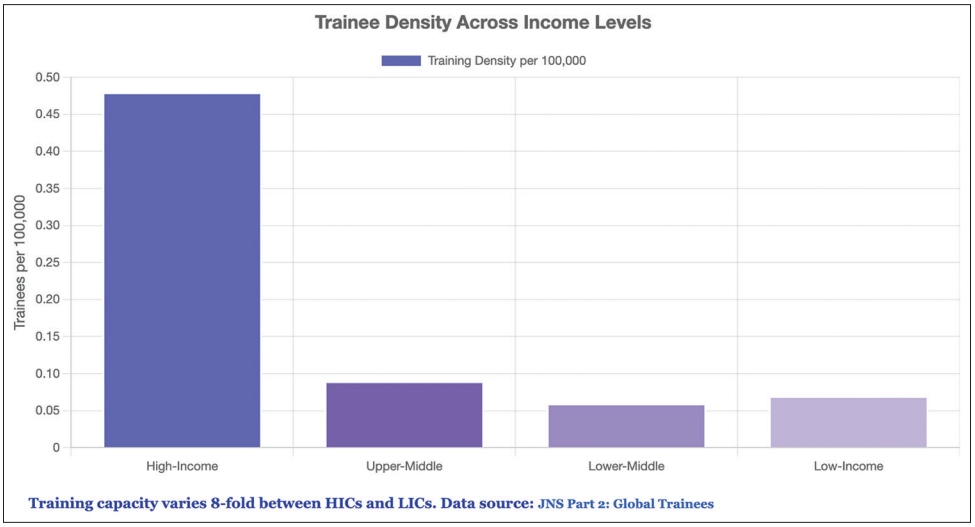

Figure 3: Training density per 100,000 population by income level

Table 1: Comprehensive Global Training Data Summary

Income Level	Programs (*n*)	Trainees (*n*)	Neurosurgeon Density per 100k	Training Density per 100k	Biplane Access (%)
High-Income (HIC)	696 (55.2%)	5,820	2.44	0.48	67.2%
Upper-Middle (UMIC)	275 (21.8%)	2,640	1.13	0.09	45.8%
Lower-Middle (LMIC)	156 (12.4%)	1,586	0.37	0.06	18.3%
Low-Income (LIC)	100 (7.9%)	500	0.12	0.07	4.5%
TOTAL/AVERAGE	1,261	10,546	0.93	0.14	34.0%

Comprehensive breakdown of global neurosurgery training infrastructure by World Bank income classification. Data source: Journal of Neurosurgery Global Workforce Mapping (2024)

participation in open surgical clippings decreased from 67.3% to 48.1% [Figure 7].[6] This trend necessitates a re-evaluation of minimum case requirements for graduation.

The competency gap

Despite increased volume, exposure does not equate to mastery. While 91% of residency programmes provide exposure to endovascular procedures, only 26% of graduating residents achieve core competency [Figure 8].[7] This 65% point gap indicates that while residents are present for these cases, the technical complexity and 'single-operator' nature of catheter-based interventions limit hands-on learning opportunities compared to open surgery.

Fellowship Programmes and Outcomes

Given the competency gap at the residency level, fellowship training has become increasingly mandatory for cerebrovascular practice.

Open cerebrovascular fellowships

The landscape for open vascular training is contracting. Currently, there are only 12 active CAST-accredited open cerebrovascular fellowships in the United States, with two programmes on probation [Figure 9].[8] These highly competitive positions place 73% of their graduates into academic positions, serving as the primary pipeline for the next generation of microneurosurgeons.

Neuroendovascular fellowship expansion

In stark contrast, neuroendovascular fellowships are expanding rapidly. The number of programmes has grown by 300% from 2015 to 2025 [Figure 10]. This growth reflects the market demand for stroke interventionists and the increasing complexity of endovascular devices.

2025 match statistics

The 2025 fellowship match data highlights the multidisciplinary nature of the field. Of the 156 applicants for 28 positions, the match rate was 82.1%.

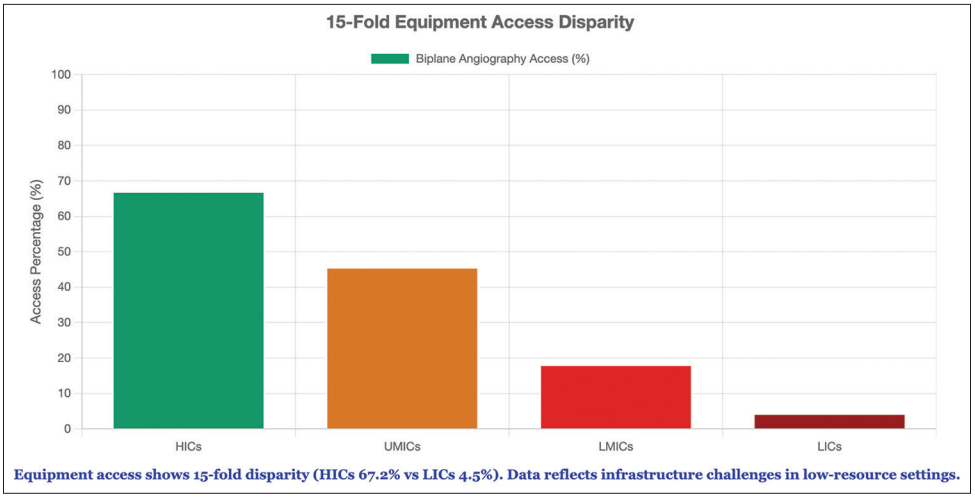

Figure 4: Access to biplane angiography equipment by income level

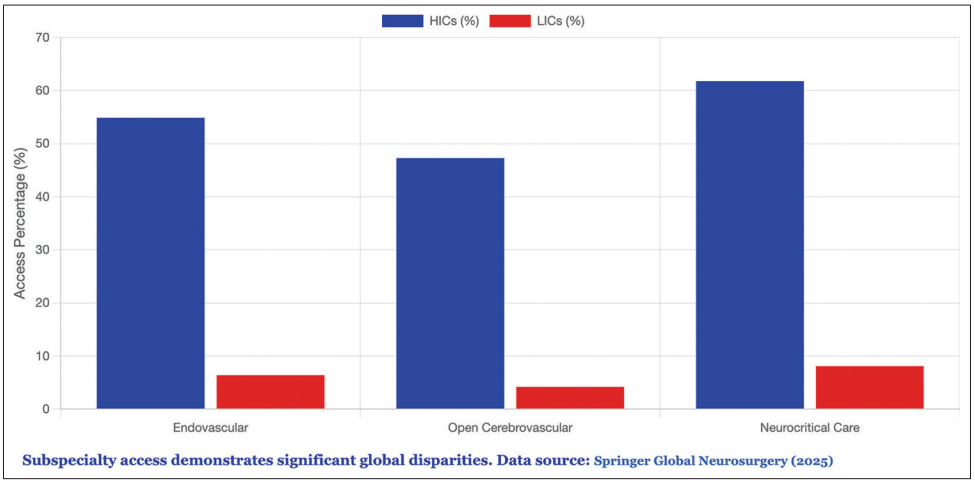

Figure 5: Subspecialty training access comparison (high-income countries vs. low-income countries)

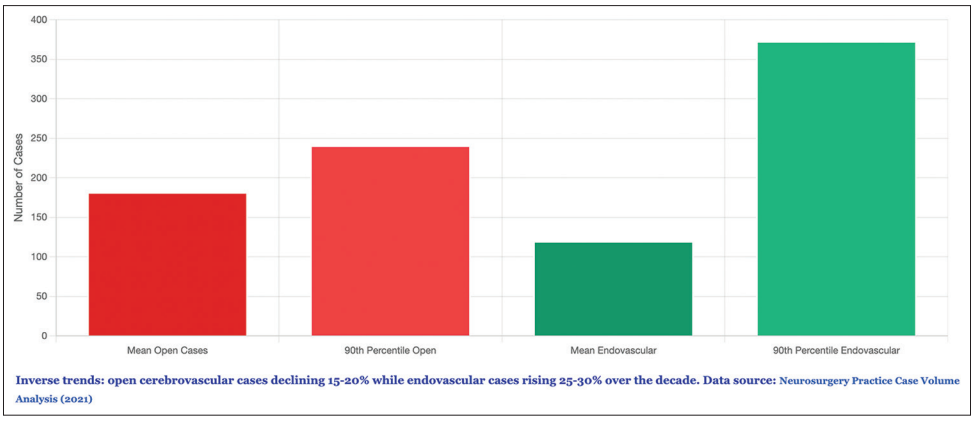

Figure 6: Cerebrovascular case volume trends during residency (3-year period)

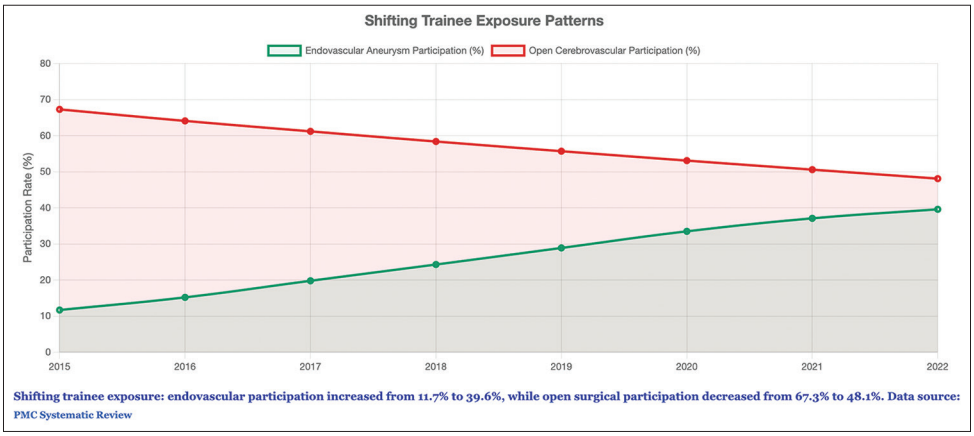

Figure 7: Trainee participation in cerebrovascular procedures (2015–2022)

Successful applicants came from diverse backgrounds:[9] neurosurgery (47%), radiology (31%) and neurology (22%) [Figure 11].[10]

Training Methodologies and Innovations

To bridge the gap between declining open volumes and the steep learning curve of endovascular techniques, training programmes are adopting new methodologies.

Simulation and Virtual Reality Integration

Simulation is no longer a luxury but a necessity. Virtual reality and augmented reality systems have seen a 34% adoption rate among training programmes. Studies indicate that simulation training leads to a 78% improvement in technical skill metrics [Figure 12].[11,12] Although the initial investment is high ($150,000–$300,000 per unit), the return on investment in terms of patient safety and accelerated skill acquisition is substantial.

While simulation offers tremendous potential, its effectiveness is contingent on curriculum integration and validated assessment tools, which are not yet universally implemented.[13] The global disparity in simulation research output – with high-income countries dominating production while LMICs contribute minimally despite bearing the greatest disease burden – further underscores the need for equitable investment in training infrastructure.[13]

International Collaborative Models

Addressing global disparities requires innovative collaboration models that transcend borders.

Successful Models

Two distinct models have shown promise. The Cameroon Visiting-Expert Model focuses on capacity building in LICs. Over an 18-month period involving 42 cases, the programme achieved 0% intraoperative mortality and successfully transferred skills to local surgeons. Conversely, the Erasmus + Neurosurgery Exchange Program in the European Union facilitates trainee mobility across 15 countries, standardising competencies and fostering a unified educational standard [Figure 13].

Future Directions and Strategic Recommendations

Looking ahead, the demand for neurosurgical care will

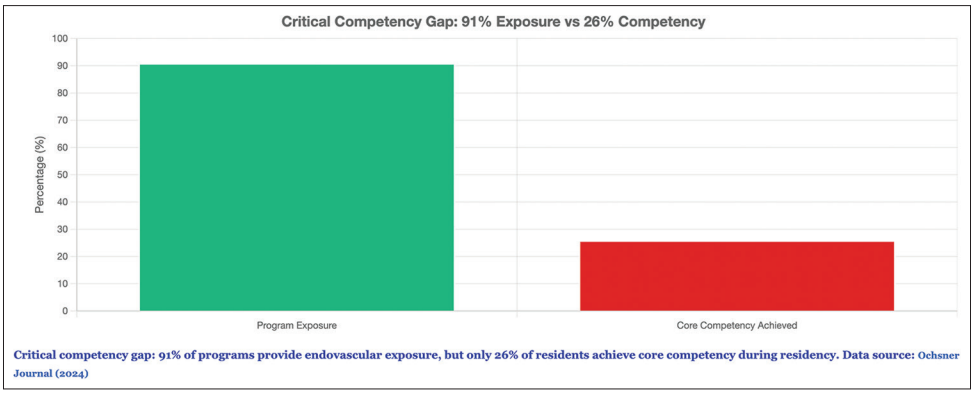

Figure 8: Endovascular training exposure versus core competency achievement

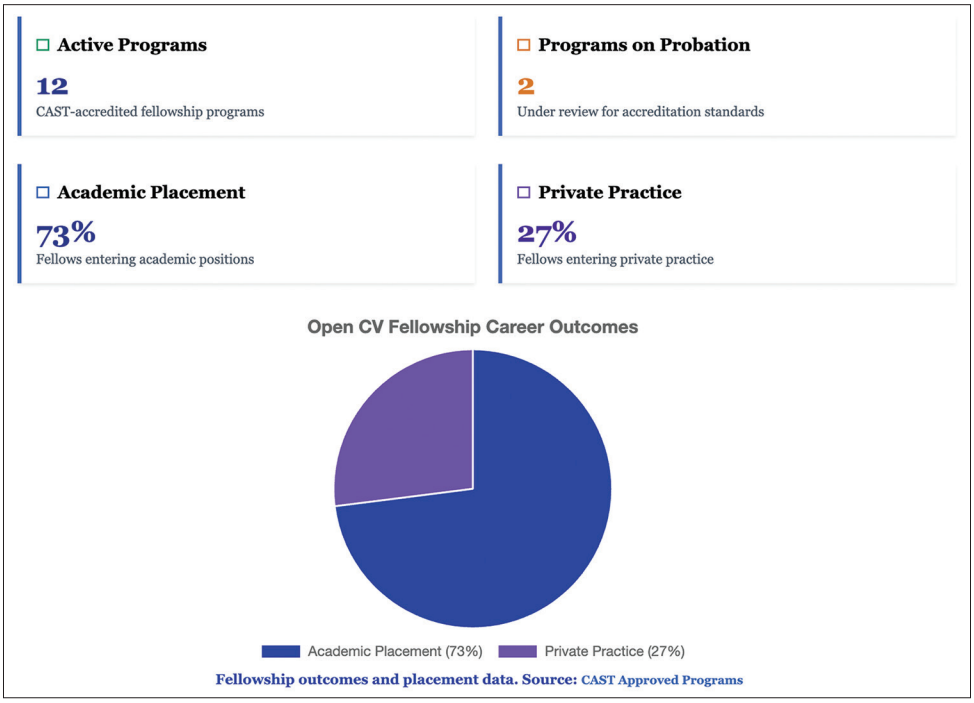

Figure 9: Open cerebrovascular fellowship landscape (United States)

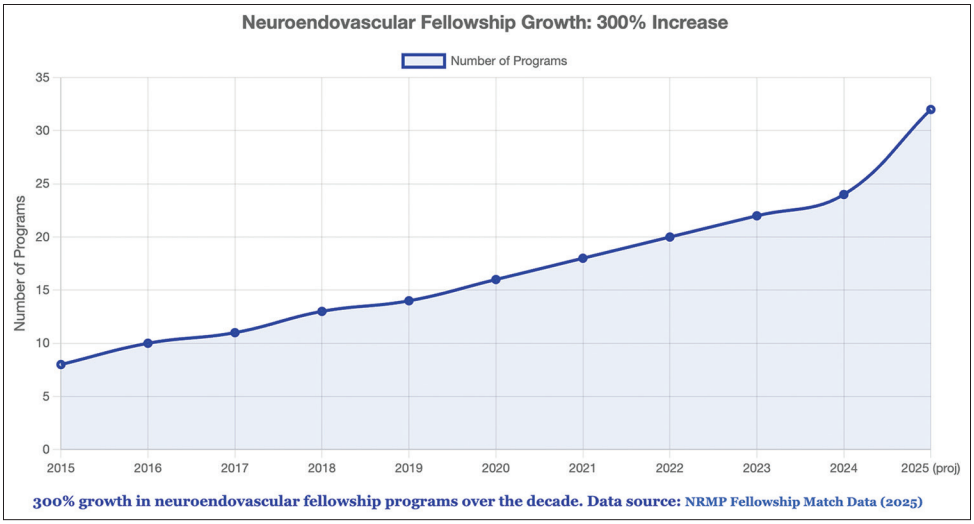

Figure 10: Neuroendovascular fellowship program expansion (2015–2025)

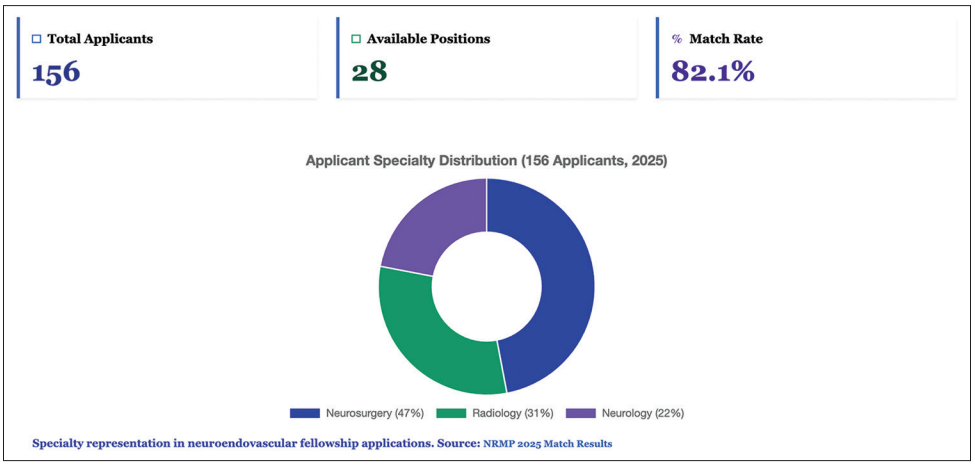

Figure 11: Neuroendovascular fellowship match statistics (2025)

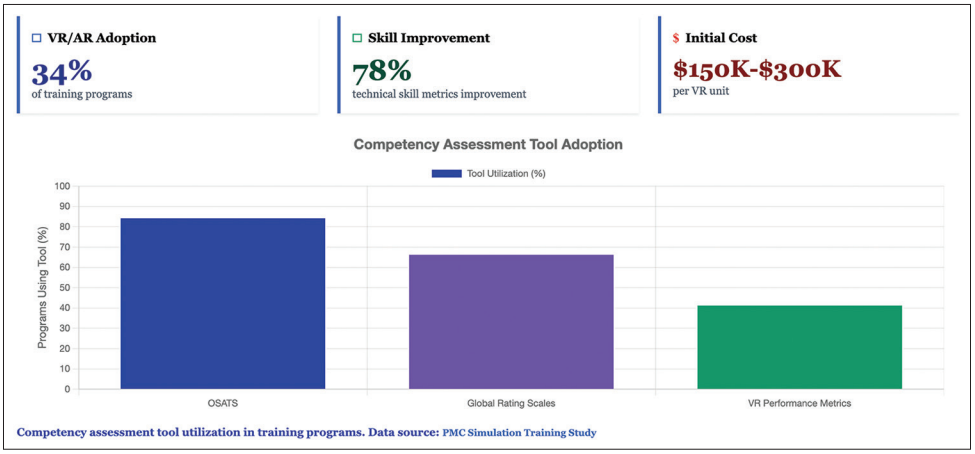

Figure 12: Virtual reality and simulation training metrics

only increase.

Workforce projections

Projections indicate a need for 95,000–110,000 neurosurgeons by 2035 to meet the global burden of disease [Figure 14]. With the current workforce at roughly 73,000, there is a projected shortage of nearly 30,000 surgeons, with 70% of this demand growth occurring in LMICs.

Strategic policy targets

To address these challenges, strategic targets for 2030 have been proposed [Figure 15]. These include a 50% reduction in global disparities, 90% achievement of dual competency among cerebrovascular trainees and 100% accreditation for training programmes.

Discussion

The data presented reveal a discipline in transition. The diverging trajectories of open and endovascular surgery necessitate a fundamental restructuring of residency curricula. The 'see one, do one, teach one' model is obsolete in an era of complex devices and high-stakes interventions. Instead, a competency-based framework, supported heavily by simulation and dual-pathway fellowship training, must become the standard.

Simultaneously, the moral imperative to address global disparities cannot be ignored. The 20-fold gap in workforce density is not merely a statistic but a reflection of systemic inequity. International partnerships, such as the visiting-expert models, provide a scalable template for capacity building but require sustained funding and political will.

Conclusions

Cerebrovascular surgery training faces unprecedented challenges but also unique opportunities. By embracing technology, restructuring education around dual competency and committing to global equity, the field can ensure that the next generation of surgeons is equipped to provide

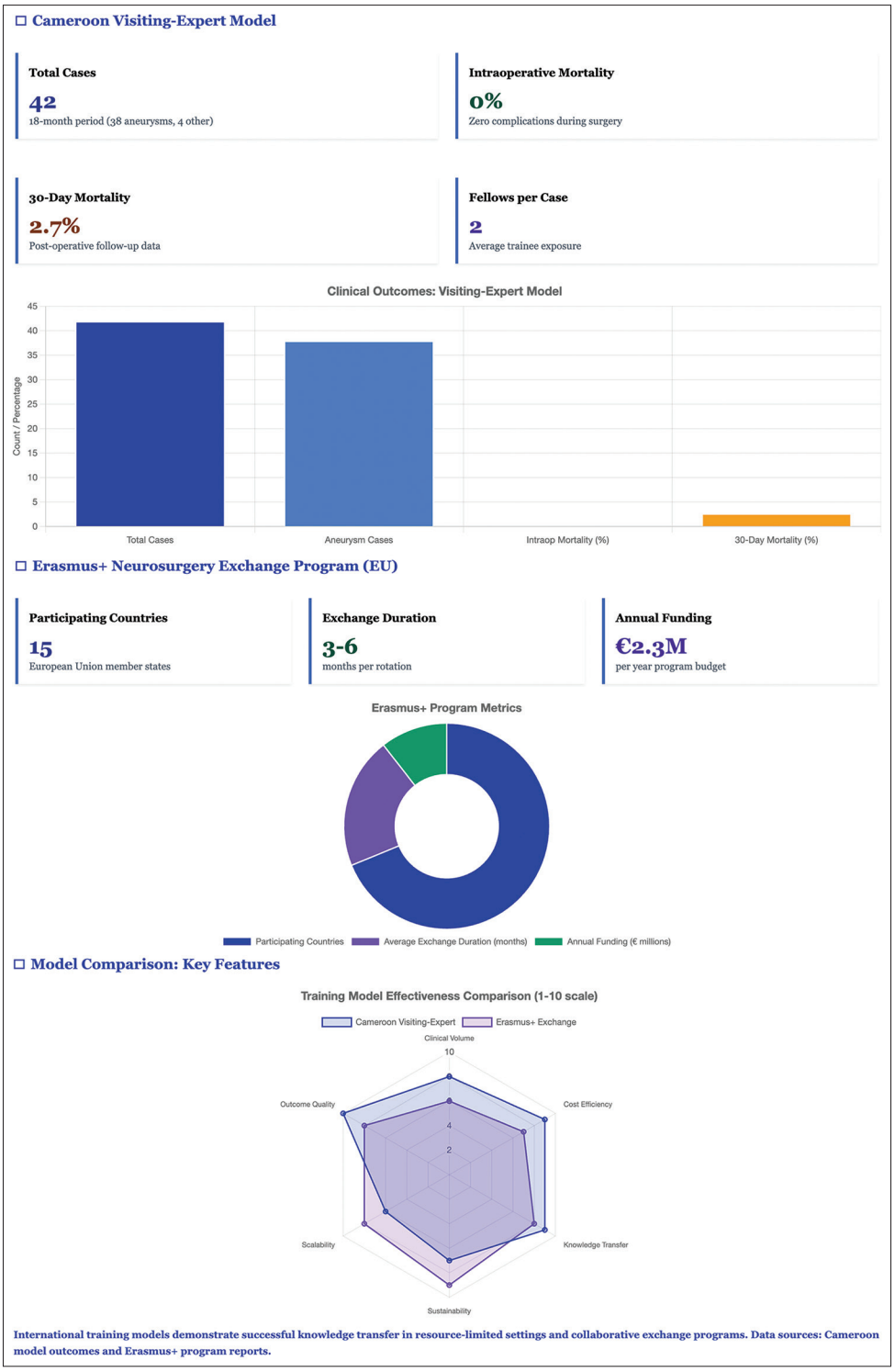

Figure 13: International collaborative training models (Cameroon and Erasmus+)

world-class care to patients regardless of geography or pathology.

Recommendations

- For programme directors: Implement longitudinal cerebrovascular rotations that integrate open and endovascular exposure early in residency. Invest in simulation infrastructure
- For policymakers: prioritise funding for essential equipment in LMICs and support visa frameworks that facilitate international training exchanges
- For international organisations: Coordinate equipment donation programmes and standardise global accreditation metrics to ensure quality control
- For trainees: Seek early exposure to both modalities

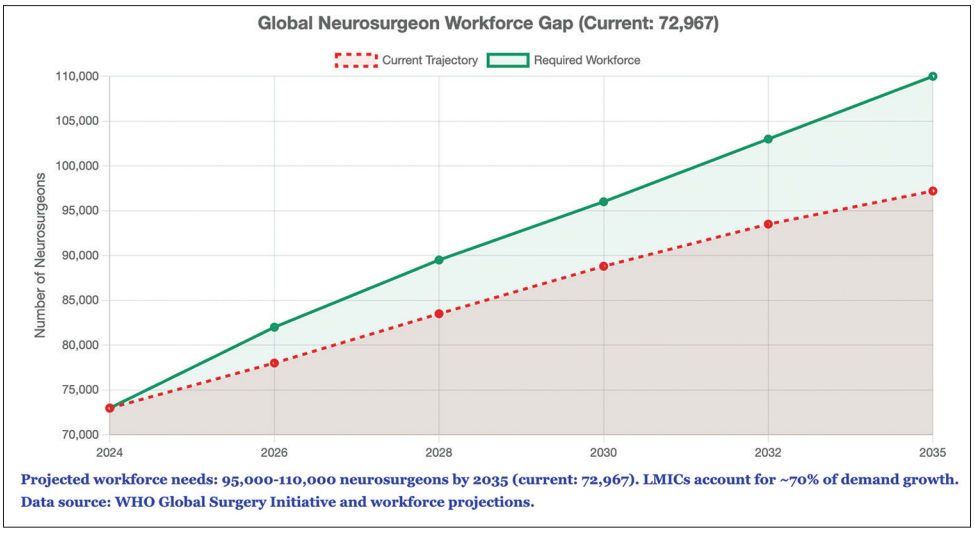

Figure 14: Global neurosurgeon workforce projections to 2035

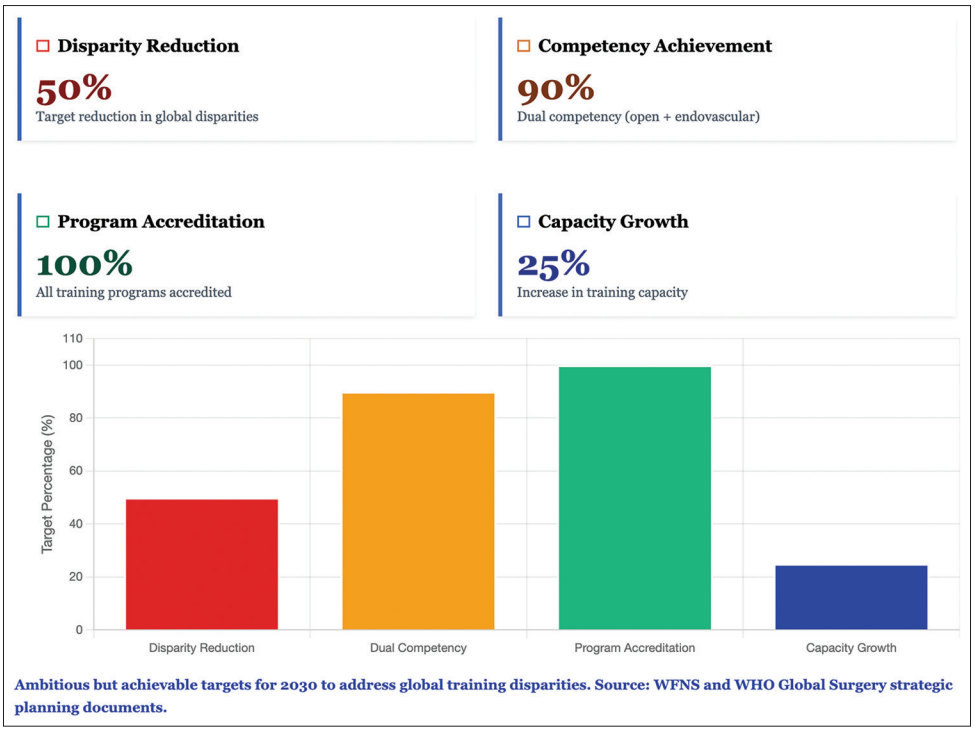

Figure 15: Strategic policy targets for 2030

and prioritise fellowships that offer comprehensive 'hybrid' training.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Venous Sinus Stenting in Idiopathic Intracranial Hypertension: Outcomes from a Single-centre Study

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Abstract

Background: Idiopathic intracranial hypertension (IIH) is characterized by elevated intracranial pressure (ICP) without identifiable intracranial pathology or abnormal cerebrospinal fluid composition. Venous sinus stenosis has been increasingly recognized as a potential contributing factor, and venous sinus stenting (VSS) is emerging as a promising treatment modality for refractory cases. Objective: To evaluate the effectiveness, safety, and clinical outcomes of venous sinus stenting in patients with IIH and radiologically confirmed venous sinus stenosis.

Materials and Methods: A prospective observational study was conducted between 2021 and 2024, including patients fulfilling the modified Dandy criteria for IIH with suspected venous stenosis on MRI/MRV. All patients underwent diagnostic cerebral venography with trans-stenotic pressure (TSP) gradient measurement using microcatheter manometry. A pressure gradient ≥10 mmHg was considered significant and taken as a cutoff for stenting. Clinical improvement was assessed using the Numerical Rating Scale (NRS) and Visual Pain Intensity Scale (VPIS) for headache and Frisen grading for papilloedema. Post-stenting follow-up was performed at regular intervals up to one year.

Results: Eighteen patients (13 females, 5 males; age range 13–50 years) were evaluated. Eight had a TSP ≥ 10 mmHg, and five underwent stenting with self-expandable open-cell stents across the stenotic segment. All patients demonstrated significant post-procedural improvement in venous flow and reduction in pressure gradient. Clinical outcomes showed marked improvement in headache in 92.8% (13/14) of patients and complete resolution of tinnitus and diplopia. Fundus evaluation revealed regression of papilloedema in all patients within one month of the procedure. MRI/MRV at six months confirmed stent patency with no in-stent thrombosis or adjacent stenosis. No major procedural or antiplatelet-related complications occurred, and all patients remained symptom-free at one-year follow-up.

Conclusion: Venous sinus stenting is a safe, effective, and durable treatment option for selected patients with IIH and significant venous sinus stenosis. It provides substantial symptomatic relief, particularly in headaches, visual disturbances, and tinnitus, with excellent safety and long-term outcomes.

Keywords: *Endovascular stenting in idiopathic intracranial hypertension, idiopathic intracranial hypertension, transverse-sigmoid sinus stenting, venous stenting in idiopathic intracranial hypertension*

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Introduction

Idiopathic intracranial hypertension (IIH) is a relatively uncommon condition characterised

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by elevated intracranial pressure (ICP) without any identifiable intracranial pathology and with normal cerebrospinal fluid (CSF) composition.[1] Several theories have been proposed regarding its pathogenesis, including obesity, excessive CSF production by choroid plexus, impaired CSF absorption through arachnoid granulations in the cortical venous sinuses and venous hypertension secondary to dural venous stenosis.[1,2] A newer hypothesis suggests a role for the glymphatic system dysfunction.[1,3] However, no single hypothesis has been definitively proven till date.

Anatomical variations and abnormalities in IIH are most frequently noted at the transverse-sigmoid junction.[1] Venous flow obstruction may be luminal or abluminal due to ICP, resulting in vicious cycle of dysfunction. The consequent rise in central venous pressure and a decrease in venous outflow secondarily result in increased pressure gradient and excess of CSF in the perivascular and subarachnoid areas.[2,4] Although the therapies in the past are targeted to reduce the CSF pressure.[5,6] Now, the focus is on eliminating the cause by reducing the venous pressure.

Venous sinus stenting (VSS) is emerging as a promising therapeutic option for patients with significant stenosis, offering symptom relief and reducing ICP by improving venous outflow.[7-10] This study evaluates the effectiveness of VSS in patients with IIH and venous sinus stenosis, assessing clinical outcomes, symptom resolution and long-term safety.

Materials and Methods

All patients who fulfilled the modified Dandy criteria for IIH and had suspected venous stenosis on magnetic resonance imaging (MRI) screening between 2021 and 2024 were included in the study. The Trans-stenotic pressure gradient (TSP) was measured using catheter angiography with a microcatheter in all patients, and a pressure gradient of 10 mmHg and more was taken as a cutoff for stenting. The symptomatic improvement was assessed using the Numerical Rating Scale (NRS) and the Visual Pain Intensity Scale (VPIS) to compare headache severity before and after stenting. Fundus photograph was taken to compare and grade papilloedema using the modified Frisen scale pre- and post-stenting.

Results

A total of 18 patients were included in the study, comprising five males and 13 females [Table 1]. The majority were in their third and fourth decades (ranging

Table 1: Patient demography

Age (years)	Sex	Complaints	Duration	MRV	TSP
35	Female	Headache	1month	Right transverse-sigmoid stenosis	7mmhg
36	Female	Tinnitus for 4 years	4 years	Left transverse-sigmoid stenosis	4mmhg
34	Female	Headache and blurring of vision for 2months	2 months	Bilateral transverse-sigmoid junctional stenosis	5.5mmhg
27	Female	Postural vertigo and tinnitus	1month	Right transverse-sigmoid stenosis	5mmhg
32	Female	Headcahe	2months	Right transverse-sigmoid critical stenosis	6mmhg
33	Female	Headache for 3 months	3 months	Right transverse-sigmoid stenosis	30mmhg
45	Female	Headache and double vision for 3 months	3 months	Right transverse-sigmoid severe stenosis and left transverse-sigmoid sinus narrowing	5mmhg
41	Female	Headache for 1 year	1 year	Right transverse-sigmoid stenosis and near total occlusion of left transverse-sigmoid sinus	13.3mmhg
28	Male	Headache and blurring of vision	1 month	Right transverse-sigmoid critical stenosis	4mmhg
50	Male	Tinnitus and headache	1 year	Posterior third SSS stenosis	3mmhg
30	Female	Headache since 11 years of age on medical management worsened for past 1 week	5months	Right transverse-sigmoid critical stenosis	15.5mmhg
29	Female	Double vision on right sided horizontal gaze	1 month	Bilateral transverse-sigmoid junctional stenosis (right > left)	Right - 19mmhg; Left - 10mmhg
24	Female	Headache and blurring of vision	1week and 3days	Right transverse-sigmoid junctional stenosis	13.6mmhg
13	Male	Headache and blurring of vision	2 months	Bilateral transverse-sigmoid narrowing	Right - 11mmhg; Left - 10.5mmhg
48	Female	Headache	4 months		
27	Male	Headache	1month	Bilateral transverse stenosis right > left	Left - 16mmhg
44	Female	Headache	1month	Right transverse-sigmoid stenosis and left hypoplastic transverse sinus	17mmhg
46	Male	Headache	1 month	Bilateral transverse sinus stenosis (right > left)	3mmhg

from 13 to 50 years) [Chart 1]. The most common symptoms include headache (77.7%), visual blurring (16.6%), tinnitus (16.6%) and double vision (11.1%). Fundus photographs were taken for all patients with visual blurring, and papilloedema was graded using the Frisen classification. MRI brain with MR Venogram (MRV) was performed in all patients, which is a useful screening tool to look for transverse and sigmoid sinus stenosis [Figure 1]. Cerebral angiogram under local anaesthesia was performed in these patients with suspected stenosis in transverse and sigmoid sinuses and transverse–sigmoid junction in the MRI, and the venous pressure was measured at pre-stenotic segment and post-stenotic segment using a microcatheter. The difference between the two pressures was defined as trans-stenotic pressure gradient (TSP). A pressure gradient of 10 mmHg and more was taken into account for stenting. Out of 18 patients, 8 patients had pressure gradient of 10 mmHg and above. Out of eight patients, five patients were eligible for the procedure and were primed initially with dual antiplatelets (tablet aspirin 75 mg once a day and tablet ticagrelor 90 mg twice daily) for 5 days prior to the procedure. During the procedure, dual femoral vessel punctures are taken for access, one in the common femoral artery and another in the common femoral vein. A 6 Fr long sheath is taken through the corresponding internal jugular vein into the sigmoid sinus.

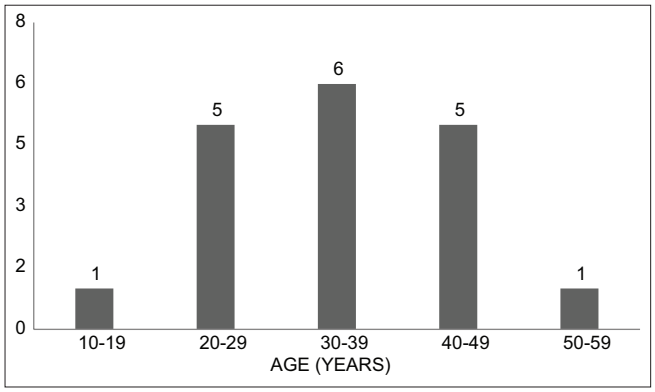

Chart 1: Distribution of patients based on age

An appropriate sized open-cell type self-expandable stent was taken across the stenotic segment and deployed slowly, spanning the stenotic segment [Figures 2 and 3]. In two cases, post-stenting balloon dilatation was done across the stented segment to stabilise the patency of the stent [Figure 2]. Post-stenting, venous pressure was measured again at the pre-stent and post-stent segment, which were noted to be significantly reduced. A check angiogram through arterial access was repeated to see the improved venous outflow across the stented segment. Post-procedure, all patients were continued on dual

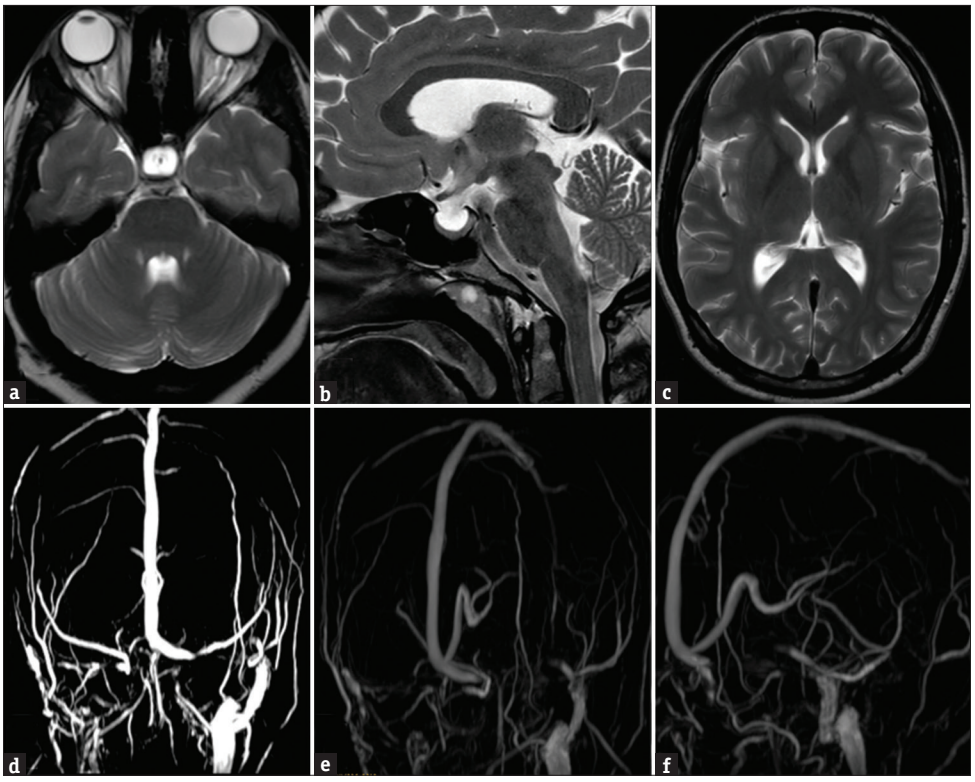

Figure 1: (Case 1) Magnetic resonance imaging brain with magnetic resonance angiogram. (a) T2-weighted (T2W) axial section showing bilateral tortuous optic nerve with increased peri-optic space and flattened posterior sclera. (b) T2W sagittal section showing empty sella sign; (c) T2W axial section showing slit like lateral ventricles. (d-f) MR Venogram (MRV) showing significant left transverse sinus stenosis and hypoplastic right transverse sigmoid sinus

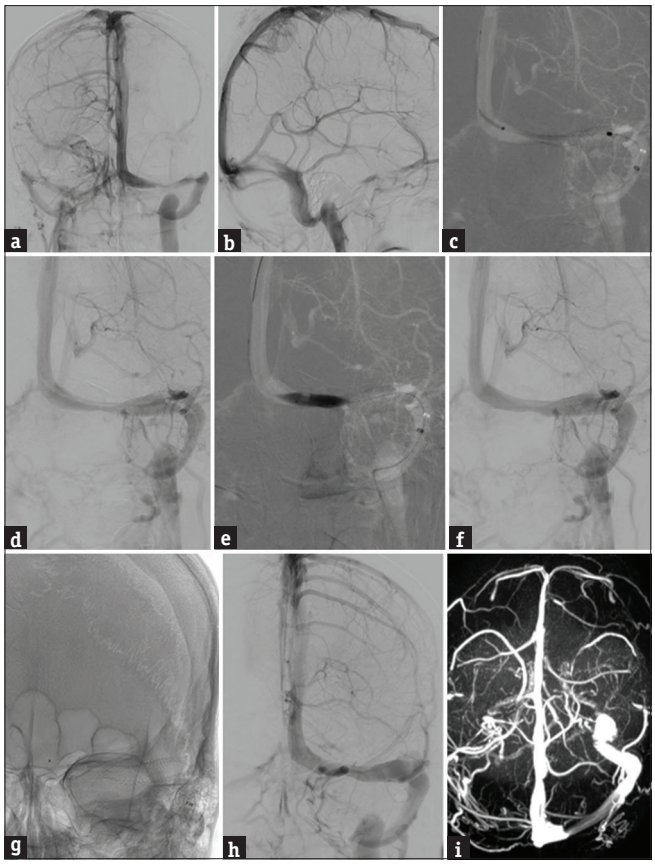

Figure 2: Cerebral angiogram showing: (a and b) anteroposterior and lateral views - dominant left transverse sinus with long-segment stenosis in the mid-segment and hypoplastic right transverse sigmoid sinus. (c) Appropriate size self-expanding stent deployed across the stenotic segment. (d) Post-stenting angiogram showed good opening of the stenosis with minimal residual narrowing. (e) Balloon dilatation of the stented residual stenotic portion was performed. (f) Post-dilatation angiogram showed satisfactory opening of the stenotic segment with good venous outflow. (g) Bone window showing left transverse stent in satisfactory position. (h) Check angiogram showing good transverse venous sinus opening and venous outflow across the segment. (i) MR Venogram (MRV) after 6 months showing stent artefact with good venous outflow

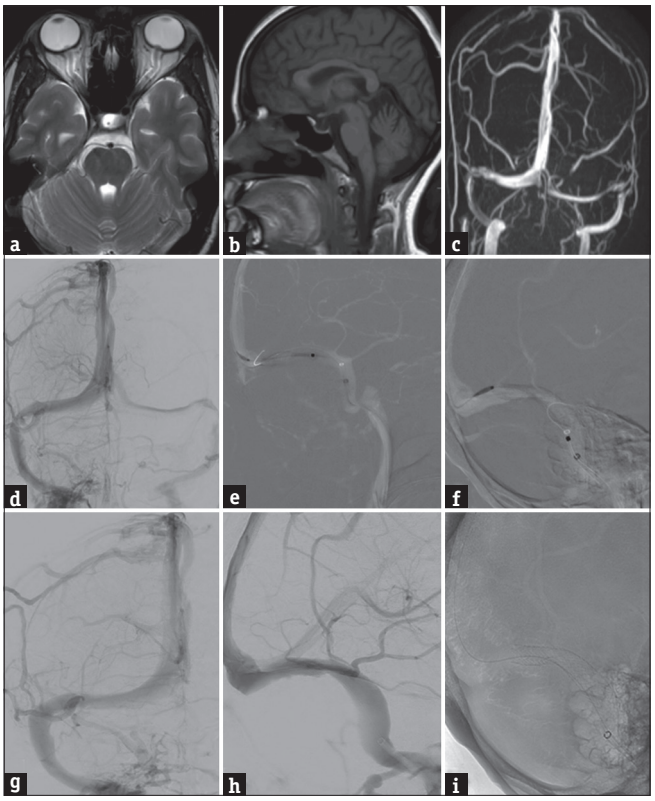

Figure 3: (Case 2) (a) Magnetic resonance imaging brain T2-weighted axial section showing bilateral tortuous optic nerves, flattened posterior sclera and optic nerve head projection. (b) T1-weighted sagittal section showing partial empty sella sign. (c) MR Venogram (MRV) showing dominant right transverse and sigmoid sinus with significant stenosis at the transverse–sigmoid junction and left hypoplastic transverse sinus. (d) Cerebral angiogram showing dominant right transverse and sigmoid sinus with transverse–sigmoid junction stenosis and hypoplastic left transverse sigmoid sinus. (e and f) Self-expanding stent deployed across the stenotic segment. (g and h) Post-stenting angiogram showing good opening of the transverse–sigmoid junction and venous outflow. (i) Bone window showing stent in satisfactory position

antiplatelets with aspirin 75 mg once a day and ticagrelor 75 mg twice daily for 6 months, then gradually tapered to aspirin 75 mg once a day and continued. All five patients were followed in the clinic and were clinically assessed at regular intervals for 1 year. All patients had improvement in their symptoms, including vision. Headache was assessed clinically using NRS and VPIS and was significantly reduced post-procedure. Out of 14 patients who had headache, 13 (92.8%) patients were relieved of headache at the end of follow-up. Fundus evaluation was done after 1 month and was graded using the Frisen scale and noted to be reduced and recovered in all patients [Figure 4]. Tinnitus and double vision were relieved in all patients post-procedure. MRI brain with MR Angiogram (MRA) and MRV was done in all patients after 6 months to look for overall venous flow [Figure 2]. No in-stent thrombosis or adjacent segment stenosis was reported in our series. No complications related to antiplatelet therapy were also noted during the follow-up period. All the patients remain symptom-free at the end of 1 year.

Discussion

IIH is characterised by ICP without a clear etiological factor.[1] The condition predominantly affects overweight women of reproductive age, with its incidence increasing alongside rising obesity rates.[1] Despite established diagnostic criteria and treatment guidelines, the exact cause of IIH remains elusive.[11] Previous hypotheses have focused on excessive CSF production or impaired reabsorption, but recent studies suggest a multifactorial aetiology, including glymphatic dysfunction, metabolic changes and venous abnormalities.[1-4] Many IIH patients exhibit transverse sinus stenosis, which can impair venous outflow and raise venous pressure.[4,11] Whether venous stenosis is a cause or consequence of elevated ICP remains debated. As our understanding of IIH

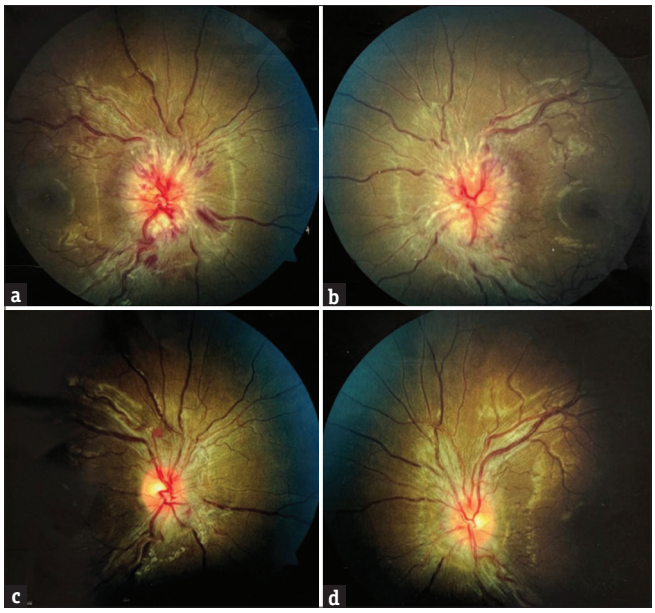

Figure 4: Fundus photograph comparing pre- and post-stenting; (a and b) pre-stenting fundus photograph showing bilateral papilloedema of Frisen grade 4. (c and d) Post-stenting showing resolving papilloedema with Frisen grade 2

pathophysiology evolves, a personalised approach to treatment selection may emerge, tailoring interventions to individual patient characteristics and underlying mechanisms of disease. Endovascular interventions, such as venous sinus stenting, have shown promising results in select IIH patients with venous stenosis.[7-11] Although the current management strategies primarily focus on reducing ICP through weight loss, carbonic anhydrase inhibitors (e.g. acetazolamide) and surgical interventions such as optic nerve sheath fenestration and CSF shunting by lumbo-peritoneal shunt.[5,6,11] Venous stenting is emerging and effective treatment option for selected patients with venous stenosis with a proven pressure gradient. First, venous sinus stenting was performed by Higgins *et al*. in 2002.[12] Following that, various studies showed promising results on venous stenting for IIH with long-term outcomes with fewer side effects.[13-41] However, there are no prospective, randomised controlled study to analyse the efficacy and long-term outcomes of venous stenting. Although, there are no guidelines for pre-requisites for venous stenting, most studies recommend trans-stenotic venous pressure gradient of 8 mmHg and more as a cutoff for venous stenting.[42] In our study, we took a pressure gradient of 10 mmHg and more as a cutoff for better outcomes. A systematic review by Starke *et al*. showed a clinical improvement in 130 of 166 patients with headache (78.3%), 84 of 89 patients with papilloedema (94.4%) and 64 of 74 patients with visual symptoms (86.5%) at a mean follow-up of 22 months.[10] A study by Dinkin and Patsalides demonstrated significant symptomatic relief in IIH patients following stenting.[14] Headaches improved or resolved in 84.7% of patients, pulse-synchronous tinnitus resolved in all cases (100%) and visual disturbances (including diplopia and transient visual obscurations) improved in all cases (100%). Objective ophthalmologic outcomes also improved, including reductions in papilloedema (measured using Frisen grading), retinal nerve fibre layer (RNFL) thickness and visual field deficits.[14] In our series, resolution or improvement in tinnitus, diplopia and visual blurring occurred in all our patients (100%) and headache in the majority (80%). Papilloedema was regressed to lower grades within 1 month of stenting [Figure 4]. A recent meta-analysis of 36 studies involving 1066 patients who underwent stenting showed a significant clinical improvement in tinnitus (95%), papilloedema (89%), diplopia or visual disturbances (88%) and headache (79%).[43] These findings suggest that VSS effectively reduces ICP and improves associated symptoms. Furthermore, the study's demonstration of improved visual fields and RNFL thickness supports the role of VSS in preventing permanent visual loss in IIH patients. Various studies reported a low incidence of complications, with no major adverse events such as stroke or intracranial haemorrhage. Minor complications included one case of retroperitoneal haemorrhage, transient head or pelvic pain and an allergic reaction to contrast dye.[43] In one series by Ahmed *et al*., the new stenosis post-stenting was reported in 6 of 52 patients (11.5%), and all underwent re-stenting.[41] Another series by Dinkin and Patsalides reported a cortical venous stasis during immediate post-stenting at the vein of Labbe and was managed with prophylactic anticoagulants for 2 weeks, without any sequelae.[14] In stent thrombosis was reported to be <20% by Ducruet *et al*. in their series of 30 patients.[44] Systematic review by Starke *et al*. reported that in-stent stenosis occurred in 3.4% and stent-adjacent stenosis occurred in 11.4% of the patients, resulting in re-stenting in 10 patients.[10] A recent meta-analysis of 1066 patients by Azzam *et al*. reported major complications and adverse events rate as 3.93% which includes subdural haematoma (0.65%), subarachnoid haemorrhage (0.28%), worsening of headache (1.41%), visual impairment (0.56%), worsening of papilloedema (0.09%), blindness (0.47%), arterial dissection (0.09%) and mortality (0.38%).[43] In our series, no major complications or in-stent thrombosis/stenosis were noted, and none of the patients required further intervention.

One of the ongoing debates in IIH research is whether venous sinus stenosis (VSS) is a cause or consequence of elevated ICP. Many studies discuss the possibility that intrinsic venous sinus stenosis (caused by structural

abnormalities such as arachnoid granulations) may be a primary factor in some patients, while in others, elevated ICP may cause secondary, extrinsic compression of the venous sinuses. The greater reduction in ICP seen in patients with intrinsic stenosis suggests that these patients may benefit the most from stenting. The idea of 'vicious cycle' in IIH, where increased ICP leads to further venous sinus narrowing, exacerbating venous hypertension and worsening the condition. By mechanically alleviating the stenosis, VSS breaks this cycle and restores normal venous outflow, leading to sustained ICP reduction. VSS may provide a more targeted and durable solution, particularly for patients with identifiable venous outflow obstruction.

Conclusion

IIH remains a complex and multifaceted disorder with no single unifying pathophysiological mechanism. Venous sinus stenting has proven to be an effective and well-tolerated treatment for patients with IIH with significant venous sinus stenosis. The symptom relief, including improvement in headaches, visual disturbances and tinnitus, is the proof of the effectiveness of the procedure. It is a safe and viable treatment option for select IIH patients.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Role of Surgical Decompression in Management of Cerebral Venous Sinus Thrombosis: An Institutional Experience

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Abstract

Introduction: Cerebral venous sinus thrombosis (CVST) is a venous stroke caused by dural venous sinuses blockage which leads to infarction of the draining brain parenchyma. This pathology is rare in the older age group and commonly occurs in the young age group between 20 and 35 years. Unlike arterial strokes, where decompressive craniectomy is widely accepted, its use in patients with venous strokes like CVST has not been widely adopted. Therefore, the aim of this study is to assess the role of decompressive craniotomy as a treatment approach for CVST.

Objective: The objective of the study was to evaluate the role and effectiveness of surgical decompression in the management of CVST.

Materials and Methods: A retrospective observational study of clinical, radiological, surgical and long-term follow-up data from patients who underwent surgical decompression for CVST in a tertiary centre from 2014 to 2023.

Results: Over a period of 9 years, a total of 24 patients of CVST underwent surgical decompression with a female preponderance noted. The most common presentation was headache, and the commonly involved sinus was the superior sagittal sinus. The decision of surgical decompression in 20 patients was made within 24 h of admission. Mean follow-up was 14 months (range 12–28 months) with 16 patients had more than 1 year of follow-up. Modified Rankin Scale (mRs) shows good clinical recovery during the follow-up period.

Conclusion: The prognosis depends on how early the treatment is initiated, the Glasgow Coma Scale at presentation, the area of brain damaged and associated prothrombotic conditions. The radiological picture appears more aggressive compared to the clinical status, and hence, a significant number of patients can be managed medically. Even though medical management is the treatment of choice, certain red flags should be identified early, and timely intervention in the form of surgical decompression in a patient with a malignant venous infarct with impending brain herniation should be considered. We feel that the timing of surgery is critical in improving outcomes.

Keywords: *Cerebral venous sinus thrombosis, decompressive craniotomy, surgical management of cerebral venous sinus thrombosis*

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Introduction

Cerebral venous sinus thrombosis (CVST) is a venous stroke caused by dural venous sinuses blockage which leads to infarction of the draining brain parenchyma. CVST is more commonly associated with general pathologies such as dehydration, infection, pregnancy, anti-phospholipid syndromes, puerperium and oral contraceptives, several local pathologies, e.g., CNS infection, brain tumours, arteriovenous malformations, etc.[1] This pathology is rare in the older age group and commonly occurs in young age group between 20 and 35 years. Female preponderance can be attributed

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to pregnancy, puerperium and excessive use of oral contraceptives.[2] CVST accounts for 10%–20% of the aetiology of young strokes in India.[3,4]

CVST usually presents with a wide variety of symptoms which include headache, seizure, visual disturbance, focal neurological deficit and altered consciousness level.[5] Due to these non-specific symptoms, diagnosis is more difficult clinically. However, the availability of non-invasive vascular imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) Brain with venography has made diagnosis easier recently.[6]

The International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) reported that the majority of deaths occur within the first 30 days of the disease.[7] The leading cause of death is haemorrhagic transformation of large venous infarcts, resulting in mass effect and cerebral herniation. CVST's long-term sequels are disabling and can lead to permanent disability.[8]

However, unlike arterial strokes, where decompressive craniectomy (DC) is widely accepted, its use in patients with venous strokes like CVST has not been widely adopted. Therefore, the aim of this study is to assess the role of decompressive craniotomy as a treatment approach for CVST.

Materials and Methods

This is a retrospective study conducted in patients who were diagnosed with CVST and underwent surgical decompression between the period of 2014 and 2023 in a single tertiary care centre. Each patient's data, including detailed history, clinical findings on the physical examination at the time of admission and radiological examination records, were collected. Patient consent was obtained from all participants prior to inclusion in this study. The diagnosis of CVST was based on clinical features and radiological investigation, such as computerised tomography (CT) scan and magnetic resonance (MR) scan with venography. In CVST cases not due to pregnancy, the thrombophilia profile was sent for each patient. The profile consisted of Protein C, Protein S, homocysteine and Factor V mutation

Indications for surgery

- Glasgow Coma Scale (GCS) <9 at the time of admission with a large infarct on the CT/MRI scan
- Clinical and radiological evidence of trans-tentorial herniation
- Significant mass effect and midline shift on CT/MRI scan
- GCS deterioration despite aggressive medical line of management.

Surgical procedure and postoperative management

DC was based on the location and size of the venous infarct. We did a large unilateral hemicraniectomy, ideally positioned over the site of the venous infarct with the largest hematoma. This facilitates extensive duroplasty using either homologous or artificial materials, aiming to alleviate raised intracranial pressure (ICP). Excision of infarcted tissue is generally not recommended. However, if there is spontaneous extrusion of the infarcted tissue, which often occurs at the site of dural opening, surgical removal may be necessary. We prefer to remove the bone flap and place it in the abdomen. In our series, in one patient, the bone flap was kept back after evacuation of the haemorrhagic infarct in the non-eloquent cortex as the brain was lax. The wound was closed in layers with the placement of a subcutaneous drain.

Postoperatively, the patients were sedated, paralysed with ventilatory support for a period of 48 h during which time mannitol was continued. Anticoagulation was started 48 h after the surgical procedure. Prophylactic antibiotics, anticonvulsants were also started. Attempts to reduce the raised ICP were made by using IV Mannitol, acetazolamide and dexamethasone.

The bone flap was repositioned once brain swelling had sufficiently decreased, typically within 3–6 months. We recommend early cranioplasty to reduce complications associated with DC, such as subdural effusions, sunken skin flap syndrome and hydrocephalus.

Modified Rankin Scale was used to evaluate patients who underwent DC and survived postoperatively to assess the outcome at discharge at 3, 6 and 12 months follow-up after surgery.

Results

Over a period of 9 years, a total of 498 patients were admitted with the diagnosis of CVST. Of the 498 patients, 21 were in the post-partum period. The thrombophilia profile was sent for the remaining 477 patients. Twenty-four patients who fulfilled the surgical criteria underwent decompressive surgery. The clinical characteristics of these patients are given in Table 1.

Radiological feature

The superior sagittal sinus was the most common dural venous sinus involved in 19/24 (79%) patients. In 18/24 (75%) patients, there was associated cortical vein involvement. In 6/24 (25%) patients, the vein of Labbe and in 3/24 (12%) patients, the vein of Trollard, were the prominent veins involved. One patient had an associated deep venous system involvement.

Midline shift >5 mm was seen in 22/24 (91.7%) patients. The mean midline shift was 8.2 mm (range 4–18). The features of subfalcine and transtentorial herniation were seen on admission in 18/24 (75%) patients.

Outcome

Out of 24 patients with CVST who underwent surgical decompression, 7 patients died. Among the patients who died, two were due to non-neurological complications. One patient had a fatal pulmonary embolism while the other succumbed due to postoperative pneumonia and sepsis. All the patients who survived were clinically evaluated at 3, 6 and 12-month intervals, and their Modified Rankin score was calculated and tabulated [Table 2]. The average follow-up was 14 months (range 12–28 months).

Table 1: Patient characteristics of surgically treated patients

Characteristics	Value, *n* (%)
Age (years)	
Mean	37.5
Range	19–60
Gender	
Male	10 (41.7)
Female	14 (58.3)
Symptom duration (days)	5.4
Range	1–14
Presenting symptoms	
Headache	17 (70.8)
Altered sensorium	13 (54.2)
Motor deficit	11 (45.8)
Seizure	8 (33.3)
Vomiting	7 (29.2)
Fever	4 (16.7)
Generalised weakness	3 (12.5)
GCS on presentation	
13–15 (good)	3 (12.5)
9–12 (mod)	8 (33.3)
<9 (poor)	13 (54.2)
Radiological Imaging showing the venous sinuses involved	
Superior sagittal sinus	11 (45.8)
Superior sagittal sinus and transverse sinus	7 (29.2)
Transverse sinus and sigmoid sinus	3 (12.5)
Only Transverse sinus	2 (8.3)
Superior sagittal sinus, transverse sinus and straight sinus	1 (4.2)
Time elapsed between presentation and surgery	
Within 6 h	16
Within first 24 h	4
Between 24–48 h	3
After 48 h	1
Thrombophilia profile	
Protein C deficiency	2 (8.4)
Protein S deficiency	4 (16.7)
Hyperhomocystinemia	3 (12.5)
Factor V mutation analysis	2 (8.4)

Illustrative Cases

Case 1

A 42-year-old female, a known case of Graves' disease, was on treatment for thyrotoxicosis. She was brought to the hospital with a headache, altered sensorium and left-sided weakness for 3 days. CT of the brain revealed a large hypodense region in the right parieto-occipital area, with areas of hyperdensity indicative of a venous infarct with haemorrhagic transformation. Further angio study revealed right transverse sinus thrombosis. Right temporo-parietal craniotomy with lax duroplasty was done. Postoperative CT scan performed after 5 days showed an organised infarct in the right parieto-occipital region with no midline shift. She gradually improved in sensorium and power and at the 3-month follow-up was Grade 5. The thrombophilia profile showed decreased Protein S level and AT–III levels [Figure 1].

Case 2

A 54-year-old male, a known case of hypertension, was brought unconscious (GCS – 10/15) to the casualty since

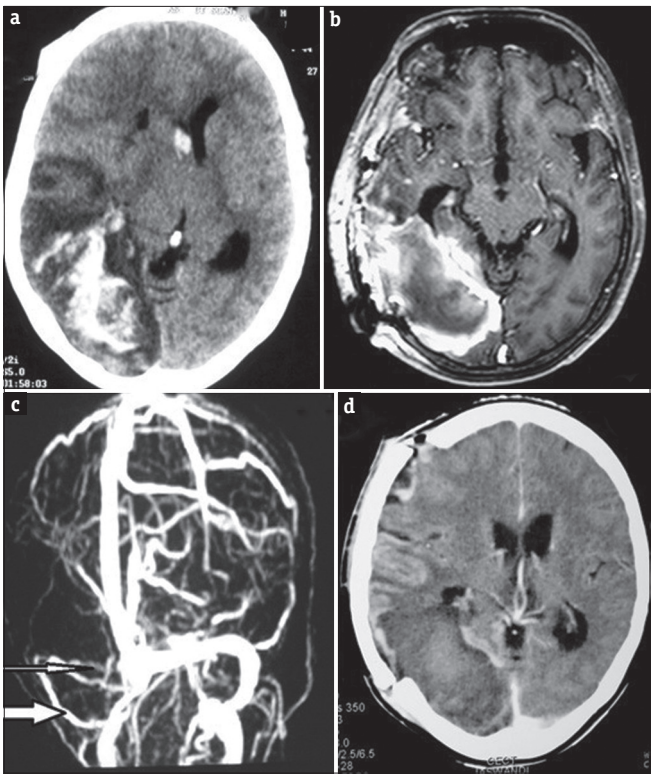

Figure 1: (a) Computed tomography (CT) brain showing a large right parietooccipital infarct with mass effect and midline shift. (b) Magnetic resonance (MR) imaging T1-weighted image showing hypo to iso intense infarct with hyperintense rim. (c) Postoperative delayed (6 months) MR Venography showing partially recanalised right transverse and sigmoid sinus with collateral formation. (d) postoperative plain CT showing resolution of midline shift and mass effect

Table 2: The modified Rankin scale of surgically operated patients

Modified Rankin scale	3 months	6 months	1 year
0	0	0	2
1	0	8	11
2	3	4	2
3	6	3	1
4	7	2	1
5	1	0	0

2 h. CT showed a large infarct in the right cerebellum with haemorrhagic transformation. Magnetic resonance angiogram showed occlusion of the right transverse and sigmoid sinus. There was proximal hydrocephalus and hence a decision to decompress the posterior fossa was taken. Suboccipital craniotomy with evacuation of the hematoma was performed. The patient was electively sedated and paralysed for 48 h. Patient was extubated later and at 3 months follow-up had moderate disability (Modified Rankin scale 3) which improved to slight disability (Modified Rankin scale 2) at 12 months follow-up. Postoperative CT showed resolution of the hematoma [Figure 2]. The thrombophilia profile showed decreased Protein C levels and moderately increased homocysteine levels.

Case 3

A 47-year-old female who had a normal delivery, G3P2 L1, had a sudden onset of headache and vomiting 1 day after parturition. She had a preference to sleep but was arousable with right-sided weakness (Power grade 2/5). CT showed a large venous infarct with haemorrhagic transformation in the left frontoparietal region. CT angiography showed thrombosis of the Superior Sagittal Sinus. As the patient was hemodynamically stable (no bradycardia), we decided to manage conservatively with anticonvulsants, cerebral decongestants and IV fluids. Patient was neurologically the same for 3–4 days, following which she showed gradual improvement. On day 10, she was relieved of headache, was mobilised and was on an oral diet. Postoperative CT after 6 months showed gliotic changes [Figure 3].

Discussion

CVST is a rare brain vascular disease accounting for 0.5%–1% of all strokes, affecting predominantly the younger age group. CVST is a multifactorial condition, with at least one associated risk factor identified in 85% of affected adults. These risk factors are usually associated with the thrombogenic triad of Virchow, which includes vessel wall injury, blood stasis and hypercoagulability.[6]

The diverse range of clinical presentations complicates the diagnosis of CVST. A high level of suspicion and

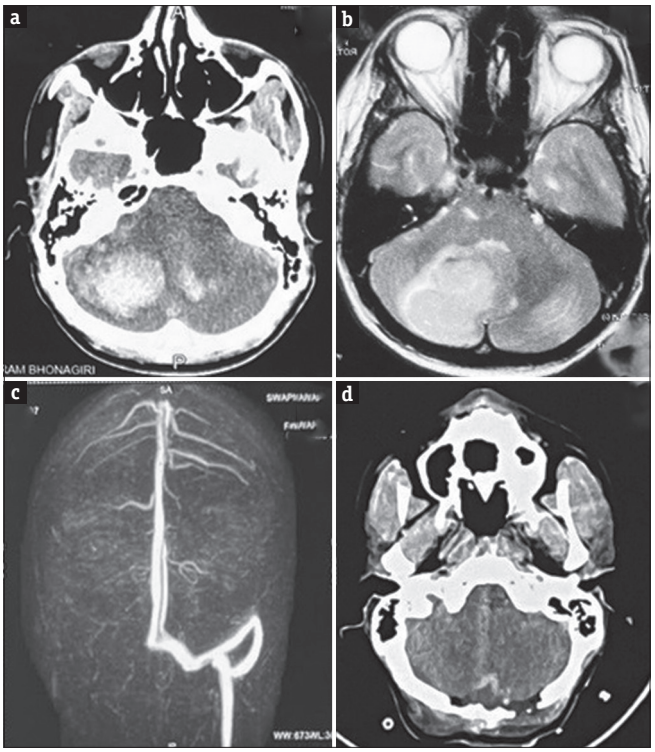

Figure 2: (a) Computed tomography (CT) brain showing right cerebellar infarct with haemorrhagic transformation. There is compression of the 4th ventricle and mass effect. (b) Shows magnetic resonance (MR) imaging, T2-weighted image showing a hyperintense lesion. (c) MR Venography showing thrombosed right-sided transverse and sigmoid sinus. (d) Postoperative plain CT showing evacuation of hematoma and resolution of mass effect

clinical expertise is crucial for identifying affected individuals. Diagnosis:

1. Laboratory Tests: In addition to routine blood investigations, a thrombophilia profile needs to be done for all patients. This is not only needed to establish a diagnosis but also to decide on the need for anticoagulation post-treatment of CVST
2. Neuroimaging
3. CT Scan
4. CT Venography
5. MRI and Magnetic Resonance Venogram
6. Digital subtraction angiography.

It needs to be noted that in CVST, our observation has been that the radiological picture (CT or MRI) appears more aggressive than the clinical picture. Hence, in patients having mild neurological deficits, a conservative trial involving decongestants, controlled mechanical ventilation, head elevation and other supportive measures to reduce ICP might tide them over the situation. In conservatively managed patients, we need to be extremely vigilant and identify neurological deterioration early to intervene surgically.

In cases of CVST, the timing of surgery is extremely important. We need to be extremely vigilant to pick

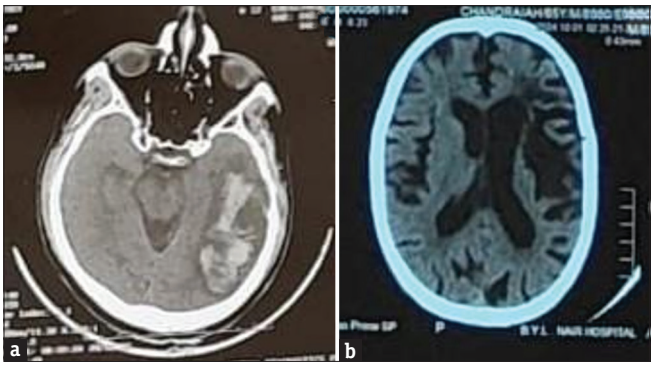

Figure 3: (a) Plain computed tomography (CT) showed a large venous infarct with haemorrhagic transformation in the left frontoparietal region with mass effect and midline shift. (b) Postoperative CT after 6 months showing gliotic changes

up the following signs, which could make us intervene surgically.

1. Unequal pupils
2. Bradycardia
3. Deteriorating GCS and clinical condition inspite of adequate medical management.

Even though medical management is the treatment of choice in these cases, the timing of surgical intervention, in indicated cases, should be appropriate to get good results.

Medical management

Anticoagulant therapy: The 2017 European Stroke Organization guidelines for the diagnosis and treatment of CSVT, endorsed by the European Academy of Neurology, recommend the following for anticoagulation therapy in CSVT:[9] Therapeutic dosage of heparin to all patients with acute cerebral venous thrombosis (CVT), even in the presence of intracerebral haemorrhage. − Low molecular weight heparin (LMWH) is preferred over unfractionated heparin, except in patients who are allergic to LMWH or when rapid reversal of anticoagulant effects is necessary. − The American Heart Association/American Stroke Association guidelines recommend anticoagulation for 3-6 months in cases of provoked CVST, 6–12 months for unprovoked CVST and potentially lifelong for recurrent CVST, venous thromboembolism following CVST, or CVST associated with severe thrombophilia, aiming for a target international normalised ratio of 2–3.[6]

Seizure control: A prospective study identified intracranial haemorrhage, cortical vein thrombosis and focal neurological deficits as independent predictors of early seizures, indicating that prophylactic antiepileptic treatment may be beneficial for these patients.[10] Another study found that focal sensory deficits and admission imaging revealing focal oedema or infarcts (both ischemic and haemorrhagic) are significant predictors of seizures in patients with CVT.[11] Several studies have also shown that the presence of supratentorial lesions is a predictor of seizures.[12] Although the duration of treatment is not well-defined, it is recommended to administer antiepileptic therapy to acute CSVT patients who present with seizures and supratentorial lesions to prevent recurrence.[9]

A. Treatment of raised ICP: Cerebral oedema is common in CSVT patients. Mild swelling usually improves with hydration and anticoagulant therapy, which helps to dissolve the thrombus, increase blood flow and decrease ICP. For patients experiencing headaches, analgesics can be administered for symptomatic relief. Transtentorial herniation of the brain is the leading cause of death in CSVT patients.[7] Carbonic anhydrase inhibitors such as acetazolamide help to lowering the ICP and alleviate headache as well as preventing visual deterioration.[13] The European Federation of Neurological Societies recommends the following: − LP can be considered before starting of anticoagulation, in the absence of parenchymal insult (large infarcts or haemorrhages) in patients with intracranial hypertension. − Acetazolamide may be considered in patients with persistent papilledema. − In patients experiencing ongoing visual deterioration despite multiple lumbar punctures and acetazolamide administration, shunting procedures such as lumboperitoneal or ventriculoperitoneal shunts, as well as optic nerve fenestration, may be considered. Steroid therapy has proven ineffective due to insufficient scientific evidence. Treatment for oedema should follow the general principles for managing elevated ICP. These include elevating the head at 30°, hyperventilation (target PaCO2 = 30–35 mm Hg) and intravenous administration of osmotic diuretics. We suggest that LP can be offered to reduce ICP in patients where the perimedullary cisterns are open
B. Effective management of CSVT requires a detailed diagnostic assessment to uncover the underlying etiological factors. This should be followed by appropriate treatment strategies tailored to address these factors.

Surgical management

Even though medical management is the treatment of choice, some patients need surgical decompressive surgery, such as craniectomy.[14] These patients are usually those who show clinical deterioration, with severe thrombosis and impending herniation due to a significant parenchymal lesion. The occurrence of CSVT during pregnancy or the postpartum period is not a contraindication for future pregnancies.[15] CSVT occurring during these periods should be treated with LMWH and continued through 6 weeks of postpartum.[16] All forms of hormonal contraception,

except progesterone-only therapies, should be discontinued in patients who develop CSVT while using oral contraceptives or hormone replacement therapy. Other forms of contraception can be used as an alternative in these patients.[17]

There are no proper randomised trials comparing decompressive surgery with optimal medical management in CVST. Unlike in arterial strokes, the effectiveness of DC in CVT is not firmly established. DC was performed in only 1.4% of cases according to the ISCVT2 study.[18] Nevertheless, it is clear that for severe cases involving life-threatening large haemorrhagic infarctions with mass effect, decompressive surgery may represent the sole life-saving intervention.[19]

We did surgical decompression within the first 24 h of admission in a total of 20/24 patients (83.33%). In CVST, perfusion and diffusion MRI show a penumbra-like condition of affected brain tissue that is metabolically compromised but still viable.[20] According to this, there is are higher possibility of late neurological symptoms improvement in cerebral tissue affected by CVST; it is advisable to avoid resecting brain tissue during surgery.

Over the years, several observational studies have indicated that decompressive surgery enhances survival and yields favourable outcomes even in patients with a clinically poor condition.[21,22]

We used the modified Rankin Score (mRS) to assess functional recovery among the survivors after surgical decompression. We had 70% of survivors having an mRs of ≤2 by 6 months of follow-up. This aligns with findings from Aaron *et al*.[14] who used the modified Rankin Scale (mRS) and reported that 68% of patients achieved an mRS score of <2 after 6 months. Similarly, Zhang *et al*. reported a good functional outcome in 56.9% of cases.[22]

Limitation of this study includes the low number of cases, and we did not include those patients in the study to whom we advised for surgical decompression but who were not willing for the surgery.

Conclusion

CVST is a highly morbid condition which is multifactorial. The prognosis depends on how early the treatment is initiated, the GCS at presentation, the area of brain damaged and associated prothrombotic conditions. The radiological picture appears more aggressive compared to the clinical status, and hence, a significant number of patients can be managed medically. Even though medical management is the treatment of choice, certain red flags should be identified early, and timely intervention in the form of surgical decompression in a patient with a malignant venous infarct with impending brain herniation should be considered. We feel that the timing of surgery is critical in improving outcomes. Since survivors after decompression experience a favourable functional outcome with minimal disability in most cases, it is crucial to conduct randomised prospective studies to establish guidelines for early surgical intervention.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Protective or Pretentious? A Critical Appraisal of Embolic Protection Devices in Carotid Artery Stenting: Four-year Experience From a High-volume Tertiary Centre

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Abstract

Introduction: Carotid artery stenosis is a significant cause of ischaemic stroke. Carotid artery stenting (CAS) is an established alternative to endarterectomy, with embolic protection devices (EPDs) introduced to reduce periprocedural embolic events.

Aim and Objective: This study aimed to compare the clinical outcomes of CAS performed with and without EPDs in patients treated at BYL Nair Charitable Hospital, Mumbai.

Materials and Methods: A retrospective analysis of 63 patients undergoing CAS between May 2020 and April 2024 was conducted. Patients were divided into two groups: CAS with EPD (n = 43) and CAS without EPD (n = 20). Clinical parameters, procedural details, complications, hospital stay and short-term outcomes were evaluated.

Results: Out of 63 cases, 40 were male and 23 were female. Hypertension and diabetes were common co-morbidities. The EPD group demonstrated a lower incidence of periprocedural transient ischaemic attack and myocardial infarction compared to the non-EPD group. Silent cerebral embolic lesions on diffusion-weighted magnetic resonance imaging were also reduced in the EPD group. Hospital and intensive care unit stays were shorter in patients with EPD use. Mortality occurred exclusively in the non-EPD group.

Conclusion: Use of EPDs during CAS is associated with reduced periprocedural complications and shorter hospitalisation. While CAS without EPD remains a viable option in selected cases, routine use of EPDs should be considered to enhance procedural safety, especially in resource-limited settings.

Keywords: *Carotid artery stenosis, carotid artery stenting, embolic protection device*

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Introduction

Stroke remains the second leading cause of death worldwide and is a principal contributor to long-term disability. One of the key underlying pathologies linked to ischaemic stroke is extracranial carotid artery stenosis, which can be managed using carotid endarterectomy (CEA) or carotid artery stenting (CAS) as revascularisation strategies. While CEA has traditionally been the mainstay of treatment, CAS has increasingly gained recognition as a viable and less invasive alternative, particularly in patients considered high risk for surgery.[1,2]

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Landmark trials such as the Carotid Revascularisation Endarterectomy versus Stenting Trial (CREST) and the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial have demonstrated comparable long-term outcomes between CAS and CEA, including similar rates of restenosis and major adverse events.[3-5] Moreover, CAS offers

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distinct procedural advantages including the avoidance of general anaesthesia, reduced risk of cranial nerve injury and maintenance of cerebral perfusion during the intervention, making it favourable in selected patient groups.[6,7]

However, the risk of distal embolisation during CAS remains a significant concern, particularly during guidewire manipulation, balloon angioplasty or stent deployment. To mitigate this risk, various embolic protection devices (EPDs) – including distal filters, distal occlusion balloons and proximal occlusion systems – have been developed and are widely used in clinical practice.[8,9] Despite their prevalent use, the actual benefit of EPDs continues to be debated. While some studies suggest that EPDs lower the risk of periprocedural stroke and transient ischaemic attack (TIA), others report no significant differences in clinical outcomes between procedures performed with or without EPDs.[10,11]

In resource-constrained healthcare settings such as those in many developing countries, the cost implications of using neuroendovascular devices like EPDs can be substantial and often borne by the patient. Thus, understanding the safety and efficacy of CAS without EPDs, particularly in the context of skilled operator performance, is of clinical relevance.

This study aims to contribute to this discussion by presenting the outcomes from a single-centre experience with CAS performed with and without use of EPDs, while also emphasizing the importance of procedural expertise as a determinant of success.

Materials and Methods

This was retrospective single-centre study conducted in patient of ICA stenosis admitted under the Department of Neurosurgery, TNMC and BYL Nair Charitable hospital, Mumbai to evaluate and compare the clinical outcomes of internal carotid artery (ICA) stenting with and without the use of EPDs. A total of 63 patients of ICA stenosis who underwent CAS between May 2020 and April 2024 were included. The study cohort comprised both symptomatic and asymptomatic individuals.

All CAS procedures were performed by experienced interventional specialist with extensive training and proficiency in carotid interventions.

Patient selection criteria

Symptomatic group

Patients were classified into symptomatic and enrolled in the study based on the following inclusion criteria:

- A documented history of a neurological event, including TIA, minor ischaemic stroke or a non-disabling major stroke affecting the territory supplied by the ipsilateral ICA, occurring within the prior 180 days
- Evidence of significant carotid artery narrowing, defined as ≥50% stenosis on digital subtraction angiography (DSA), or ≥70% stenosis on non-invasive imaging such as duplex ultrasonography, computed tomography angiography (CTA) or magnetic resonance angiography (MRA)
- Determination of medical fitness for carotid stenting by both neurological and cardiovascular assessment
- Ability to provide informed consent and adhere to follow-up protocols after the procedure.

Asymptomatic group

Patients with no recent cerebrovascular symptoms were classified into asymptomatic and included if they fulfilled the following criteria:

- Absence of any history of ipsilateral TIA, stroke or transient visual disturbance (amaurosis fugax) within the past 6 months
- Detection of ≥60% ICA stenosis, measured according to the North American Symptomatic CEA Trial (NASCET) criteria, confirmed via DSA or validated non-invasive imaging modalities (ultrasound, CTA or MRA)
- Presence of one or more high-risk imaging features, including:
  - Ulcerated or irregular plaque morphology
  - Documented rapid progression of stenosis on follow-up imaging
  - High-grade stenosis or occlusion in the contralateral carotid artery
  - Impaired cerebrovascular reserve on functional perfusion studies.

Case scenario

- A 65-year-old male presented with recurrent right-sided TIAs. DSA demonstrated severe, ulcerated right ICA stenosis. A distal embolic protection device was deployed across the lesion, followed by controlled balloon angioplasty and placement of a self-expanding stent. Completion angiography showed excellent luminal restoration with minimal residual stenosis. The patient remained neurologically stable with no post-procedure DWI lesions. This figure illustrates the standard technique of EPD-assisted CAS with angioplasty in high-risk plaque morphology [Figure 1].
- A 50-year-old patient with symptomatic left ICA stenosis underwent CAS using a distal embolic protection device. Due to favourable vessel

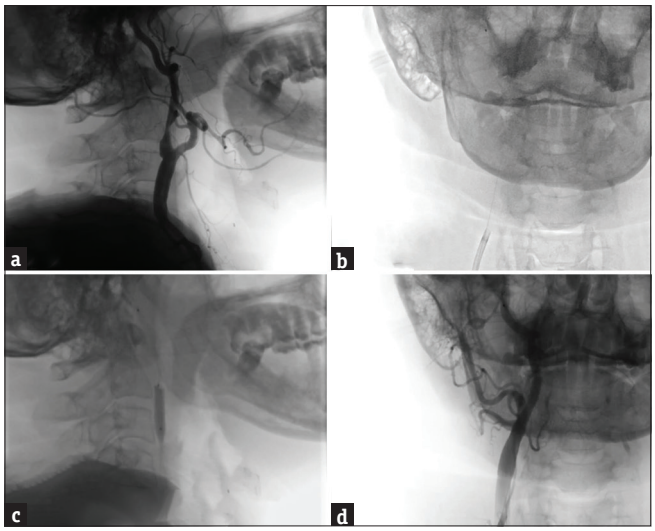

Figure 1: Embolic protection device with angioplasty. (a) Right common carotid artery and internal carotid artery (ICA) Pre-operative digital subtraction angiography (DSA) lateral view. (b) Right ICA with protection device deployed anteroposterior view. (c) Right ICA with balloon angioplasty done Lateral view. (d) Right ICA Post-stenting DSA with stent *in situ*

Table 1: Patient demographics, co-morbidities and presenting symptoms in patients undergoing carotid artery stenting with and without embolic protection devices

Variable	CAS with use of EPD	CAS without use of EPD
Total cases	43	20
Age (years)		
Mean±SD	61.4±9	59.6±10.2
Range	52–70	54–68
Gender		
Male	27	13
Female	16	7
Comorbidity		
Hypertension	34	13
Dyslipidaemia	29	6
DM	31	10
CAD	12	3
PAD	7	1
Symptoms		
Symptomatic	33	16
Asymptomatic	10	4

EPD: Embolic protection devices, PAD: Peripheral arterial disease, CAD: Coronary artery disease, DM: Diabetes mellitus, SD: Standard deviation, CAS: Carotid artery stenting

diameter and soft plaque characteristics, direct stenting was performed without pre- or post-dilatation. Angiography confirmed satisfactory stent expansion and restored antegrade flow. The patient experienced no peri-procedural neurological deficits. This figure demonstrates an EPD-assisted CAS approach where angioplasty is avoided to reduce embolic burden in select

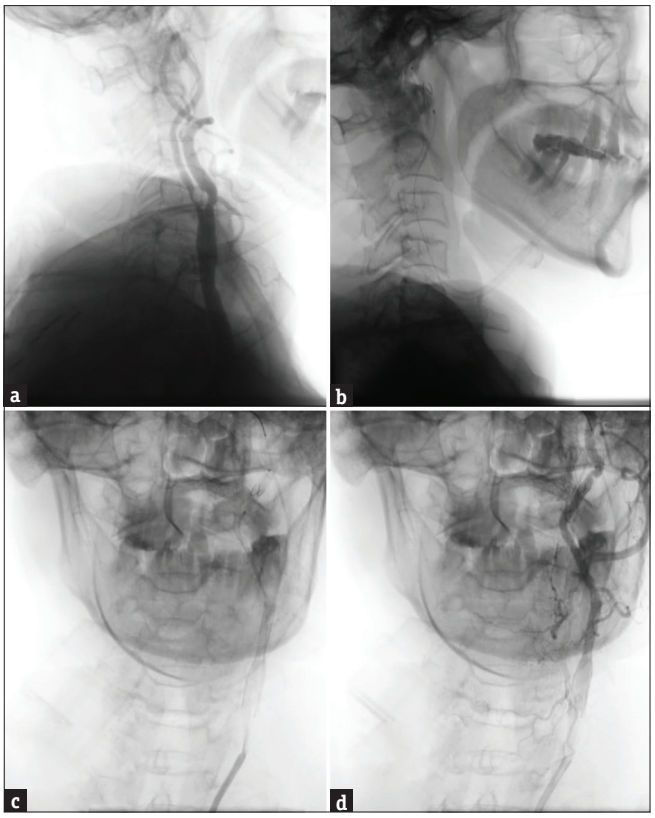

Figure 2: Embolic protection device without angioplasty. (a) Left common carotid artery (CCA) internal carotid artery (ICA) stenosis pre-operative digital subtraction angiography with stenosis lateral view. (b) Left ICA with protection device deployed lateral view. (c) Left CCA ICA stent deployed anteroposterior (AP) view. (d) Left ICA runs post-stenting AP view

anatomical and plaque-related scenarios [Figure 2].

- A 58-year-old male with significant cardiac comorbidities and a Type III aortic arch underwent CAS for high-grade right ICA stenosis. Due to severe arch tortuosity and anticipated difficulty in safely advancing a protection device, stenting was performed without EPD. A self-expanding stent was deployed successfully with good angiographic outcome. Post-procedure MRI revealed a small silent DWI lesion, but the patient remained asymptomatic. This figure highlights selective unprotected CAS in challenging vascular anatomy [Figure 3].

Angiographic and clinical data collection

Demographic data such as age, gender and symptomatic status were recorded. Pre- and post-procedure angiographic evaluations were conducted using DSA. Arterial lesion characteristics included lesion length, percent stenosis (measured using NASCET criteria), plaque morphology and lesion configuration (contiguous or sequential/remote).

Table 2: Lesion characteristics, aortic arch type, angioplasty details and stent outcomes in patients undergoing carotid artery stenting with and without embolic protection devices

Variable	CAS with use of EPD	CAS without use of EPD
Side of ICA involved		
Right ICA	25	13
Left ICA	18	7
Stenosis (%)		
50–69	24	11
≥70	19	9
Length of plaque (mm)		
Mean±SD	28.3±2.5	27.5±2.4
Range	16–34	14–31
Characteristics of plaque		
Smooth	25	15
Irregular	12	3
Ulcerated	6	2
Aortic arch		
Type 1	37	17
Type 2	4	2
Type 3	2	1
Angioplasty		
Pre-stent dilatation only	31	13
Post-stent dilatation only	4	2
Both pre and post stent dilatation	5	3
No angioplasty	3	2
Angioplasty rate (%)	93.02	90.0
Type of stents used		
Residual stenosis (%)		
<20	39	17
20–40	3	2
>40	1	1

SD: Standard deviation, ICA: Internal carotid artery, EPD: Embolic protection devices, CAS: Carotid artery stenting

Table 3: Intensive care unit and overall hospital stay in patients undergoing carotid artery stenting with and without embolic protection devices

Variable	CAS with use of EPD	CAS without use of EPD
ICU stay (days)		
Mean±SD	1.4±1.0	1.7±1.1
Range	1–5	1–8
Overall hospital stay (days)		
Mean±SD	2.2±1.7	2.8±1.9
Range	2–9	2–13

SD: Standard deviation, ICU: Intensive care unit, EPD: Embolic protection devices, CAS: Carotid artery stenting

Plaque morphology was assessed categorised as smooth, irregular or ulcerated. Lesion length was measured in millimetres from the proximal to distal extent of the maximum stenosis.

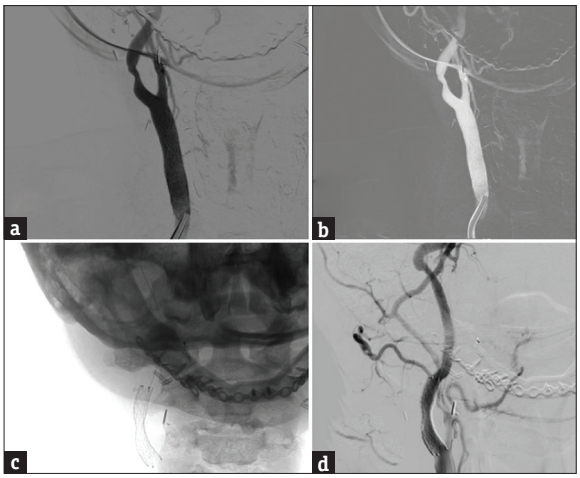

Figure 3: Internal carotid artery (ICA) stenting without embolic protection device. (a and b) Right ICA stenosis pre-operative digital subtraction angiography (DSA) image anteroposterior view. (c) Right ICA with stent deployed in stenosed segment. (d) Right ICA with post-stenting DSA image with stent *in situ*

Embolic protection device usage protocol

The use of EPDs was documented and categorised. EPD deployment was selectively determined based on plaque morphology and vascular diameter.

EPDs were employed in cases with
1. Unstable or mobile plaques
2. Circumferential severe ulcerations
3. Irregular surface morphology.

The study population of 63 patients undergoing CAS was divided into two groups based on the use of EPDs. A 43 patients received CAS with the deployment of an EPD during the procedure (EPD group), while 20 patients underwent CAS without EPD assistance (non-EPD group). The decision to use an EPD was made selectively, based on plaque morphology, vessel diameter and judgement of interventional specialist to optimise procedural safety.

The comparison focused on immediate post-procedural complications, the occurrence of peri-procedural stroke or myocardial infarction, mortality rates and the long-term risk of ipsilateral stroke. Additional subgroup analysis was performed based on plaque type, lesion length and percentage of stenosis.

Follow-up and outcome assessment

Post-procedure, patients were monitored for 30 days for the occurrence of any stroke (unilateral or bilateral) of any severity, myocardial infarction and all-cause mortality. Patients underwent regular clinical and imaging follow-up for a mean duration of 12 months, with some patients followed for up to 2 years. During a long-term follow-up, particular attention was given

Table 4: Clinical and radiological outcomes of carotid artery stenting with and without embolic protection devices

Variable	CAS with use of EPD	CAS without use of EPD	*P*
Functional			
TIA	1	5	0.037 (significant)
Stroke	0	0	1.0
Vasospasm	0	4	0.047 (significant)
Myocardial infarction	0	1	0.337
Mortality	0	2	0.115
Radiological			
Stent thrombosis	0	1	0.337
Stent migration	0	0	1.0
Silent embolic lesion	0	3	0.083

EPD: Embolic protection devices, TIA: Transient ischaemic attack, CAS: Carotid artery stenting

to the incidence of ipsilateral stroke, restenosis and any delayed adverse events related to the stenting procedure.

Statistical analysis

All the data were analysed using the SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). The continuous variables such as age, plaque length and hospital stay were expressed as mean ± standard deviation and compared between the groups using the independent Student's *t*-test. Given the small sample size and low event rates, categorical variables, including co-morbidities, plaque morphology, procedural details and peri-procedural complications were analysed using Fisher's exact test. $P < 0.05$ was considered statistically significant.

Ethics approval

Ethical approval for the study was provided by Institutional ethics committee at BYL Nair Hospital, Mumbai on 14/06/2025.

Results

This was retrospective single-centre study conducted in patient of ICA stenosis admitted under the Department of Neurosurgery, TNMC and BYL Nair Charitable hospital, Mumbai.

A total of 63 patients underwent internal CAS at TNMC and BYL Nair Charitable Hospital between May 2020 and April 2024. Of these, 43 (68.3%) procedures were performed with use of EPDs, while 20 (31.7%) performed without use of EPDs. The mean age of the cohort was 61.4 ± 9 years in CAS with EPD cohort, whereas 59.6 ± 10.2 in CAS without EPD cohort, with a male predominance in both groups. In this study, hypertension followed by DM was the most common comorbiditiy to be found, whereas coronary artery disease (CAD) and peripheral arterial disease (PAD) were the less common [Table 1].

Symptomatic patients accounted for 77% (33/43) of cases in the EPD group and 80% (16/20) in the non-EPD group. Right ICA involvement was noted in 58% (25/43) of patients with EPD and 65% (13/20) without EPD.

Regarding stenosis severity, 56% (24/43) of patients with EPD had 50%–69% stenosis, while 44% (19/43) had ≥70%. In the non-EPD group, 55% (11/20) had 50%–69% stenosis and 45% (9/20) had ≥70% stenosis. Mean plaque length was similar between groups: 28.3 ± 2.5 mm in the EPD group and 27.5 ± 2.4 mm in the non-EPD group.

Plaque morphology differed between groups, with smooth plaques being the most common, observed in 58% (25/43) of patients in the EPD group and 75% (15/20) in the non-EPD group. Irregular plaques were seen in 28% (12/43) of EPD cases and 15% (3/20) of non-EPD cases. Ulcerated plaques were noted in 14% (6/43) of patients with EPD and 10% (2/20) without EPD. Most patients had a Type 1 aortic arch (86% in EPD group, 85% in non-EPD group).

Angioplasty was performed in the majority of cases, with a rate of 93.02% in the EPD group and 90% in the non-EPD group. Pre-stent dilatation only was the most frequent approach in both groups. Residual stenosis post-procedure was <20% in 91% (39/43) of EPD cases and 85% (17/20) of non-EPD cases [Table 2].

The mean intensive care unit stay was 1.4 ± 1.0 days for EPD patients and 1.7 ± 1.1 days for non-EPD patients. Overall hospital stay averaged 2.2 ± 1.7 days in the EPD group and 2.8 ± 1.9 days in the non-EPD group [Table 3].

Clinical complications included TIAs in five patients of non-EPD group. Vasospasm, myocardial infarction and mortality occurred exclusively in the non-EPD group, affecting 4, one and two patients, respectively. Radiologically, silent embolic lesions were detected in three patients without EPD [Table 4].

Discussion

Stroke remains a major global cause of death and is a leading contributor to long-term disability. CAS has emerged as a less invasive alternative to CEA, especially in high-surgical risk patients. Recent literature[12,13] suggests that endovascular interventions for carotid artery disease are associated with a risk of cerebral ischaemia and other complications that are comparable to those seen with conventional surgical techniques.

Furthermore, studies[14,15] indicate that the use of EPDs during these procedures may minimise the risk of intracranial embolisation, thereby reducing the incidence of major neurological complications and yielding outcomes similar to those of CEA.

The mean age in our cohort was 61.4 ± 9 years in the EPD group and 59.6 ± 10.2 years in the non-EPD group, with a clear male predominance in both groups. These findings align with broader epidemiological data demonstrating higher prevalence of carotid atherosclerosis in middle aged to elderly males.[1,2] The age and gender distribution in our study is comparable to the CREST trial,[3] which reported mean ages in the low 60s and male predominance amongst participants undergoing CAS or CEA.

Hypertension was the most prevalent comorbidity in both groups, followed by diabetes mellitus and dyslipidaemia. CAD and PAD were the less common. This distribution is consistent with prior reports emphasising hypertension and diabetes as dominant risk factors for carotid artery disease.[4,5] The presence of multiple vascular risk factors underscores the systemic nature of atherosclerosis and reinforces the need for comprehensive cardiovascular management alongside revascularisation.

Symptomatic patients comprised 77% of the EPD group and 80% of the non-EPD group, which is comparable to patient selection in large randomised trials such as SAPPHIRE[4] and CREST.[3] The comparable proportion of symptomatic patients suggests that both groups had similar baseline cerebrovascular risk, allowing for a balanced comparison of outcomes.

Stenosis severity was similar between groups, with approximately 55% having moderate stenosis (50%–69%) and 45% having severe stenosis (≥70%). Plaque morphology predominantly featured smooth plaques, but irregular and ulcerated plaques were also present, slightly more in the EPD group. This distribution is consistent with previous studies highlighting the predominance of smooth plaques but with significant proportions of complex morphology plaques in high-risk patients.[6,7] The higher prevalence of irregular and ulcerated plaques in the EPD group likely guided the selective use of EPDs to mitigate embolic risk.[8]

Angioplasty was performed in over 90% of cases in both groups, primarily as pre-stent dilatation, which is the standard technique for optimizing stent deployment.[9] Residual stenosis post-procedure was <20% in 91% of EPD cases and 85% in non-EPD cases, demonstrating effective luminal restoration in both groups. These rates are comparable to outcomes reported by Brott *et al*. in CREST,[3] reinforcing the technical success of CAS regardless of EPD use.

Mean ICU stay was slightly shorter in the EPD group (1.4 ± 1.0 days) versus the non-EPD group (1.7 ± 1.1 days), while overall hospital stay was also shorter in the EPD group (2.2 ± 1.7 days vs. 2.8 ± 1.9 days). This difference may reflect a trend towards quicker recovery or fewer complications with EPD use, consistent with studies indicating fewer periprocedural neurological events when EPDs are used.[10,11]

Clinically, TIAs occurred in five patients in non-EPD group which was statistically significant as compared to one patient in EPD group. However, vasospasm occurred in four patients exclusively in the non-EPD group, alongside one myocardial infarction and two deaths, whereas none were reported in the EPD group. Radiologically, silent embolic lesions were detected in the three patients of non-EPD group. These findings support the protective effect of EPDs against cerebral embolisation during CAS, echoing previous reports that demonstrate reduced rates of TIA and silent embolic lesions with EPD use.[12,16]

Nonetheless, some studies argue that CAS without EPDs can be performed safely in experienced hands,[13,14] as reflected in our relatively low overall complication rates. The decision to use EPDs was tailored to plaque morphology and lesion complexity, which likely contributed to minimizing adverse events in both groups.

This study has several limitations, including its retrospective, single-centre design and relatively small sample size. The use of stent without of EPD primarily done during the early phase of our institutional experience, with varying interventional specialists expertise and techniques, potentially influencing outcomes. Although interventional specialists gained more experience and used protection devices more consistently in later cases, patient complexity differed over time. Despite these limitations, this remains one of the larger single-centre analyses with detailed data collection and independent neurological assessments, providing valuable insights that warrant validation in larger prospective studies.

Conclusion

CAS is a complex procedure where careful patient selection and individualized assessment of anatomical and clinical factors are essential to optimise outcomes. Our experience indicates that cerebral EPDs are effective in reducing distal embolisation during CAS, particularly in the immediate periprocedural period. Nevertheless, their influence on long-term

embolic complications is still not clearly established. Successful use of EPDs requires a significant learning curve, and these devices are not without potential complications. Our findings highlight the need for tailored use of EPDs, weighing their benefits against risks based on patient and anatomical factors. Larger, randomised studies are necessary to clarify the definitive role of embolic protection in improving CAS outcomes.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Exploring the Role of Systemic Inflammatory Index, Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio in Moyamoya Disease: A Case–Control Study

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Abstract

Background: Moyamoya disease (MMD) is a rare cerebrovascular condition of uncertain aetiology. Immune-inflammatory markers, such as the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and systemic immune-inflammation index, have garnered interest for their potential to elucidate the immune-inflammatory state in various conditions.

Objective: To investigate the role of immune-inflammatory markers in patients with MMD.

Methods: A total of 105 patients were included, comprising 55 MMD patients (cases) and 50 age- and sex-matched controls with degenerative spine disease. Complete blood count parameters were analysed to calculate the immune-inflammatory markers.

Results: The mean levels of immune-inflammatory biomarkers were significantly higher in the case group compared to the control group ($P < 0.001$). Notable sex-based differences were observed with significantly elevated markers in female patients compared to males ($P = 0.025$). However, no significant differences were found between paediatric and adult subgroups ($P = 0.5$) or between haemorrhagic and ischemic subgroups ($P = 0.5$).

Conclusion: This study demonstrated significantly elevated immune-inflammatory markers in patients with MMD, with notably higher levels observed among females, suggesting a possible hormonal influence. However, as our study did not include direct hormonal assessments, this association remains speculative. No significant differences were noted between paediatric and adult populations or between ischemic and haemorrhagic presentations. Further well-designed studies incorporating hormonal profiling are necessary to clarify the underlying mechanisms and validate the observed sex-related inflammatory variation.

Keywords: *Immune-inflammatory marker, moyamoya disease, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, systemic immune-inflammation index*

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Introduction

Moyamoya disease (MMD) is a non-atherosclerotic cerebrovascular structural abnormality first described by Japanese scholars Takeuchi and Shimizu in 1957.[1] Despite extensive research, the exact pathophysiological mechanism underlying MMD remains elusive. However, an abnormal immune response has been hypothesised as a potential trigger. Histopathological studies of intracranial vessels in MMD patients have revealed smooth muscle hyperplasia, T-cell proliferation and macrophage infiltration within

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the vessel walls. Immunohistochemical analyses further demonstrated abnormal expressions of immunoglobulin G and S100A4 proteins in vascular smooth muscle cells.[2] In addition, elevated plasma levels of inflammatory mediators such as monocyte chemoattractant protein-1, interleukin-1 β (IL-1 β) and stromal cell-derived factor-1α have been observed, supporting the theory of an immune-inflammatory pathology in MMD.[3,4] Recently, the platelet–lymphocyte ratio (PLR) and neutrophil–lymphocyte ratio (NLR) have emerged as easily accessible and cost-effective biomarkers of systemic inflammation. These indices have been validated in various immune-inflammatory diseases, including MMD.[5,6] In the absence of infection, PLR and NLR are considered reliable indicators of systemic inflammation. Notably, the combined use of NLR and PLR enhances the predictive accuracy for inflammatory and mucosal diseases compared to using either marker alone.[2] Building on this, Hu *et al*. proposed the systemic immune-inflammation index (SII), a comprehensive metric derived from peripheral lymphocyte, neutrophil and platelet counts, which has been shown to be more precise in capturing systemic immune-inflammatory status than NLR or PLR alone.[7]

$$\text{Systemic Inflammatory Index} = \text{Platelet count} \times \frac{\text{Neutrophil}}{\text{Lymphocyte}}$$

Compared to the individual use of PLR and NLR, the SII offers a more comprehensive reflection of the systemic immune-inflammatory state. Notably, SII is a simple, convenient, cost-effective, readily available and non-invasive biomarker.[1] Despite its advantages, the clinical significance of SII in MMD remains underexplored due to limited literature on its application in this condition. Considering that MMD is likely a disease influenced by both inflammatory and immune mechanisms, we investigated the clinical value and significance of SII, alongside NLR and PLR, in patients with MMD. This exploration aims to enhance our understanding of these biomarkers and their potential role in the pathophysiology and clinical management of MMD.

Materials and Methods

We retrospectively analysed 105 patients, including 55 diagnosed cases of MMD at a tertiary centre, from January 2019 to December 2021. For the control group (n = 50), we selected patients admitted to our ward with degenerative spine disease. Age and sex matching were performed for both groups after excluding individuals with comorbidities or routine drug use. Blood samples were not drawn specifically for the study, as total leucocyte count (TLC), differential leucocyte count (DLC) along with platelet counts are part of the routine pre-operative work-up at our centre. All samples were collected on the 1st day of admission from fasting venous blood. Written informed consent was obtained from all participants in both the case and control groups. This study was approved by the Institutional Ethics Committee (2024-119-mch-EXP-59).

Inclusion criteria

A diagnosis of MMD was confirmed through cerebral angiography based on the following findings:

1. Stenosis of the distal portion of internal carotid artery, the middle cerebral artery or anterior cerebral artery
2. Presence of abnormal collateral vessels near the site of arterial occlusion or stenosis
3. Bilateral involvement meeting criteria 1 and 2.

Exclusion criteria

1. History of infectious, inflammatory, neoplastic or haematological diseases, organ infarction or trauma, hypertension, diabetes, smoking and alcohol consumption habits
2. Combined cerebral arteriovenous malformations, cavernous haemangiomas
3. Atherosclerosis
4. Patients treated with glucocorticoids, permanent immunomodulatory drugs or anti-inflammatory drugs
5. Autoimmune diseases
6. A lack of venous blood test data.

The stage of MMD was determined by digital subtraction angiography (DSA) based on Suzuki's staging.

Demographic and laboratory data

Clinical and demographic data were collected retrospectively at the time of admission, including:

a. Patient demographics: Age, sex, risk factors for cerebrovascular disease (e.g., hypertension, diabetes and hyperlipidemia) and personal history (e.g., smoking and alcohol use)
b. Laboratory parameters: Neutrophil count, lymphocyte count, TLC, DLC, platelet count and calculated NLR, PLR and SII
c. Suzuki stage of MMD as determined by DSA.

Statistical analysis

This was done in IBM SPSS (Statistical Software for the Social Sciences) Statistics Version 20.00 (IBM SPSS Inc., Chicago, IL, USA). Continuous variables were expressed with mean ± standard deviation or median values (1st quartile - 3rd quartile), while categorical variables were expressed with frequency and related percentage. The normality of the data for continuous variables was verified using the Shapiro–Wilk test.

The means of two continuous normally distributed variables were compared by independent samples using the Student's *t*-test or ANOVA test and non-parametric test like Mann–Whitney test. For categorical variables, the Chi-square test and Fisher's exact test were done. P <0.05 was considered statistically significant.

Results

The study involved a total of 105 patients, comprising 55 individuals diagnosed with MMD and 50 age- and sex-matched controls. The control group included patients with degenerative spine disease. The mean age of participants in the MMD group was 25.3 (range: 12–40) years, while that of the control group was 29.8 (range: 15–45) years, with no statistically significant difference between the two groups (P = 0.323). The key inflammatory markers, including the SII, NLR and PLR, were compared between the MMD and control groups. The mean values of SII, NLR and PLR in the MMD group were significantly elevated compared to in the control group (P < 0.001), (P = 0.03) and (P < 0.001), respectively [Table 1 and Figures 1-3].

Further subgroup analyses were conducted within the MMD cohort. When stratified by sex, significant differences in SII, NLR and PLR were observed between female (n = 25) and male (n = 30) patients (P < 0.05). Females exhibited higher median values for SII (639, interquartile range [IQR]: 498–681), NLR (2.16, IQR: 1.6–2.52) and PLR (10.5, IQR: 8.7–13.09), compared to males, whose median values were SII: 494 (IQR: 367–608), NLR: 1.70 (IQR: 1.9–2.10) and PLR: 8.39 (IQR: 6.5–10.4) [Table 2]. No significant difference in SII, NLR and PLR was identified when comparing paediatric (age <18 years, n = 17) and adult (age >18 years, n = 38) subgroups within the MMD cohort. The median and IQR of SII, NLR and PLR in the paediatric subgroup were 507 (417–705), 1.90 (1.47–2.12) and 9.08 (7.15–10.76), respectively. In adults, these values were SII: 574 (441–823) (P = 0.5), NLR: 1.81 (1.47–2.52) (P = 0.43) and PLR: 10.14 (7.44–13.30) (P = 0.41), respectively, [Table 3].

Patients with MMD were also classified into haemorrhagic (n = 30) and ischemic (n = 25) subgroups, based on cranial MRI results and clinical history. While the haemorrhagic subgroup exhibited higher median values of SII (608, IQR: 435–760), NLR (1.94, IQR: 1.47–2.12) and PLR (9.08, IQR: 7.15–10.76) compared to the ischemic subgroup SII (506 IQR: 367–698) (P = 0.5) NLR (1.70 IQR: 1.44–2.34) (P = 0.43) and PLR (8.79 IQR: 6.67–11.87) (P = 0.41), respectively, [Table 4].

In summary, the study highlights a significant elevation in inflammatory markers SII, NLR and PLR in MMD patients compared to controls. In addition, sex-specific differences were observed, with females exhibiting higher inflammatory indices. However, no significant differences were noted between paediatric and adult MMD subgroups or between ischemic and haemorrhagic

Table 1: Comparison of demographic features and clinical characteristics between the study and control groups

Parameters	Cases (n=55)	Controls (n=50)	P
Age (years)	25.36 (12–40)	29.82 (15–45)	0.605
Male, n (%)	28 (56)	34 (68)	0.216
SII (mean)	686±571.2	311±170.8	**<0.001**
NLR	2.17±1.4	1.6±0.688	**0.03**
PLR	10.25±6.13	6.59±3.54	**<0.001**
Platelets (×10^9/L)	306±99	200±76.1	**<0.001**
Lymphocyte (×10^9/L)	34.5±10.2	34±6.9	0.96
Neutrophil (×10^9/L)	63.0±10.6	54.9±7.09	**<0.001**
TLC (×10^9/L)	10.75 (9.4–13)	7.67 (6.6–9.81)	**<0.001**

Values are mean±SD. Boldface-type indicates statistical significance with a P<0.05 (Student's *t*-test). SII: Systemic immune-inflammation index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, TLC: Total leucocyte count, SD: Standard deviation

Table 2: Comparison of immune inflammatory biomarkers in male and female subgroups

Parameters	Male (n=30)	Female (n=25)	P
SII, median (IQR)	494 (367–608)	639 (498–681)	**0.025**
NLR	1.70 (2.10–1.9)	2.16 (1.6–2.52)	**0.034**
PLR	8.39 (6.5–10.4)	10.5 (8.7–13.09)	**0.037**

Bold values represent statistically significant. SII: Systemic immune-inflammation index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, IQR: Interquartile range

Table 3: Comparison of biomarkers in paediatric and adult subgroup

Parameters	<18 years	18 years and above	P
SII, median (IQR)	507 (417–705)	574 (441–823)	0.507
NLR, median (IQR)	1.90 (1.47–2.12)	1.81 (1.47–2.52)	0.439
PLR, median (IQR)	9.08 (7.15–10.76)	10.14 (7.44–13.30)	0.418

SII: Systemic immune-inflammation index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, IQR: Interquartile range

Table 4: Comparison of immune-inflammatory biomarkers in ischemic and haemorrhagic subgroups

Parameters	Haemorrhagic stroke	Ischemic stroke	P
SII, median (IQR)	608 (435–760)	506 (367–698)	0.507
NLR, median (IQR)	1.94 (1.63–2.19)	1.70 (1.44–2.34)	0.439
PLR, median (IQR)	10.15 (7.53–12.00)	8.79 (6.67–11.87)	0.418

SII: Systemic immune-inflammation index, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, IQR: Interquartile range

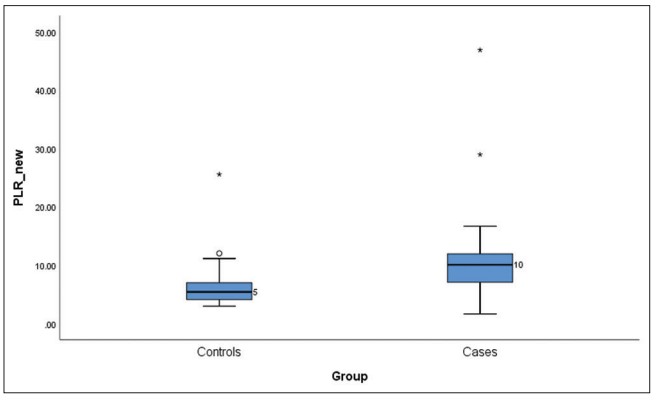

Figure 1: Box plot showing platelet-to-lymphocyte ratio

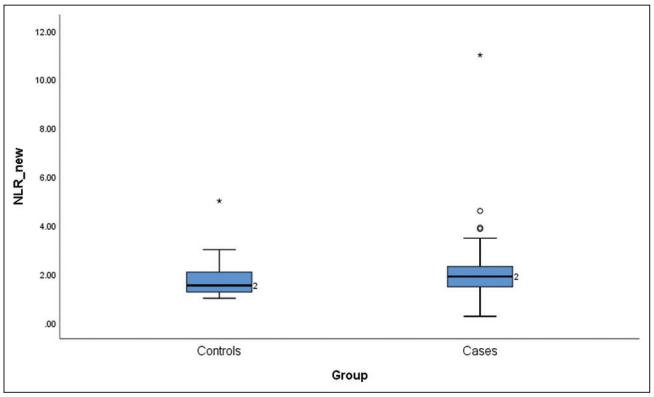

Figure 2: Box plot showing neutrophil-to-lymphocyte ratio

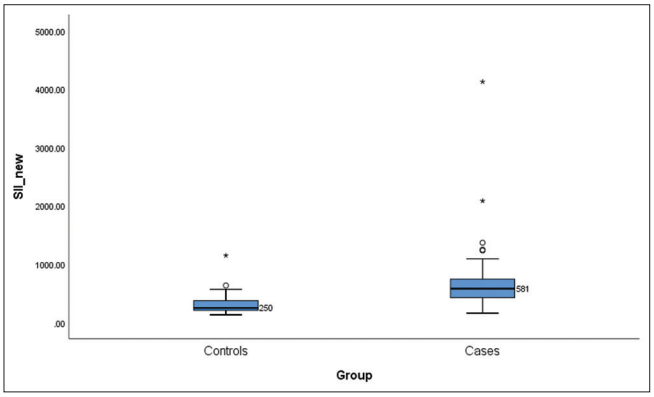

Figure 3: Box plot showing systemic inflammatory ratio

presentations of the disease, despite a trend toward higher values in the haemorrhagic subgroup [Table 5].

Discussion

MMD has long been recognised as a condition of unknown aetiology. However, recent advancements in research suggest that the disease arises from multifactorial influences, with viral infections such as Epstein-Barr virus, Cytomegalovirus and Varicella Zoster virus playing potential role in triggering its onset.[8,9] Acute inflammation, as well as persistent overactivity of the immune system in autoimmune disorders, has also been implicated in the progression of MMD.[10] Notably, the discovery of the *RNF213* gene as an immunosensor in MMD patients represents a pivotal breakthrough, linking immune dysfunction to the disease pathogenesis.[11] Further investigations into immune-mediated mechanisms by Kim *et al*. using serological analysis of recombinant cDNA expression library identified various autoantibodies in the cerebrospinal fluid of MMD patients, including PC326 (of unknown function), sex determining region Y and peroxisomal D3, D2-enoyl-coa isomerase.[12] This highlights the potential role of autoimmunity in disease progression.

Table 5: Comparison using logistic regression used for multivariable analysis

	Adjusted OR	95% CI for adjusted OR		*P*
		Lower	Upper	
MRS				0.08
MRS (1)	0	0		0.998
MRS (2)	0.194	0.046	0.811	0.025
P	1.016	1.004	1.028	0.007
Lymphocyte	1.135	1.044	1.234	0.003
Neutrophil	1.08	1.009	1.156	0.027
SII_new	1.006	1.001	1.011	0.012

Logistic regression used for multivariable analysis. CI: Confidence interval, OR: Odds ratio, SII: Systemic immune-inflammation index, MRS: Modified Rankin Scale

The link between exaggerated immune responses and MMD is further supported by the observations of disease exacerbation following cytokine storms such as those seen in COVID-19 infections. In addition, the progression of MMD in individuals with Graves' disease has been associated with elevated thyroid hormone levels, a phenomenon more frequently observed in adult female patients, opening new avenues for exploring hormonal and autoimmune contributions to disease pathology.[13] The SII, a marker derived from routine blood counts of platelets, neutrophils and lymphocytes, offers a practical, cost-effective tool for assessing immune and inflammatory status. Its affordability and accessibility make it particularly suitable for integration into clinical practice, even in resource-limited settings. As a readily available measure, SII enables healthcare providers to monitor immune activity efficiently, benefiting both primary care and specialised healthcare settings.[2]

Liu *et al*. demonstrated that patients with MMD had significantly higher SII, NLR and PLR compared to controls in a non-emergent outpatient setting.[1] Their study reported mean values of 754 ± 499 vs. 411 ± 205 for SII ($P < 0.001$), 2.83 ± 1.98 vs. 1.81 ± 0.72 for NLR ($P < 0.001$) and 152 ± 64 vs. 120 ± 42 for PLR ($P < 0.001$), respectively. These findings align

with our study, which also demonstrated significantly higher SII, NLR and PLR values in MMD patients compared to controls ($P < 0.001$). In our study, the SII, NLR and PLR values were also significantly higher in female patients compared to males. Although the sample sizes of the male ($n = 30$) and female ($n = 25$) subgroups were limited, this finding suggests a potential hormonal influence on immuno-inflammatory markers and disease progression. Larger studies are needed to confirm whether this association is genuine or merely coincidental.

Interestingly, while Liu *et al*. found that the SII, NLR and PLR values were significantly higher in the haemorrhagic MMD patients compared to the ischemic cases, our findings did not reveal a statistically significant difference between these subgroups.[1] Nonetheless, a trend towards a higher value of SII in the haemorrhagic subgroup was observed.[5] This discrepancy may reflect population-based variability in immune-inflammatory marker expression or could be attributed to the smaller sample size in our study. When comparing paediatric and adult MMD subgroups, no significant differences in SII, NLR and PLR values were found, suggesting a shared underlying pathogenesis across age groups. This indicates that the immuno-inflammatory mechanisms driving the disease likely function similarly in children and adults, providing a unified framework for understanding and treating MMD regardless of age. However, further research is necessary to validate this consistency.

This study holds significant clinical value. By identifying elevated SII, NLR and PLR levels as potential markers of MMD, we gain tools for early detection and disease monitoring, aiding in the prediction of disease occurrence and progression. Furthermore, these findings emphasise the need for treatments targeting the immune-inflammatory response, which could potentially slow or halt disease progression. By offering insights into the immune processes underlying MMD, our study paves the way for improved diagnostic and therapeutic strategies. These advancements could not only enhance patient outcomes but also lead to more personalised approaches to managing this complex disease. As research continues, integrating immune and inflammatory markers into clinical practice could transform how we diagnose, monitor and treat MMD.

Conclusion

Patients with MMD exhibit significantly elevated levels of SII, NLR and PLR compared to control groups, including those with degenerative spine disease patients. These findings suggest a critical role of immuno-inflammatory mechanisms in the etiopathogenesis of MMD, highlighting their potential as valuable markers for predicting disease onset and monitoring progression. Although higher marker levels were observed in female patients, this finding was incidental, and our study did not include hormonal assessments; therefore, no definitive conclusions regarding hormonal influence can be drawn. Dedicated studies incorporating hormonal profiling and larger stratified cohorts are required to clarify this possible association. By identifying immune-inflammatory pathways as therapeutic targets, this study opens avenues for treatments aimed at slowing or halting disease progression. However, additional research is essential to ensure their safety and efficacy. Overall, these findings represent a significant step toward improving the understanding and management of MMD.

Limitation

This study has several limitations that should be acknowledged. First, the relatively small sample size in each subgroup may limit the statistical power and generalisability of our findings. Larger, multicentre studies are needed to confirm and validate the observed trends and associations. Secondly, our study did not include an analysis of key pro-inflammatory cytokines, such as IL-6, IL-17, IL-23 and tumour necrosis factor-alpha, which are known to play pivotal roles in the pathogenesis of MMD. These cytokines are involved in activating the *RNF213* transcription pathway, a critical mechanism believed to trigger neovascularisation and intimal thickening, hallmark processes in MMD. Including these cytokines in future research could provide deeper insights into the molecular pathways underlying the disease and help establish more comprehensive immunological profiles for affected patients. Addressing these limitations in future studies could strengthen our understanding of the immuno-inflammatory mechanisms driving MMD, ultimately contributing to improved diagnostic and therapeutic strategies.

Ethics approval

The study was approved by the Institutional Ethics Committee.

Consent to participate

As this is a retrospective study, the patients' consent to participate was waived off by the Institutional Ethics Committee (2024-119-mch-EXP-59).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Haemodynamic Stroke Due to Total Chronic Carotid Occlusion: Is There a Role for Revascularisation?

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Abstract

Ischaemic stroke can arise from the stenosis and occlusion of a carotid artery by a clot (embolic) or local thrombosis. Haemodynamic stroke is one of the types of ischaemic stroke that occurs due to discrepancy between demand and supply of cerebral blood flow because of cerebral arterial occlusion or high-grade stenosis but can also arise with systemic conditions reducing blood pressure. Treatment of haemodynamic stroke focuses on increasing blood flow to the affected brain region by best medical therapy (BMT) and managing blood pressure (potentially keeping it slightly higher than normal) and may include considering procedures like extra-intracranial flow augmentation bypass surgery (revascularisation surgery) in specific cases when necessary to improve perfusion. Traditionally, revascularisation surgery has been used in the treatment of skull base tumours requiring sacrifice of a large intracranial artery; complex intracranial aneurysms requiring trapping; and distal revascularisation and moyamoya disease. Current evidence does not support routine use of revascularisation in symptomatic cerebrovascular steno-occlusive disease but suggests that carefully selected patients with refractory haemodynamic symptoms may still be candidates. This review summarises the current historical background and knowledge regarding challenges in the field of haemodynamic stroke and their management, putting forward a clinical and research strategy on the effects of revascularisation in terms of cerebral haemodynamic change, cognition and quality of life of patients in the case of symptomatic cerebral atherosclerotic stenosis and occlusion. This review will also help readers understand the importance of revascularisation in this type of ischaemic stroke.

Keywords: *Atherosclerotic, haemodynamic, ischaemic, revascularisation, thrombectomy*

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Introduction

Ischaemic stroke is a broad category that includes a wide variety of stenotic and occlusive diseases of the carotid artery. Extracranial atherosclerotic internal carotid artery (ICA) occlusion and large-artery intracranial atherosclerotic disease (ICAD), including ICA and/or middle cerebral artery (MCA) stenosis and occlusion, are examples of this type of stroke.[1] Complete carotid artery occlusion is responsible for approximately 10% of transient ischaemic attack (TIA); 15%–25% of ischaemic strokes in the carotid artery territory; and 10%–15%, a 2-year risk of subsequent ipsilateral ischaemic stroke in the context of BMT.[2] Haemodynamic stroke is one of the types of ischaemic stroke that is caused by hypoperfusion due to discrepancy between the metabolic demand and supply of blood flow to various regions of the brain at a certain time. This discrepancy occurs due to arterial occlusion or high-grade stenosis due to atherosclerotic disease or moyamoya disease/syndrome.[3-7] It can also arise in systemic conditions like

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heart failure and hypotension. Haemodynamic stroke is associated with high morbidity and mortality.[4-7] It has a high risk of recurrence associated with it; therefore, timely recognition by relevant investigation and management is required.[8,9] These strokes are managed by increasing blood flow to the affected area, either systemically or by enhancing local perfusion, which can be achieved by best medical therapy (BMT), increasing blood pressure above normal values and revascularisation surgery.

As treatment protocols for Moyamoya disease-associated strokes are well established in the literature, treatment strategies for total chronic carotid occlusion are not well described in the literature.

Cerebral revascularisation is a procedure that restores blood flow to the hypo-perfused brain by bypassing blocked or damaged blood vessels and thereby preventing stroke, alleviating symptoms and improving overall brain function in patients with cerebrovascular disorders, especially moyamoya disease and symptomatic cerebral atherosclerotic stenosis and occlusion.[1,10,11] Recent randomised clinical trials are in favour of revascularisation surgery in the case of moyamoya disease, showing its beneficial effects, while in the setting of cerebrovascular atherosclerotic steno-occlusive disease, its indication has been whittled down.[10,11] Dementia is a well-documented symptom that results from occlusion of the ICA, and cognitive impairment can occur even in the absence of cortical infarction.[13-15] Revascularisation surgery has resulted in functional improvement in terms of neuropsychological status of patients with symptomatic ICA occlusive disease in some studies, while other studies find no difference in post-operative cognitive performance.[15]

This review summarises the current historical background and knowledge regarding challenges in the field of haemodynamic stroke and their management, putting forward a clinical and research strategy on the effects of revascularisation in terms of cerebral haemodynamic change, cognitive decline and quality of life of patients in case of total chronic carotid occlusion. This review will also help the readers in understanding the scope of revascularisation for this subset of patients.

Clinical Manifestations

Clinical manifestations of haemodynamic stroke or TIA may be indistinguishable from thromboembolic causes. However, they present with some non-localised or diffuse non-specific symptoms, like the sudden onset of neurological symptoms such as dizziness, confusion, weakness or visual disturbances. They are often triggered or precipitated by activities that lower blood pressure, like standing up quickly, exercising or taking certain medications.[4-7] They may also manifest as 'limb shaking episodes' (coarse limb movements frequently accompanied by paresis and typically lasting <5 min that can be mistaken for seizures) and ocular manifestations like retinal claudication that presents as temporary visual change[16,17] [Figures 1 and 2].

One of the observational studies showed 70% of patients with symptomatic vertebral artery stenosis had both focal and non-focal transient neurological attacks as compared with 26% of patients with symptomatic ICA stenosis.[18] These clinical features are precipitated by standing up quickly, exercise, antihypertensive medication, transition from a cold to a warm environment, coughing, acute haemorrhage and looking into bright light.[19]

Cognitive decline resulting from occlusion of the ICA is a well-documented phenomenon,[7,14,19] and cognitive impairment can occur even in the absence of cortical infarction.[13-15,20] It is one of the underrecognised morbidities in patients with total carotid artery stenosis.

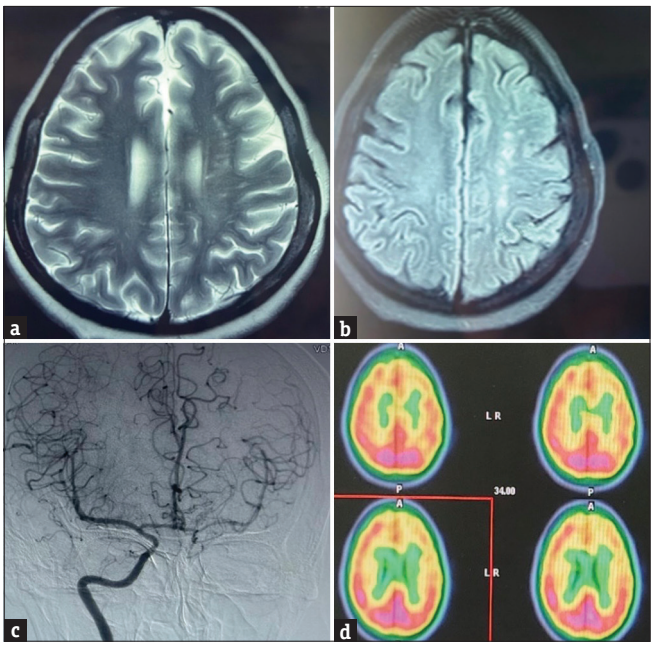

Figure 1: A 54-year-old female with transient right hemiparesis with slurring of speech for 6 months. Pre-operative Montreal Cognitive Assessment (MoCA) score was 19. (a and b) Magnetic resonance (MR) imaging brain revealed Fazeka's grade-I ischemic/microangiopathic changes (c) Diagnostic digital subtraction angiography run showed a complete occlusion of the supra-clinoid internal carotid artery with left anterior cerebral artery and middle cerebral artery (MCA) filling through A-com and left P-com arteries with pial feeders from left posterior cerebral artery. (d) MR perfusion images. Superficial temporal artery-MCA flow augmentation revascularisation with encephalo-duro-myo-synangiosis was done. Postoperatively, the patient had subjective improvement in power in the right upper limb with no further evidence of stroke and improvement in speech in follow-up. Her MoCA score also improved to 24 in follow-up

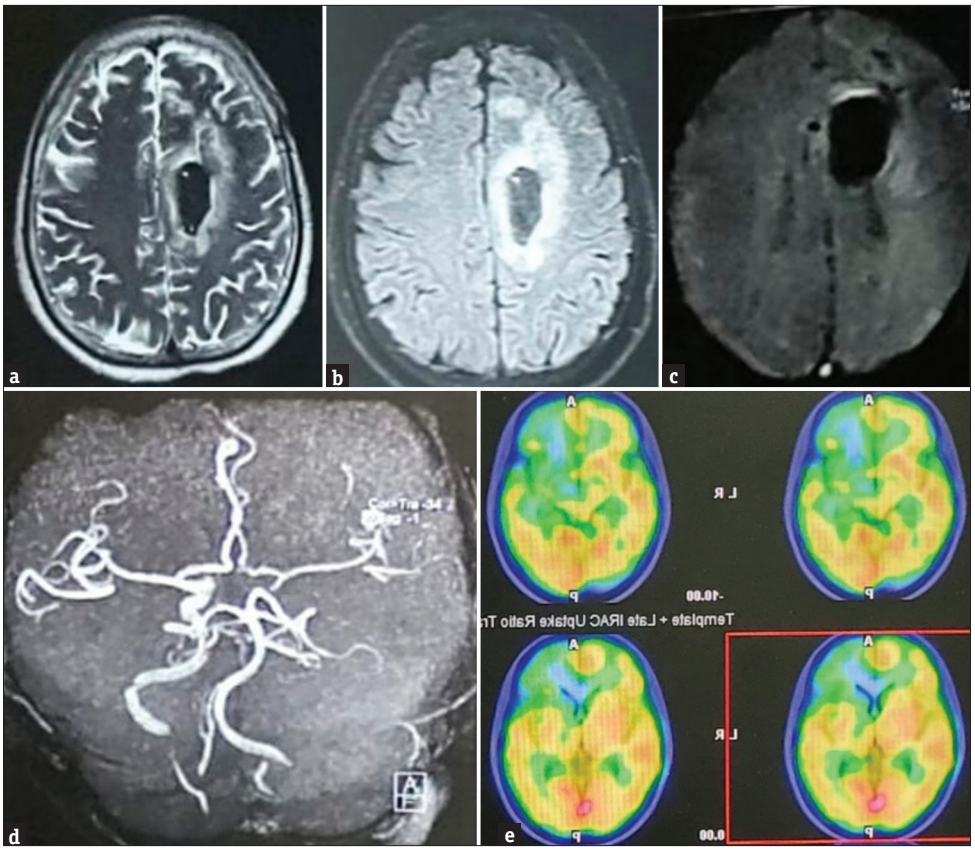

Figure 2: A 69-year-old female with sudden quadriparesis and speech loss for 2 months with pre-operative Montreal Cognitive Assessment (MoCA) score of 22. (a-c) Magnetic resonance (MR) imaging head revealed altered signal intensity on T2 and flair images with blooming on GRE. (d) Diagnostic digital subtraction angiography demonstrated left internal carotid artery (ICA) thrombosis with no filling of the left ICA (e) MR perfusion scan. A double-barrel left-sided superficial temporal artery-middle cerebral artery bypass with encephalo-duro-myo-synangiosis was done. Postoperatively, the patient experienced no complications with subjective improvement in power and speech and no further evidence of stroke. MoCA score was 26 in follow-up

It is likely due to impaired haemodynamics from reduced cerebral perfusion rather than micro-embolic ischaemic injury. The severity of cognitive decline varies from mild decline to severe dementia. Cognitive impairment affects patient well-being and their ability to live independent, productive lives. It places a large demand on societal, hospital and financial resources.[15,20]

Imaging

Haemodynamic stroke has no gold standard investigation that can specifically diagnose this type of stroke; but in the past 20 years, there has been considerable progress in imaging techniques, which has enabled physicians to identify conditions including haemodynamic ischaemia and poor collateral circulation as well as patients at high risk of recurrent stroke like computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) as shown in Figures 1 and 2.

Imaging modalities for chronic total carotid occlusion can be divided into Structural/haemodynamic and Functional/physiological modalities. Structural modalities include CT, MRI, transcranial doppler (TCD) and color-coded duplex sonography, while functional modalities include PET, BOLD MRI, Xenon CT and perfusion CT.

Structural/Haemodynamic Imaging

CT scan or MRI should first be performed for general examination of chronic total ICA occlusion like determining the presence of haemorrhage or infarction. CTA, magnetic resonance angiography, digital subtraction angiography and ultrasound directly measure the length of the occluded artery, the degree of reverse filling by the distal blood flow of the occluded artery, the shape of the ICA residue at the occlusion and the degree of compensation by the collateral circulation. Doppler (TCD) and color-coded duplex sonography have been used for the evaluation of extra- and intracranial cerebrovascular disease, including haemodynamic features, stroke cause and risk prediction. These techniques are highly operator-dependent, but their advantages, including safety, bedside availability, high temporal and spatial resolution and cost-effectiveness, outweigh their limitations.[38-40]

Table 1: Clinical trials on intracranial atherosclerotic steno occlusion

Trials	Study type	Results	Interpretation	Limitations
EC-IC bypass Trial[1]	BMT versus BMT plus revascularisation surgery	Total patients: 1377 Mean follow-up: 5 years BMT (*n*=714) 30-day ischaemic events: 3% 30-day major (non) fatal stroke: 1% 5-year (non) fatal stroke: 29% BMT plus bypass surgery (*n*=663) Bypass patency: 96% Surgical mortality: 1% 30-day ischaemic events: 12% 30-day major (non) fatal stroke: 4.5% 5-year (non) fatal strokes: 31%	Revascularisation Surgery added no effect on the risk of recurrent stroke to BMT	The study didn't take haemodynamic impairment as a factor for the selection of patients
COSS trial[12]	BMT versus BMT plus revascularisation surgery	Total number of patients: 195 Mean follow-up 2 years BMT (*n*=98) 30-day ipsilateral stroke: 2% 2-year stroke rate: 23% BMT + EC-IC bypass (*n*=97) Bypass patency: 98% 30-day ipsilateral stroke: 14% Difference: 12.4% (95% CI, 4.9%–19.9%)* 2-year stroke rate: 21% Difference: 1.7% (95% CI, −10.4% to 13.8%)	Revascularisation Surgery added no effect on the risk of recurrent stroke to BMT	Inadequate selection of patients with haemodynamic impairment using semi-quantitative PET OEF-ratios 12% of patients with contralateral ≥60%-stenosis-occlusion
JET[12]	BMT versus BMT plus revascularisation surgery.	Total number of patients: 196 Completed follow-up of 2 years BMT (*n*=98) Primary end point: 14.3% BMT + EC-IC bypass (*n*=98) Primary end point: 5.1%	The incidence of stroke recurrence in the surgically treated group was significantly lower than that in the medically treated group (*P*=0.046)	Nil
Sasoh *et al*.[15]	To assess cognitive impairment in symptomatic patients with haemodynamic cerebral ischaemia and determine the efficacy of EC-IC bypass in restoring neuropsychologic integrity	Total number of patients: 25	Pre-operative study of patients revealed significant impairment in cerebral blood flow and metabolism as well as reduced WAIS-R score Elevated regional oxygen extraction fraction and reduced regional cerebral metabolic rates of oxygen were significantly associated with pre-operative cognitive impairment (*P*=0.0032 and *P*=0.0255, respectively) Cerebral blood flow and metabolism improved significantly after bypass surgery, and the WAIS-R score increased	Nil

Contd...

Table 1: Contd...

Trials	Study type	Results	Interpretation	Limitations
CMOSS trial[37]	BMT versus BMT plus revascularisation surgery	Total number of patients: 306 Completed follow-up of 2 years BMT (*n*=155) Primary end point: 12.3% 30-day stroke/death: 1.8% BMT+EC-IC bypass (*n*=151) Primary end point: 8.6% Difference: −3.6% (95% CI, −10.1% to 2.9%) HR, 0.71 (95% CI, 0.33–1.54) 30-day stroke/death: 6.2%	EC-IC bypass surgery did not reduce the risk of recurrent stroke or death at 2 years compared with BMT alone	Potential inadequate selection of patients with haemodynamic impairment using CTP
Younkin *et al*.[59]	Effects of superficial temporal-middle cerebral artery anastomosis on CBF, neurologic examination and cognitive functions	Total number of patients: 44	At 3 months, there was a significant improvement in all variables At 9 months, CBF was no longer significantly greater, but neurologic examination and cognitive functions had further improved	None of the pre-operative measurements predicted post-operative clinical improvement

BMT: Best medical therapy, CBF: Cerebral blood flow, EC-IC: Extracranial–intracranial, MCA: Middle cerebral artery, PET: Positron emission tomography, SPECT: Single-photon emission computed tomography, Xe CT: Xenon computed tomography, HR: Hazard ratio, CI: Confidence interval, OEF: Oxygen extraction fraction, CTP: Computed tomography perfusion, WAIS-R: Wechsler Adult Intelligence Scale-Revised, JET: Japanese EC-IC Bypass Trial, CMOSS: Carotid and middle cerebral artery occlusion surgery study

Functional/Physiological Imaging

CT and MR perfusion imaging help in identifying haemodynamic insufficiency. Normal imaging doesn't measure the CPP directly but can assess changes in cerebral blood flow (CBF) after a vasodilatory stimulus, mean transit time (MTT), CBF, cerebral blood volume (CBV) and oxygen extraction fraction (OEF).[21] OEF is considered to provide the strongest indication of the need for recanalisation surgery.[22,38] PET scans have been used since the late 1970s to measure OEF and oxygen consumption (CMRO2) with the help of oxygen-15-labeled O2 inhalation PET with arterial tracer measurements in areas with reduced CBF, and they also allow 3-dimensional mapping of brain perfusion. A disadvantage of PET scans with O-15 tracers is that this technique is not widely available, has a failure rate between 20% and 40% for obtaining complete quantitative data, mostly due to technical difficulties, requires longer scan times and is associated with higher costs compared to other methods like CT perfusion or MRI.[22,23] Misery perfusion[24] and increased CBV were considered markers of compromised haemodynamic reserve, and hence, vasodilatory drugs such as acetazolamide were used to evaluate the cerebral vasodilatory capacity, which is assessed using PET scans. PET, as well as MR- or CT-perfusion studies, is also used for mapping arterial MTT, which linearly reflects the CPP and is thereby used to assess haemodynamic impairment.[25-27]

Perfusion CT or MRI often identifies perfusion-diffusion mismatch, characterised by a severe delay of brain perfusion in the ICA territory, accompanied by a normal regional CBV and no change in diffusion-weighted imaging. CT perfusion studies are used for mapping of CBF, CBV, MTT and time to maximal contrast concentration.[34-35] Time to maximal contrast concentration is one of the markers of viable tissue in acute ischaemic stroke. It is physiologically related to MTT.[34-35] Xenon CT is another CT method used for quantitative CBF measurement, and intravenous acetazolamide is used to measure vasodilatory reserve.[36] Kamath *et al*.,[37] in their study, compared PET measurements of CBF, MTT and OEF with CTP in 6 patients with carotid occlusion. CTP-CBF correlated well with PET (R^2 = 0.796; P < 0.001), and the relative MTT correlated with the PET OEF ratio (R^2 = 0.59, P < 0.001). Recently, the CMOSS trial (Carotid and MCA Occlusion Surgery Study) used CTP measurements of CBF (>5% reduction) and MTT (>4-s increase) to select symptomatic patients with intracranial or extracranial arterial occlusion for surgical bypass.[37]

Newer Advanced Techniques

Cerebrovascular reserve capacity (CVR) is a crucial diagnostic tool when evaluating CTO of the ICA. This variable has been identified as a predictor of ischaemic stroke. BOLD MRI in combination with a standardised

carbon dioxide application as a vasoactive stimulus is another advanced technique that is used to measure the CVR, which is associated with recurrent ischaemic stroke.[28-32] TCD studies are often used to assess vasoreactivity and have suggested that in patients with CTO of the ICA, a breath-holding index of <0.69 is correlated with a high risk of subsequent stroke.[38]

Management

No specific treatment has proven effective for stroke risk reduction in case of haemodynamic impairment due to atherosclerotic occlusive cerebrovascular disease. Management of haemodynamic stroke focuses on increasing blood flow to the affected brain region by BMT, managing blood pressure, potentially keeping it slightly higher than normal and may include considering procedures like extra-intracranial flow augmentation bypass surgery in specific cases when necessary to improve perfusion. Previous trials with Level I evidence like COSS (terminated prematurely) and CMOSS were not in favour of surgical bypass in preventing stroke in atherosclerotic carotid occlusion patients.[12,36] Blood pressure control; addressing modifiable risk factors like cholesterol by lipid-lowering agents, smoking and diabetes; dual antiplatelets for 3 months followed by monotherapy and using imaging techniques like TCD to assess blood flow and guide treatment decisions are some of the measures taken for managing haemodynamic stroke due to symptomatic cerebral atherosclerotic stenosis and occlusion.[12,41,42]

The literature has limited data for standard blood pressure targets in neurologically stable patients with haemodynamic impairment. The COSS[12] and SAMMPRIS[43] trials found no increased risk for stroke in patients with systolic blood pressure (SBP) <140 mm/Hg as compared to other trials, while SOpHIA sub-study[37] and a VERiTAS[44] (Stroke Risk and Haemodynamic in ICAD) were in favour of increased stroke risk for patients with ICA disease and haemodynamic impairment with SBP <140 mm/Hg.[43,45] Hence, in the absence of consensus, individualised blood pressure targets should be considered, balancing stroke risk from hypoperfusion with haemorrhagic risks from hypertension.[46]

Various endovascular therapies have gained importance in the past for steno-occlusive cerebrovascular disease, which includes mechanical thrombectomy[47] for acute proximal intracranial occlusions and angioplasty with stenting and carotid endarterectomy[48] for symptomatic carotid stenosis. Carotid artery stenting is an alternative treatment to carotid endarterectomy for stroke prevention in patients who are older than 70 years with a symptomatic 50%–99% atherosclerotic stenosis, irrespective of the stroke mechanism.[48] Endovascular revascularisation via angioplasty with stenting may be considered when medical therapy fails in case of haemodynamic failure resulting from other cervical artery diseases like dissection, inflammation or vasospasm.[49] The SAMMPRIS[41] and CASSISS[50] trials favoured the superiority of BMT over intracranial stenting as an initial treatment for symptomatic intracranial atherosclerosis due to high periprocedural stroke risk and because some patients with haemodynamic stroke at presentation did not benefit from intracranial stenting.[50,51]

Hence, intracranial angioplasty and/or stenting is an optional therapy for selected patients with symptomatic severe (>70%) intracranial arterial stenosis causing haemodynamic impairment despite BMT. Literature also had limited evidence in favour of angioplasty with stenting in patients receiving mechanical thrombectomy for an acute ischaemic stroke caused by a clot-on-plaque.[51] Current endovascular therapies have limited utility in chronic total occlusions, but may be considered in select dissection/inflammatory aetiology.

Various new therapies have been developed in the last few decades with an aim to improve clinical outcomes in the acute phase of haemodynamic strokes due to symptomatic carotid occlusion disease. Cerebral revascularisation (EC-IC or superficial temporal artery [STA]-to- MCA bypass) is one of them that has proven to play an important role in the management of these strokes in some studies. This flow augmentation bypass restores blood flow to the hypoperfused areas of the brain, thereby preventing further strokes. It has shown benefits in nonrandomised studies for patients with symptomatic ischaemic moyamoya disease, but studies showing its beneficial effects in symptomatic carotid occlusion disease are still lacking.[52-54]

Revascularisation by extracranial–intracranial (EC-IC) bypass surgery was first performed by Yasargil, who utilised it for treating occlusive cerebrovascular disease. The direct bypass surgery is mainly performed by connecting the STA to the MCA.[55]

Previous trials have FAILED to demonstrate benefit to surgical revascularisation in patients with symptomatic cerebrovascular atherosclerotic steno-occlusive disease. Best medical therapy (BMT), including optimisation of atherosclerotic and stroke risk factors as well as dual antiplatelet therapy, still fails to prevent strokes in a small number of patients, who may present with recurrent TIAs and/or strokes.[3,56] The literature is in favour of the fact that no study has investigated the role of revascularisation surgery in this patient group. The

first trial of cerebral revascularisation in patients with symptomatic non-moyamoya vasculopathy was published in the New England Journal of Medicine in 1985, which failed to show any benefits and in stratifying patients by risk to determine who would receive the greatest benefit from intervention.[57] Later, the St. Louis Carotid Occlusion Study came, which identified patients who were at the highest risk for recurrent stroke in the setting of cerebrovascular stenosis and occlusion by using PET OEF.[1,58] Subsequently, the COSS was then designed on this premise. Patients in the COSS underwent PET OEF to determine whether patients with symptomatic cerebral atherosclerotic stenosis and occlusion who are at the highest risk of recurrent stroke would benefit from revascularisation, which was later randomised to BMT versus surgical revascularisation.

Despite numerous criticisms, the ultimate outcome showed that surgical revascularisation provided no benefit over the BMT, mostly due to the impressive natural history of medical therapy and the perioperative surgical risk associated with revascularisation.

The EC-IC Bypass trial in 1985 investigated whether EC-IC arterial bypass [Table 1], in addition to BMT, was superior to BMT alone in patients with ischaemic cerebrovascular disease, including extracranial ICA occlusion. The study revealed a bypass patency rate of 96%, a 30-day perioperative stroke rate of 12.2% for cerebral or retinal ischaemic events ranging from 'trifling symptoms to fatal strokes', a major stroke rate of 4.5% and a perioperative mortality rate of 1.1%. The incidence of fatal and nonfatal ischaemic strokes was not significantly different in patients randomised to EC-IC arterial bypass versus those patients randomised to medical therapy alone; hence, there was a widespread reduction in EC-IC bypass surgery for patients with ischaemic cerebrovascular disease, including those with extracranial ICA occlusion.

The COSS study [Table 1] was driven by the good outcomes of the medically managed patients and the perioperative morbidity associated with revascularisation surgery, but was prematurely terminated due to futility analysis. Perioperative stroke risk in the COSS was similar to that of the original EC-IC bypass trial (14%). This made the revascularisation surgery wane for patients with symptomatic steno-occlusive cerebrovascular disease after the publication of the COSS. Hence, further research was needed into this patient group, even after the COSS study, to assess the risk of further stroke after initial therapy as well as to determine optimal treatment modalities. One of the conclusions of the COSS trial was that EC-IC bypass could be an appropriate option to consider in patients with haemodynamic compromise in the future, if the risk of perioperative stroke could be significantly reduced. Although the COSS did stratify patient risk by using haemodynamic imaging modalities, it did not specifically investigate patients in whom BMT failed [Table 1].

Similar to COSS, the Japanese EC-IC Bypass Trial (JET) was a multicentre, randomised controlled trial designed to test the hypothesis that STA-MCA cortical branch anastomosis, in addition to best medical therapy, could significantly reduce subsequent ischaemic events in patients with recently symptomatic haemodynamic cerebral ischaemia from chronic occlusive lesions of the ICA or MCA. Overall, surgical patients experienced a significant reduction in the study's primary end point (major stroke or death in the 2-year period after surgery) as compared with the medical patients with a mean follow-up period of 15 months (5.1% vs. 14.3%, respectively; $P = 0.046$).[12,57] But the results of the Japanese EC-IC trial can't be considered confirmatory and in favor of revascularisation surgery in symptomatic chronic carotid occlusion, as the interim and final results of the trial have not been published in any peer-reviewed journal till yet.

Haemodynamic strokes have significant cognitive impairment that is only partially alleviated with EC-IC bypass surgery. Cognitive impairment in ischaemic stroke occurs due to the involvement of specific regions important for higher cerebral functions. If multiple infarctions disturb multiple localised functions, dementia may result. It may also be due to ischaemic damage of large-scale networks between cortical or subcortical regions. EC–IC bypass did not adversely affect post-operative cognitive function, but also improved some cognitive domains, including verbal memory, visual memory, executive function, attention and psychomotor speed by correcting cerebral haemodynamic.[14,59] Effects of bypass surgery for cognitive function have always remained controversial. Some investigators are in favour of functional improvement in patients with symptomatic ICA occlusive disease by EC-IC bypass, while others did not find significant post-operative improvement in cognitive performance. Yamauchi *et al*.,[14,60,61] in their study, reported widespread cortical hypometabolism in these patients. Masayuki Sasoh *et al*.,[15,61] in their study (Level III evidence), reported improvement in cognition postoperatively and association of cognition with increases in rCBF and decreases in rOEF. These findings suggest that bypass surgery has heterogeneity in study findings, and in future, longitudinal, controlled studies are needed before firm conclusions can be drawn.

Surgical Complications

Revascularisation in neurosurgery is a double-edged sword with both benefits and certain risks and complications. Complications include infections, adverse reactions to anaesthesia, intraoperative and post-operative bleeding, neurological complications such as stroke, brain damage or cognitive impairment, cerebral infarction and cerebral hyperperfusion syndrome. The 'watershed shift phenomenon' was proposed by Hayashi *et al.* to be responsible for cerebral infarction among paediatric moyamoya diseases, which is an intrinsic haemodynamic ischaemia at the adjacent cortex to the STA-MCA bypass. Retrograde blood supply from the STA-MCA bypass interferes with the anterograde blood flow from the proximal MCA, resulting in the temporary decrease in CBF at the cortex supplied by the adjacent branch of the MCA.[29] Besides the watershed shift phenomenon, thromboembolic complications originated from the anastomosed site[30] and the mechanical compression by the swollen temporal muscle flap could also cause cerebral ischaemia in the acute stage.[62,63] Wessels *et al*. in their study showed an overall surgical complication rate of 6.5% and perioperative ischaemic stroke rate of 4.3% in their study with an overall 1-year ischaemic/TIA event rate of 6.1%.[54] Hence, CBF measurement and MR imaging/angiography in the acute stage are necessary for the accurate diagnosis and prompt perioperative management of these complications.

Patients with total chronic carotid occlusion are a subset of patients, which requires special attention. These patients experience recurrent haemodynamic stroke despite the BMT, and chronic hypoperfusion may lead to cognitive impairment. As these patients are not candidates for endovascular or surgical flow restoration procedures, they can be a good choice for revascularisation surgery if there is no improvement after the BMT. Further clinical studies are needed to establish the role of flow augmentation surgery in the form of STA-MCA bypass for patients with total chronic carotid occlusion with haemodynamic strokes.

Conclusion

The management of haemodynamic stroke due to symptomatic steno-occlusive carotid disease represents a significant challenge for neurosurgeons and other health professionals. The appropriate therapeutic approach should be based on the thorough evaluation of the haemodynamic profile of patients, considering his or her medical history, neurological status and specific anatomical features. Cerebral revascularisation for non-moyamoya symptomatic steno-occlusive cerebrovascular disease has not been shown to provide statistical clinical benefit in various studies but may remain a potential option in carefully selected refractory patients, though evidence for benefit is limited. However, patients with total carotid occlusion remain a special subset of patients who require further studies to assess the clinical benefit of revascularisation.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Microsurgical Clipping of Distal Anterior Cerebral Artery Aneurysms: Technical Nuances and Clinical Outcomes from a 15-year Institutional Experience

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Abstract

Background: Distal anterior cerebral artery (DACA) aneurysms are a rare subset of intracranial aneurysms, accounting for 1%–9% of cases. Their deep interhemispheric location, small-caliber vessels and proximity to cortical perforators make surgical management challenging. Microsurgical clipping remains the treatment of choice for ruptured or complex DACA aneurysms.

Materials and Methods: We retrospectively analysed 38 patients who underwent microsurgical clipping for DACA aneurysms at our tertiary neurosurgical center between January 2008 and December 2022. Data collected included demographics, comorbidities, clinical presentation (Hunt–Hess and world federation of neurosurgical societies (WFNS) grades), aneurysm morphology, operative details, post-operative complications and functional outcomes. Functional recovery was assessed using the Glasgow Outcome Scale and modified Rankin Scale (mRS) at discharge and follow-up.

Results: The cohort included 23 males (61%) and 15 females (39%), with a mean age of 43.2 ± 13 years (range: 26–68). The common comorbidities were hypertension (42%), smoking/tobacco use (24%), diabetes (16%) and chronic alcoholism (13%). Most patients presented with ruptured aneurysms (89.5%). Aneurysms predominantly involved the A3 segment (55.3%) and were saccular in 89.5% of cases. Temporary proximal clipping was used in 78.9% of patients (mean duration: 114 ± 26 s). Complete aneurysm occlusion was achieved in 97.4% of patients. Intraoperative rupture occurred in 13.2% of patients and 30-day mortality was 2.6%. At a 1-year follow-up, 84.2% of patients had favourable functional outcomes (mRS ≤2).

Conclusion: Microsurgical clipping of DACA aneurysms is safe and effective, offering high rates of aneurysm obliteration and good functional recovery. Success depends on meticulous interhemispheric dissection, temporary proximal control and careful preservation of distal perforators.

Keywords: *Distal anterior cerebral artery aneurysm, interhemispheric approach, microsurgical clipping, surgical outcome*

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Introduction

An aneurysm is defined as a focal, abnormal dilatation of an arterial wall involving all three layers: intima, media and adventitia, resulting from structural weakness and haemodynamic stress.[1] Among intracranial vascular pathologies, cerebral aneurysms represent the localised dilations of cerebral arteries, most commonly occurring at arterial bifurcations within the circle of Willis.[2] Saccular (berry) aneurysms represent the most common type of intracranial aneurysm and are particularly prone to rupture, resulting in subarachnoid haemorrhage (SAH).[3] Ruptured berry aneurysms are a major cause

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of non-traumatic SAH, carrying high morbidity and mortality despite advances in neurocritical care.[4]

Within the spectrum of intracranial aneurysms, distal anterior cerebral artery (DACA) aneurysms constitute a rare subset, accounting for approximately 1%–9% of all cerebral aneurysms.[5,6] These aneurysms arise distal to the anterior communicating artery complex, typically along the pericallosal or callosomarginal arteries.[7] Because of their deep interhemispheric location, small caliber of parent vessels and complex anatomical relationships with bridging veins and cortical branches, DACA aneurysms pose significant challenges in both surgical and endovascular management.[8,9]

Clinically, most DACA aneurysms present with rupture, often associated with intracerebral haematoma within the interhemispheric fissure or corpus callosum, which worsens the outcome.[6] Microsurgical clipping remains the preferred treatment for ruptured DACA aneurysms, owing to their distal location, small sac size, often broad neck, and frequent association with intraparenchymal haematoma, which allows simultaneous aneurysm obliteration and haematoma evacuation.[10,11] However, the advent of advanced endovascular tools such as microcatheters, low-profile stents and flexible coils has expanded the therapeutic options even in distal arterial territories. Despite this, the narrow vessel diameter and acute angulations still limit endovascular access in many cases.[8]

Recent studies suggest comparable long-term outcomes between clipping and coiling in selected DACA aneurysms, although surgical clipping remains preferred for ruptured or complex lesions.[12,13] Nonetheless, data focusing exclusively on microsurgical outcomes in DACA aneurysms remain limited, often derived from small retrospective cohorts. Therefore, this study aims to analyse demography clinical characteristics, radiological features, surgical outcomes and complications in patients undergoing microsurgical clipping of DACA aneurysms at our tertiary care centre.

Materials and Methods

Study design and setting

This retrospective observational study was conducted at the department of neurosurgery in our institute. It included patients who underwent microsurgical clipping of DACA aneurysms between January 2008 and December 2022. All eligible cases during this 15-year period were reviewed to assess clinical presentation, operative findings and outcomes.

Inclusion and exclusion criteria

Inclusion criteria

1. Patients with ruptured or unruptured aneurysms located distally in the anterior cerebral circulation (beyond the A1–A2 junction)
2. Diagnosis confirmed by pre-operative angiography, including computed tomography (CT) angiography, magnetic resonance angiography or digital subtraction angiography
3. Patients who underwent definitive microsurgical clipping as the primary treatment.
4. Availability of complete surgical and follow-up records.

Exclusion criteria

1. Cases in which clipping was not performed or converted to endovascular treatment
2. Patients managed exclusively by coiling
3. Incomplete documentation or loss to follow-up before discharge
4. Patients who died before surgical intervention.

After applying these criteria, a total of 38 patients were included for the analysis.

Data collection and variables

Patient records, operative notes, radiological archives and follow-up outpatient data were retrospectively reviewed to extract the clinical, radiological and operative details. Demographic and clinical information included age, sex, comorbidities such as hypertension, diabetes and smoking status, Hunt and Hess and WFNS grade at admission (only for ruptured cases) and presence of subarachnoid haemorrhage, intracerebral haematoma, intraventricular haemorrhage or hydrocephalus. Aneurysm morphology was documented in terms of location (A2, A3, A4 or pericallosal branches), maximum dome diameter, neck size, aspect ratio, multiplicity and shape (saccular, fusiform or irregular). Operative details included surgical approach (interhemispheric or parasagittal), side of craniotomy, use of proximal temporary clipping, intraoperative rupture, need for adjunct measures such as temporary trapping, bypass or wrapping, clip type and configuration and intraoperative complications. Post-operative and outcome parameters included angiographic result (complete occlusion or residual remnant), complications such as rebleeding, infarction, infection or new neurological deficits, duration of hospital stay and mortality. The functional outcomes were assessed at discharge and during the last follow-up using the Glasgow Outcome Scale (GOS) or modified Rankin Scale (mRS). A good outcome was defined as GOS 4–5 or mRS ≤2, while a poor outcome was defined as GOS ≤3 or mRS >2. The duration of follow-up was calculated from the date of surgery to the last clinic visit or death and expressed in months.

Surgical technique

All surgeries were performed under general anaesthesia using the standard microsurgical techniques. A unilateral interhemispheric or parasagittal approach was selected according to the side and configuration of the aneurysm. After positioning the patient supine with mild head flexion, a bicoronal or parasagittal craniotomy was fashioned. The interhemispheric fissure was dissected under the operating microscope to expose the pericallosal and callosomarginal arteries, which were traced to the aneurysm neck. Temporary proximal control was established when required, and sharp dissection was used to separate the aneurysm when preserving perforators and branch vessels. The aneurysm was clipped using suitable titanium clips to ensure the complete exclusion of the neck without compromising the parent artery. Intraoperative rupture, when encountered, was managed with controlled temporary clipping and suction decompression. After achieving haemostasis, the dura was closed in a watertight manner and the bone flap replaced.

In selected cases, intraoperative indocyanine green angiography was used to confirm adequate aneurysm occlusion and preservation of parent and perforating vessels.

Post-operative care and follow-up

Post-operative CT or CT angiography was performed within 24 h to assess clip position and detect any haemorrhage, infarction or hydrocephalus. Patients were managed in the neurosurgical intensive care unit with strict blood pressure control and maintenance of euvolemia. External ventricular drainage was used in cases of acute hydrocephalus. Prophylactic antiepileptic therapy was administered to all patients during the post-operative period and was tapered gradually during the follow-up based on clinical status. Clinical condition was recorded daily during hospitalisation and at the follow-up visits. Follow-up imaging was performed during scheduled outpatient visits or when clinically indicated, particularly in patients with new neurological symptoms or suspicion of aneurysm recurrence.

Statistical analysis

Descriptive statistical analysis was performed using the standard methods. The continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Data were analysed using Microsoft Excel. Due to the limited sample size, the analysis was primarily descriptive.

Ethical statement

The present study was a retrospective observational analysis based on anonymised patient records collected during routine clinical care. Institutional Review Board approval was not required as this was a retrospective observational study with no new intervention. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Results

In our study, the mean age was 43.2 ± 13 years (range, 26–68), with a male predominance (60.5%). The common comorbidities included hypertension (42.1%), smoking/tobacco use (23.7%), diabetes (15.8%) and chronic alcoholism (13.2%). Most patients presented with ruptured aneurysms (89.5%), while 10.5% were unruptured. Among ruptured cases, the majority had Hunt and Hess Grades 2 (26.5%) and 4 (23.5%). WFNS grading showed that 32.4% of patients were Grade 2, followed by 23.5% classified as Grade 3 [Table 1].

Aneurysm laterality was slightly more common on the right side (55.3%). The majority were located in

Table 1: Demographic and clinical characteristics of patients

Variable	Number of patients (%)
Age	
Mean±SD	43.2±13
Range	26–68
Sex	
Male	23 (60.5)
Female	15 (39.5)
Pre-operative comorbidities	
Hypertension	16 (42.1)
Diabetes	6 (15.8)
Smoking/tobacco	9 (23.7)
Chronic alcoholism	5 (13.2)
IHD	5 (13.2)
Clinical presentation	
Ruptured	34 (89.5)
Unruptured	4 (10.5)
Hunt and Hess Grade (*n*=34)	
1	7 (20.6)
2	9 (26.5)
3	7 (20.6)
4	8 (23.5)
5	3 (8.8)
WFNS Grade (*n*=34)	
1	7 (20.6)
2	11 (32.4)
3	8 (23.5)
4	5 (14.7)
5	3 (8.8)

SD: Standard deviation, IHD: Ischaemic heart disease, WFNS: World federation of neurosurgical societies

the A3 segment (55.3%), followed by A2 (26.3%) and A4/pericallosal branches (18.4%). Morphologically, most aneurysms were saccular (89.5%), with fusiform (7.9%) and irregular/lobulated (2.6%) types being less frequent. Neck diameters were predominantly small (<5 mm, 84.2%), with a mean of 3.48 ± 1.4 mm, while dome diameters averaged 6.1 ± 2.4 mm, most measuring <5 mm. Associated cerebrovascular findings included multiple aneurysms (7.9%), vascular occlusion (5.3%), AVF (2.6%) and moyamoya disease (2.6%). Among ruptured cases, the Modified Fisher grade distribution was Grade 1 (20.6%), Grade 2 (38.2%), Grade 3 (26.5%) and Grade 4 (14.7%) [Table 2].

Temporary proximal clipping was utilised in 78.9% of patients, with a mean duration of 114 ± 26 s. Clip selection included curved clips in 55.3% and straight clips in 36.8% of cases. The mean operative time was 145 ± 41 min, with an average blood loss of 186 ± 68 ml [Table 3].

Intraoperative rupture occurred in 13.2% of cases, while parent artery injury, bridging vein injury and cortical contusion/brain retraction injury were uncommon (2.6%). Postoperatively, cerebral vasospasm was noted in 13.2% of patients, hydrocephalus requiring external ventricular drainage or shunt in 7.9%, and other complications, including infarction, rebleeding, seizures, meningitis and surgical site infection, occurred in 2.6% each. Angiographic results demonstrated total occlusion in 97.4% of aneurysms [Table 4].

Functional outcomes improved over time. At discharge, 30 patients (78.9%) had a favourable GOS (4–5), increasing to 33 (86.8%) at 1-year follow-up. Similarly, favourable mRS scores (0–2) were observed in 28 patients (73.7%) at discharge, rising to 32 (84.2%) at 1 year. The mean ICU stay was 4.1 ± 1.5 days, with total hospital stay averaging 10.5 ± 2.1 days. The mean follow-up duration was 18.2 ± 5.8 months [Table 5].

Table 2: Aneurysm characteristics

Variable	Number of patients (%)
Aneurysm laterality	
Right	21 (55.3)
Left	17 (44.7)
Aneurysm location	
A2	10 (26.3)
A3	21 (55.3)
A4/pericallosal branches	7 (18.4)
Morphology	
Saccular	34 (89.5)
Fusiform	3 (7.9)
Irregular/lobulated	1 (2.6)
Aneurysm size	
Neck diameter (mm)	
Small (<5 mm)	32 (84.2)
Medium (5–15 mm)	6 (15.8)
Large (>15 mm)	0
Mean±SD	3.48±1.4
Range	2.4–12
Diameter of dome (mm)	
Small (<5 mm)	27 (71.1)
Medium (5–15 mm)	10 (26.3)
Large (>15 mm)	1 (2.6)
Mean±SD	6.1±2.4
Range	2.9–15.6
Associated cerebrovascular findings	
Multiple aneurysm	3 (7.9)
Arterio-venous fistula	1 (2.6)
Vascular occlusion	2 (5.3)
Moyamoya disease	1 (2.6)
Intracerebral haematoma	2 (5.3)
Modified Fisher grade (*n*=34)	
0	0
1	7 (20.6)
2	13 (38.2)
3	9 (26.5)
4	5 (14.7)

SD: Standard deviation

Table 3: Operative details

Variable	Number of patients (%)
Temporary clip used	
Yes	30 (78.9)
No	8 (21.1)
Duration of temporary clip (s) (mean±SD)	114±26
Type of permeant clip	
Straight	14 (36.8)
Curved	21 (55.3)
Fenestrated	3 (7.9)
Operative time (min) (mean±SD)	145±41
Mean blood loss (ml) (mean±SD)	186±68

SD: Standard deviation

ILLUSTRATIVE CASE

A 42-year-old female presented with severe new-onset headache for 1 day. She had initially consulted a local physician who advised CT brain imaging along with analgesics. CT brain demonstrated interhemispheric subarachnoid haemorrhage with intraventricular extension. CT angiography revealed two aneurysms – one at the anterior communicating artery (ACOM) and another at the DACA. Four-vessel digital subtraction angiography confirmed filling of both aneurysms from the right internal carotid artery [Figure 1].

The patient subsequently underwent surgical clipping. In the supine position, a modified pterional craniotomy was performed. The ACOM aneurysm was clipped first, followed by interhemispheric dissection and clipping

of the DACA aneurysm [Figure 2]. The patient was electively ventilated for 6 h postoperatively. Triple-H therapy and nimodipine were administered. The patient recovered well, was extubated without neurological deficit and discharged on the post-operative day 10.

Discussion

DACA aneurysms represent a surgically challenging pathology, and their optimal management continues to be an area of clinical interest in cerebrovascular neurosurgery. These aneurysms arise distal to the anterior communicating artery, most commonly along the pericallosal or callosomarginal branches, and are associated with considerable surgical complexity due to their deep interhemispheric location, small-caliber parent vessels and intimate relationship with cortical perforators and bridging veins.[6] The majority of DACA aneurysms are saccular in morphology and carry a significant risk of rupture, frequently resulting in subarachnoid haemorrhage and, in some instances, intraparenchymal haematoma.[3] Microsurgical clipping remains the treatment modality of choice for ruptured DACA aneurysms, permitting definitive aneurysm obliteration when allowing concomitant evacuation of associated haematomas when present.

In the present series of 38 patients, the mean age was 43.2 ± 13 years, with a male predominance of 60.5%. This demographic profile aligns closely with the study conducted by Shukla *et al*. and Lehecka *et al*.,[10,11] which have described mean ages in the fourth to fifth decade and a slight male predominance, reflecting the common age group affected by intracranial aneurysms. Notably, the majority of patients (89.5%) presented with ruptured aneurysms, a finding that corroborates reports by Take *et al*., and Orz *et al*., where distal anterior circulation aneurysms frequently manifested as acute SAH.[5,6]

Analysis of the neurological status at presentation revealed that most ruptured patients were graded as Hunt and Hess II–IV, indicating moderate-to-severe neurological compromise. Similarly, WFNS grading reflected comparable distributions, suggesting a significant proportion of patients presented with altered consciousness or focal neurological deficits. These observations underscore the aggressive clinical course of ruptured DACA aneurysms and highlight the need for timely and effective surgical intervention.

Pre-operative comorbidities are prevalent among patients with DACA aneurysms, influencing both surgical planning and outcomes. In our cohort, hypertension was observed in 42.1% of patients, aligning with the findings from a study by Zhang *et al*., which identified hypertension as a significant

Table 4: Intra- and post-operative complications

Variable	Number of patients (%)
Intra-operative complication	
Intraoperative rupture	5 (13.2)
Parent artery injury	1 (2.6)
Bridging vein injury	2 (5.3)
Cortical contusion/brain retraction injury	1 (2.6)
Post-operative complications	
Cerebral vasospasm	5 (13.2)
Infarction/ischaemic stroke	1 (2.6)
Rebleeding/aneurysm rupture	1 (2.6)
Hydrocephalus requiring EVD/Shunt	3 (7.9)
Seizures	1 (2.6)
Meningitis	1 (2.6)
Surgical site infection	1 (2.6)
Mortality within 30 days	1 (2.6)
Angiographic result	
Total occlusion	37 (97.4)
Incomplete occlusion	1 (2.6)

EVD: External ventricular drainage

Table 5: Surgical outcome and functional scores

Parameter	Number of patients				
	Pre-operative	Post-operative (discharge)	Follow-up (3 months)	Follow-up (1 year)	Follow-up (2 years)
GOS					
Favourable (4–5)	18	30	32	33	33
Unfavourable (1–3)	20	8	6	5	5
mRS					
Favourable (0–2)	14	28	31	32	32
Unfavourable (3–5)	24	10	7	6	6
Post-operative stay (days) (mean±SD)					
ICU stay			4.1±1.5		
Hospital stay			10.5±2.1		
Mean follow-up duration (months) (mean±SD)			18.2±5.8		

GOS: Glasgow Outcome Score, mRS: Modified Rankin Scale, SD: Standard deviation, ICU: Intensive care unit

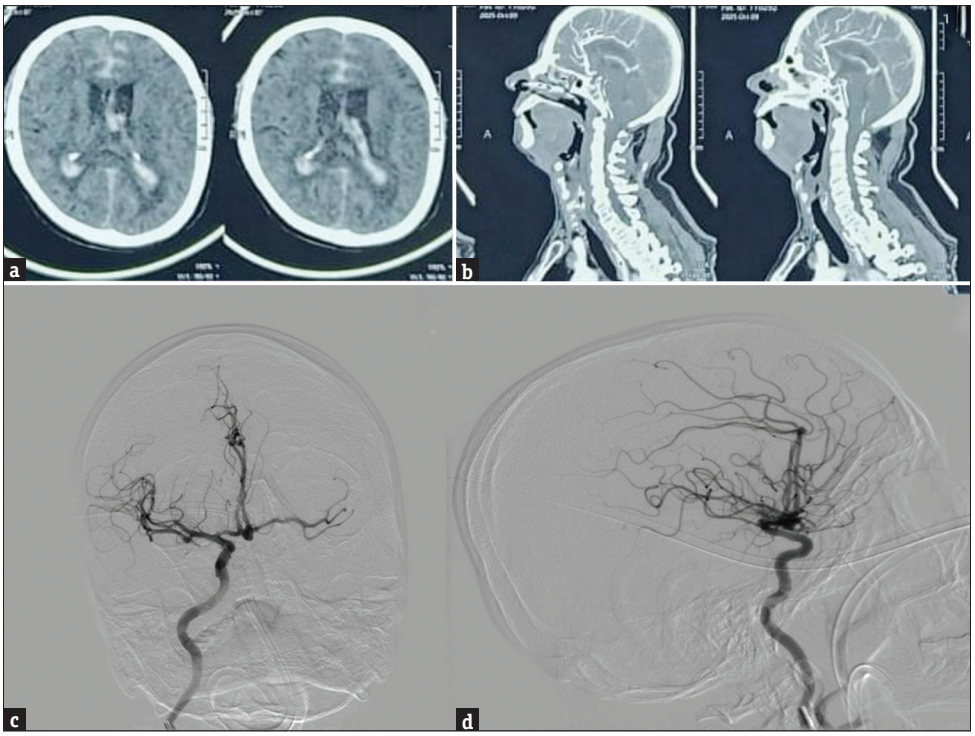

Figure 1: (a) Shows plain computed tomography (CT) brain with subarachnoid haemorrhage in interhemispheric fissure and intraventricular extension. (b) Shows reconstructed CT angiography lateral view showing both ACOM and distal anterior cerebral artery (DACA) aneurysms. (c) Shows Digital subtraction angiography (DSA) right internal carotid artery run anteroposterior view and (d) shows DSA Lateral view which shows both ACOM and DACA aneurysms filling up

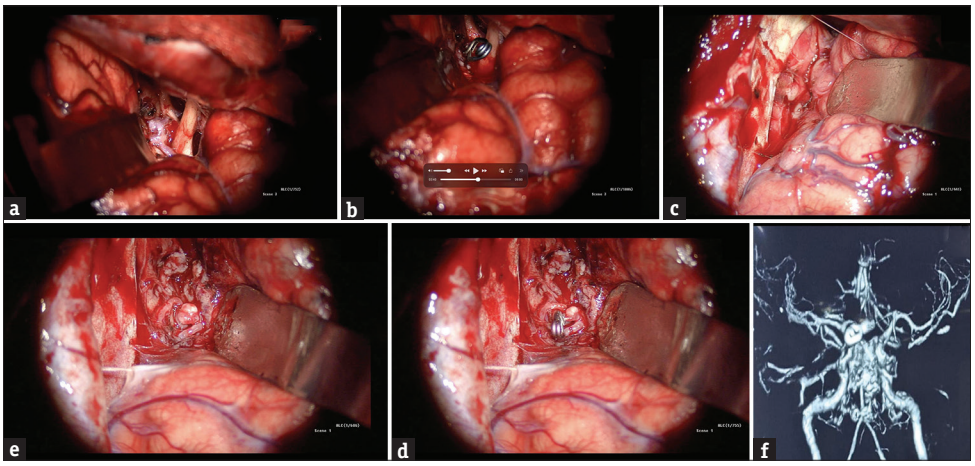

Figure 2: (a) Shows intraoperative picture of ACOM aneurysm. (b) Shows post-clipping status of ACOM artery aneurysm. (c) Shows interhemispheric approach to dissect the distal anterior cerebral artery (DACA) aneurysm. (d) Shows the intraop picture of DACA aneurysm. (e) Post-clipping status of DACA aneurysm. (f) Shows the post-operative computed tomography reconstructed image showing clip in place

risk factor for intracranial aneurysms.[14] Smoking or tobacco use was reported in 23.7%, diabetes mellitus in 15.8%, chronic alcohol consumption in 13.2% and ischaemic heart disease in 13.2%. These observations are consistent with data reported in recent studies on distal intracranial aneurysms.[13,14] These comorbidities require meticulous pre-operative evaluation, as they may elevate perioperative risk and influence intraoperative and post-operative management strategies.

In our cohort, the majority of DACA aneurysms were located in the A3 segment (55.3%), followed by A2 (26.3%) and A4/pericallosal branches (18.4%). The A3 predominance in our series is consistent with prior reports by Proust *et al*., who documented that the majority of DACA aneurysms arise in the A3 segment, highlighting the tendency for distal pericallosal involvement in this patient population.[15] In addition, saccular aneurysms were most common (89.5%), with

small necks (<5 mm) observed in 84.2% of cases. These characteristics are consistent with the study by Steven *et al*., which also identified saccular morphology and small necks as prevalent features in DACA aneurysms.[16]

In the present study, the mean dome diameter of DACA aneurysms was 6.1 ± 2.4 mm, with 71.1% measuring <5 mm and only one aneurysm exceeding 15 mm. Associated cerebrovascular anomalies were observed in 7/38 (18.4%) of patients, including three cases of multiple aneurysms (7.9%), vascular occlusion (5.3%) and isolated cases of arteriovenous fistula and moyamoya disease (2.6% each). The majority of patients presented with lower Fisher Grades (1–2: 58.8%), while Grades 3 and 4 accounted for 41.2%.

Compared with findings of Zhu *et al*., their cohort demonstrated a slightly smaller mean dome diameter and 35% of patients with Fisher Grades 3 and 4, indicating a comparable haemorrhagic burden. These differences likely reflect population characteristics, referral patterns and imaging protocols, emphasising the importance of early detection and meticulous pre-operative planning to optimise surgical outcomes for DACA aneurysms.[13]

In our series, temporary clipping was utilised in 78.9% of cases for proximal control, with a mean duration of 114 ± 26 s. This emphasises its importance in preventing intraoperative rupture in distal, small-caliber vessels. In comparison, Sharma *et al*.[17] also reported the utilisation of temporary clips, albeit with longer durations. Although temporary clipping is a valuable tool for proximal control, careful attention to duration and patient selection is crucial to minimise ischaemic complications and optimise functional recovery.

The selection of permanent clips favoured curved configurations (55.3%), reflecting the anatomical complexity and angulation of the pericallosal and callosomarginal arteries, which necessitates precise alignment for secure aneurysm neck obliteration. Operative metrics, including a mean surgical duration of 145 ± 41 min and average blood loss of 186 ± 68 ml, demonstrate that DACA aneurysm clipping can be accomplished efficiently with meticulous microsurgical technique, despite the challenges posed by deep interhemispheric access and delicate vascular structures.

Intraoperative complications occurred in 9/38 (23.7%) cases, with intraoperative rupture was most common occurred in 5/38 (13%). Other intraoperative events included parent artery injury in 1/38 (2.6%), bridging vein injury in 2/38 (5.3%) and cortical contusion/brain retraction injury in 1/38 (2.6%). Post-operative complications were observed in 11/38 (28.9%) patients, most commonly cerebral vasospasm in 5/38 (13%) and hydrocephalus requiring external ventricular drainage or shunt in 3/38 (7.9%). Less frequent complications included infarction, rebleeding, seizures, meningitis and surgical site infection (each 1/38, 2.6%). These complication rates are comparable with previous studies.[15,18] Complete aneurysm occlusion was achieved in 37/38 (97.4%) patients, which is comparable to the study conducted by Lee JY *et al*.,[19] who reported complete occlusion rate 90%. 30-day mortality observed in our series was 1/38 (2.6%), which is lower than previously reported study by Zhu *et al*.[13] These findings support that microsurgical clipping of DACA aneurysms offers high rates of aneurysm obliteration with an acceptable complication profile and low mortality. The data highlight the importance of temporary proximal clipping, careful interhemispheric dissection and precise handling of distal vessels to optimise both procedural safety and functional outcomes.

In our cohort, the mean ICU stay was 4.1 ± 1.5 days and the total hospital stay averaged 10.5 ± 2.1 days. These durations are reflective of a relatively uncomplicated post-operative course in the majority of patients and suggest effective perioperative care, early mobilisation and timely management of complications. Short ICU and hospital stays are clinically significant as they reduce the risk of nosocomial infections, lower healthcare costs and indicate efficient surgical and anaesthetic management in complex DACA aneurysm surgeries.

The mean follow-up duration in our series was 18.2 ± 5.8 months, which allowed adequate assessment of both functional recovery and potential delayed complications such as hydrocephalus, vasospasm-related deficits or aneurysm recurrence. Long-term follow-up is particularly important in distal aneurysms due to their complex anatomy and higher surgical risk, as it ensures the early identification and management of late morbidity, providing a comprehensive evaluation of the effectiveness and durability of microsurgical clipping.

In our series of 38 patients undergoing microsurgical clipping of DACA aneurysms, favourable outcomes were observed in a majority of patients. At discharge, 30 patients (78.9%) had a favourable GOS (4–5), which increased to 33 patients (86.8%) at 1- and 2-year follow-up. Similarly, favourable mRS (0–2) scores were recorded in 28 patients (73.7%) at discharge, improving to 32 patients (84.2%) at 1- and 2-year follow-up. Sharma *et al*.[17] reported comparable outcome, with 24/28 (85.7%) patients with favourable GOS at a long-term follow-up. Contrary, Zhu *et al*. reported favourable outcomes in only 59.6% of patients at a

2-year follow-up, reflecting real-world multicentre data.[13] In our series, functional outcomes continued to improve during follow-up, with favourable GOS and mRS scores increasing from discharge to 1–2 years. No late aneurysm recurrence was observed on follow-up imaging, underscoring the durability and efficacy of microsurgical clipping for DACA aneurysms. Our findings reinforce that meticulous microsurgical technique, careful interhemispheric dissection and temporary proximal control are critical for optimising the outcomes in this challenging subset of aneurysms.

In our series, several factors appeared to influence the surgical outcomes. Patients presenting with lower Hunt and Hess or WFNS grades generally had better functional recovery, while those with higher grades were more likely to experience post-operative complications such as vasospasm or hydrocephalus. Similarly, aneurysm characteristics, including larger dome size, complex morphology or involvement of critical branches, were associated with increased technical difficulty and higher risk of intraoperative rupture. These observations are consistent with prior studies,[5,6,10,11,17,20] suggesting that pre-operative neurological status, aneurysm morphology and careful surgical planning serve as key prognostic indicators in DACA aneurysm management. Such risk stratification can guide perioperative decision-making, optimise resource allocation and improve patient counselling regarding expected outcomes.

Limitation

This study has several limitations. It is a retrospective, single-centre analysis, which may limit the generalisability of the findings. The sample size was relatively small (n = 38), restricting the statistical power to analyse rare complications or subgroup outcomes. In addition, there was no comparative group or randomised controlled trial (RCT) design, so direct conclusions regarding the relative efficacy of microsurgical clipping versus endovascular management cannot be drawn. Prospective multicentre studies or RCTs are needed to better evaluate optimal treatment strategies for DACA aneurysms. In addition, variations in surgeon experience over the 15-year study period may have influenced operative strategies and outcomes.

Conclusion

DACA aneurysms constitute a rare and surgically demanding subset of intracranial aneurysms. Microsurgical clipping of DACA aneurysms is safe and effective, providing high rates of complete aneurysm obliteration with low perioperative morbidity and mortality. Success depends on meticulous interhemispheric dissection, temporary proximal control and careful preservation of distal perforators. Functional recovery improves progressively postoperatively, emphasising the durability and efficacy of precise microsurgical management in this challenging subset of aneurysms.

Future prospective multicentre studies comparing microsurgical clipping with evolving endovascular techniques are warranted to better define optimal treatment strategies and long-term outcomes for DACA aneurysms.

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Conflicts of interest

There are no conflicts of interest.

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Case Report

Hypertrophied Atrophy: Two Patient Case Report of Post-stroke Post-gamma Knife Radiosurgery Hypertrophic Olivary Degeneration

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Abstract

The study on patients presenting with tremors gives us deep knowledge of the connections in the motor circuits of the basal ganglia and brainstem. The large amplitude, low frequency tremors involving the limbs which has been variedly described as bird flapping or an alien hand movement of limbs is the rubral tremor associated with disturbances in the brainstem circuit involving the structures of Guillain–Mollaret triangle (GMT) which include red nucleus, dentate nucleus and the inferior olivary nucleus (ION). The afferent cut off to the ION results in pathological degeneration with volumetric expansion of the nucleus observed radiologically or also called the hypertrophic olivary degeneration (HOD). Two patients with different aetiologies of pontine bleed and ION afferent disconnection presented with a delayed rubral tremor. Both showing T2/FLAIR magnetic resonance imaging hyperintense signal in the olivary nucleus on the same side of the primary pathology completing the aetio-clinico-radiological diagnosis of HOD. Case literature is limited to few single case reports, and amongst them, the most common aetiologies include the vascular pathologies such as brainstem bleed, infarct or cavernous malformation or it has been observed post-tumour excision near the brainstem. The 2nd case in our report is the 1st such report of a gamma knife radiosurgery (GKRS) induced HOD. Sound knowledge of brainstem anatomy and physiological pathways involved in motor activity and judicious intervention of areas either surgically or by GKRS is essential to avoid HOD-related sequalae. In the patients presenting with rubral tremors, HOD must be kept in mind owing to its self-limiting natural history and partial response with dopaminergic agents and sodium valproate.

Keywords: *Gamma knife radiosurgery, Gullian–Mollaret triangle, hypertrophic olivary degeneration, stroke*

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Introduction

Hypertrophic olivary degeneration (HOD) is a type of disconnection syndrome due to varied aetiological pathologies which disrupt the connections of the dentate-rubro-olivary pathway.[1] It is a transneuronal multi or uni-synaptic degeneration which involves the olivary nucleus afferent disconnection leading to vacuolar degeneration and gliosis causing a paradoxical hypertrophy of the nucleus with functional loss. The dentato-rubro-olivary pathways, also known as the Guillain–Mollaret triangle (GMT),[2] includes the red nucleus located in the ventral midbrain of one side, inferior olivary nucleus (ION) located in the superior medulla of the same side and dentate nucleus of the cerebellum of the opposite side interconnected via tracts between all the three structures [Figure 1a]. The inciting pathology in the development of HOD is the afferent cutoff to the ION which can be at three levels; central tegmental tract (CTT), cerebellar or its peduncle lesions and the pontine lesions.

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Magnetic resonance imaging (MRI) of the brain reveals an increase in the volume of the olivary nucleus with an associated hyperintensity on T2 sequence and FLAIR and without contrast enhancement. The pathological findings on HOD include increased volume or mass of the olivary nucleus involved with microscopic findings suggestive of cytoplasmic vacuolar degeneration and relative increase in the number of astrocytes.[3]

Pathophysiology and Case Series

The GMT is formed by three epicentres and three connections between them, the epicentres include the ION, contralateral dentate nucleus and ipsilateral red nucleus. The efferents or the pathway tracts from dentate nucleus pass to the red nucleus through the dentatorubral tract which travel in the superior cerebellar peduncle and get decussation in the midbrain to enter the opposite side red nucleus.[1] The efferents from the red nucleus descend down the brainstem as the CTT or the rubroolivary tract which run in the dorsal paramedian pontine region. The triangle is completed by the olivocerebellar tracts which arise from the ION and through the inferior cerebellar peduncle reach the contralateral dentate nucleus.[4] The dentato-rubro-olivary circuit is complete triangle with afferent and efferent tracts with synaptic connections, the disynaptic pathway starts from the opposite dentate nucleus via the superior cerebellar peduncle crossing at the midbrain reaches and relays in the red nucleus and the efferent tracts from it pass via the CTT to the ION, the Monosynaptic pathway runs through the same course without relaying in the red nucleus.

The HOD is transsynaptic degeneration due to loss of afferents to the ION, the efferent fibers from the ION to the contralateral dentate nucleus when affected is generally not associated with the development of HOD.[5] The lesions occur at various places and the pattern of involvement of HOD varies accordingly. 1st pattern of involvement includes the lesions at the CTT which affect the brainstem [Figure 1b], 2nd pattern of involvement includes the lesions in the cerebellum which may affect the dentate nucleus or the superior cerebellar peduncle which causes the afferent loss at a proximal or presynaptic level to the contralateral ION involving the dentatorubral pathway [Figure 1c]. 3rd pattern of involvement includes the lesions in pons which affects both the central tegmental descending fibers and the decussating fibres of the contralateral dentatorubral tracts [Figure 1d].

Case report 1

A 42-year-old male, resident of northern India, presented with a history of ictus and development of left hemiplegia in May 2020, patient was evaluated to have a diffuse pontine bleed [Figure 2b], managed conservatively then and the patient improved over the next 3 months with improvement in power with physiotherapy. The patient noticed an insidious onset, progressively increasing left-sided abnormal movements over the next few months which were increasing in intensity with movement, nature of the movement as patient describes them as a bird wings flapping. He did not give any history of abnormal movement of the palate or eyes or any new onset acute headache or ictus like history.

Non-contrast computed tomography of the head was done which showed gliotic focus of the old pontine bleed [Figure 3a], contrast MRI of the brain revealed a T1-hypo, T2-hyper [Figures 2a and 3b] and FLAIR-hyperintense [Figure 3c]. Non-contrast-enhancing [Figure 2c] intra-axial lesion in the ventral right lower medullary area restricted to the ION which showed choline peak on MR spectroscopy and no diffusion restriction on diffusion-weighted imaging. The patient was considered with differential of low-grade glioma at one of the local centres and

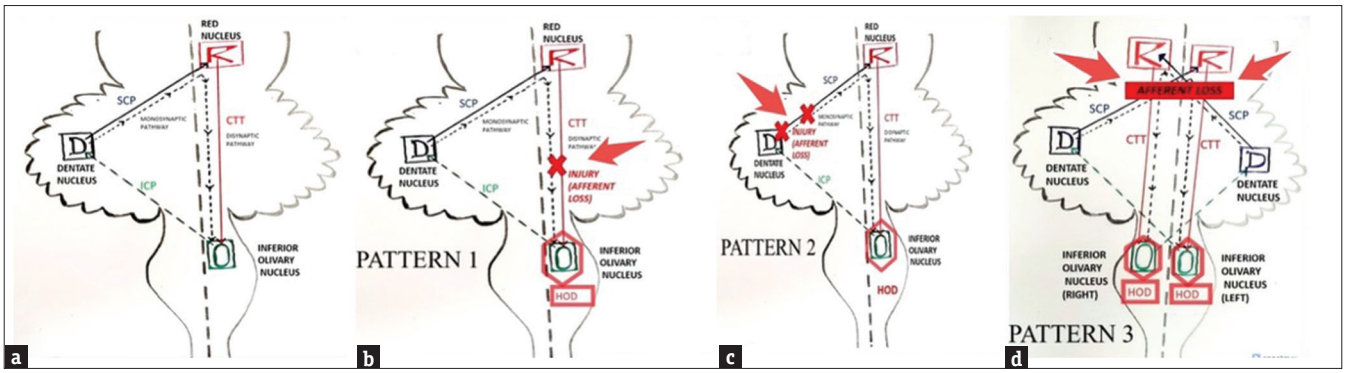

Figure 1: (a) Guillain–Mollaret triangle components and its pathways (Bisynaptic and monosynaptic), 1 (b-d) depicting the patterns of afferent disconnection to inferior olivary nucleus leading to hypertrophic olivary degeneration (arrows pointing towards lesion sites)

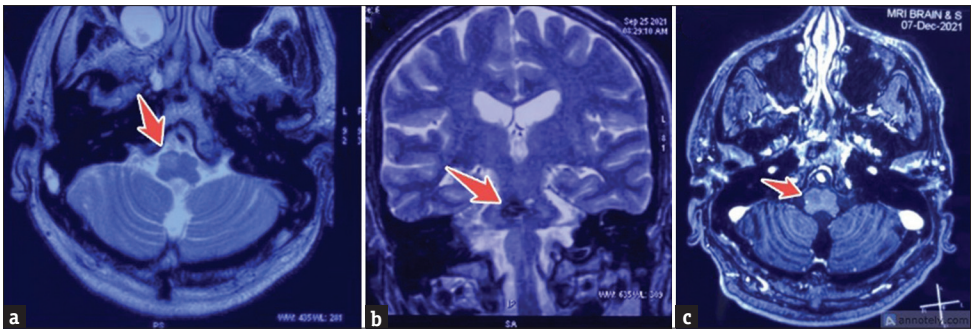

Figure 2: (a) Typical lesion of hypertrophic olivary degeneration (HOD) T2-Hyperintense involving the lower ventral medulla of the inferior olivary nucleus area. (b) Depicting the same sided Pontine bleed in coronal T2 sequence. (c) No contrast enhancement of the HOD lesion on T1* (Arrows depicting the lesions)

was planned for sequential scanning for understanding the natural history of the lesion as intervention in this critical area was associated with more risk than benefit.

Second differential at a different centre considered the diagnosis of a medullary cavernoma and referred the case to our institute for gamma knife radiosurgery (GKRS) of the lesion. The patient was started on dopaminergic agonist drugs, and on follow-up of 1 year, the patient is doing well with gradual improvement of symptoms.

This case depicts a typical temporal sequalae of pontine bleed affecting the CTT and type 1 pattern of ION disconnection leading to HOD and also reflects its self-limiting natural history.

Case report 2

A 50-year-old diabetic female, who presented to our institute with a history of sudden onset severe headache and right-sided weakness in 2016, which on evaluation revealed an arteriovenous malformation (AVM) associated bleed at the middle cerebellar peduncle and left cerebellum. The patient was managed conservatively in the acute phase and the AVM was targeted with GKRS (Session 1). The patient gradually improved and was able to do her daily activities normally. Follow-up imaging showed a residual nidus of size 1.5 cm × 1.2 cm × 1 cm with feeders from left anterior inferior cerebellar artery and left superior cerebellar artery which then underwent endovascular onyx embolisation in April 2020. She had 2nd ictus in October 2020 with a rebleed in the same area from the residual nidus. The nidus was targeted with 2nd stage GKRS with a prescription dose of 23.0 Gy at 50% isodose on 12th January 2021 and discharged in the stable condition.

The patient presented 6 months post 2nd session of GKRS with complaints of abnormal movement of right-sided extremities (similar clinical features to case 1). A repeat MRI was done at 9 months post-GKRS which showed a significant reduction in nidus size but with a development of a new lesion T2-Hyper [Figure 4a]. FLAIR hyperintense with no contrast uptake [Figure 4b] at the ION on the left side which was T2 hyperintense and non-contrast enhancing, the patient was diagnosed with HOD with rubral tremors and was started on clonazepam, escitalopram 20 mg with regular physiotherapy. The patient last presented to our GKRS OP in January 2025 on regular interval follow-ups with a significant improvement in tremors and weakness.

The analysis from this case includes that of new aetiological basis of HOD with involvement of the pontine long tracts along with CTT post-GKRS. The temporal correlation of events and intervention point out towards a GKRS induced afferent cutoff and HOD development and also its subsequent natural resolution.

Review of Literature

The review of the literature [Table 1] has case reports with single or two cases with majority of the HOD cases in patients of brainstem cavernoma, in patients with brainstem infarcts or bleed and also few post-surgical excision of brainstem lesions. Palatal tremor was one of the most common symptoms along with the holmes (rubral) tremor or a cerebellar sympatomology.

Discussion

Aetiology

The HOD which is an interruption in the afferent tracts to the ION can be caused due to varied pathologies which commonly include haemorrhage, infarction, vascular malformations, toxic, trauma or surgery.[6] The vascular pathologies are the major stakeholders with upcoming new aetiologies of post-surgical and post-intervention (GKRS) to the brainstem causing lesions within the GMT.

Pathological and radiological characteristics

The changes which include astrocytic hypertrophy, neuronal vacuolar degeneration, apparent hypertrophy and gliosis occur over a period of time after the primary

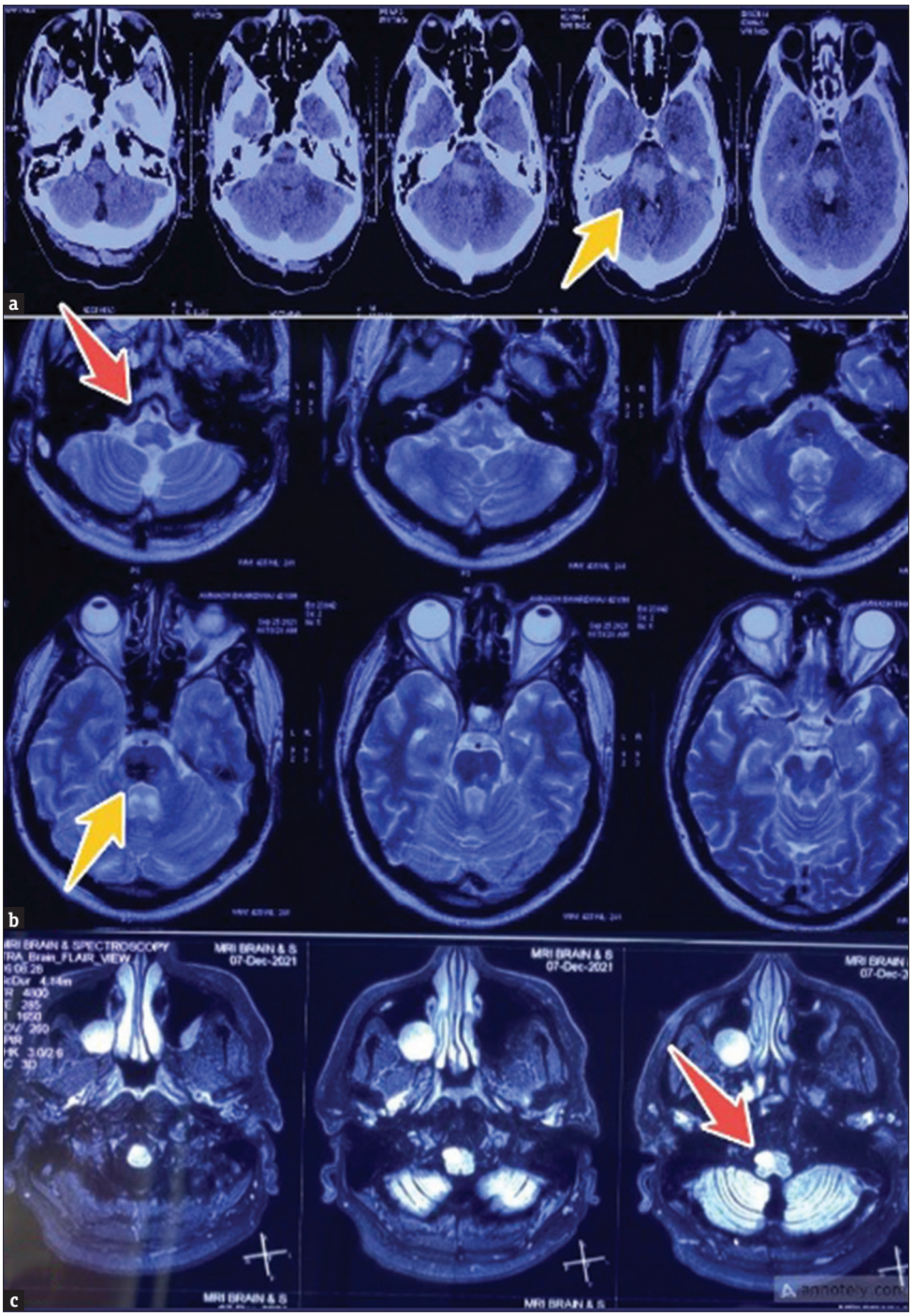

Figure 3: (a) Non-contrast computed tomography findings of Pontine bleed with which the patient initially presented. (b) Depicting the same sided inferior olivary nucleus involvement to the bleed (Type 1 Pattern). (c) Showing the typical FLAIR hyperintensity of hypertrophic olivary degeneration (HOD) lesion. (Red Arrows pointing to HOD lesions, Yellow arrows-pointing right sided Pontine bleed)

insult. The first change observed pathologically is the degeneration of the white matter capsule which generally occurs at 2–7 days, followed by the olivary nucleus neurons hypertrophy which starts at 3 weeks post insult, increase unto a maximum at around 8.5 months, then the phase of pseudo-hypertrophy with degeneration of neurons and replacement by the large astrocytes occurs, followed by a functional and morphological atrophy of the ION.[7]

The vacuolar degeneration with increased fluid component reflects as a T2-hyperintensity on MRI-brain at the ION located in the ventrolateral part of the medulla. Initially, the intensity signal from ION increases without apparent hypertrophy of the nucleus; the 2nd stage which is the typical characteristic of HOD with T2-hyperintensity with hypertrophy of the ION; which is followed by the phase where there is apparent volume loss and shrinkage

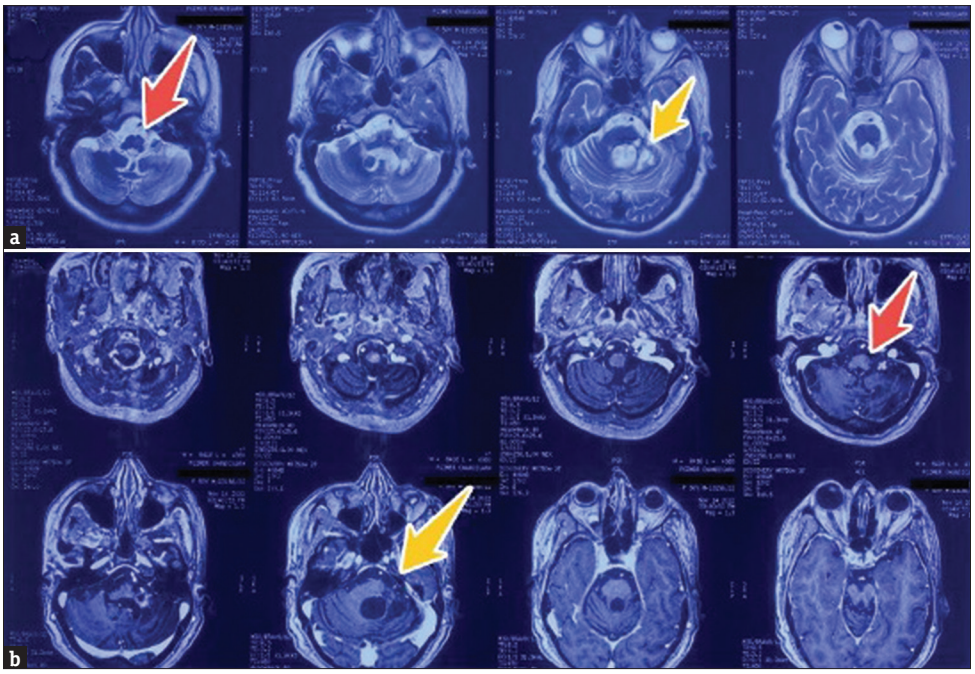

Figure 4: T2-MRI Axial cuts (a) and T1-Contrast (b) of the patient post 2 stage gamma knife radiosurgery and onyx embolisation of an twice ruptured pontine arteriovenous malformation with a delayed presentation with rubral tremors and MRI depicting the hypertrophic olivary degeneration lesion in the left olivary nucleus(red arrows) on the same side on the pontine lesion and old bleed with gliosis(yellow arrows)

of the nucleus with persistent T2-hyperintensity. The characteristic feature which differentiates HOD from most other pathologies which present with similar radiological findings is that the lesion in HOD does not show contrast uptake. The imaging findings on DTI suggest a secondary demyelination pattern[8] with associated neuronal degeneration which is suggestive of transneuronal degeneration.

Clinical presentations and differential diagnosis

The most common presentation of HOD is a movement disorder which generally involves the palate as a palatal tremor[9] -stereotypic, rhythmic contractions of the palate with a frequency of 1–3 Hz which occurs in a specified timeline, usually within 11 months of the insult to the structures in the GMT.[10] The palatal tremors are characteristic of patients with HOD and is considered as a hallmark symptom, but not all patients of HOD present with the symptom complex. The other movement disorders which have been explained are the dentatorubral tremors, ocular myoclonus and nystagmus. The rubral tremor [Video 1] is also a well-defined movement disorder in which there is a resting and also intentional component of an large amplitude, slow frequency predominantly action tremor which also presents after an certain delay of the primary insult.

The key differentials of a patient who presents with a movement disorder and MRI findings of a T2 hyperintense lesion in the medulla include demyelination, tumours, ischaemia and infectious and inflammatory pathologies. The characteristics which point more towards a HOD is a typical movement disorder with delay in symptoms from the inciting insult with a typical contrast non-enhancing T2-hyperintense enlargement of ION[11] which is limited to ION and serial MRI shows the temporal evolvement with the detection of a remote lesion in the same sided red nucleus or tegmentum of pons or in the opposite cerebellar dentate nucleus.

Treatment and prognosis of hypertrophic olivary degeneration

It has been observed that majority of the patients with HOD are subclinical and have a self-limiting course. The different treatment regimens which have shown some response in patients include dopaminergic agents, sodium valproate, clonazepam, carbamazepine, tryptophan or trihexyphenidyl.[12]

Conclusion

Sound knowledge of anatomical basis and physiological pathways involving the motor circuits help us plan intervention of the brainstem lesions from surgery to gamma knife to conventional radiotherapy. The posterior fossa ischaemic or haemorrhagic stroke patients should be kept on follow-up and observed for delayed new-onset tremors which when confirmed clincoradiologically, the patient can be reassured and unnecessary intervention can be avoided.

Table 1: All the articles reporting hypertrophic olivary degeneration, the major aetiologies involved in them are cerebellar haemorrhage or infarction or cases post-surgical excision of brainstem lesions

References	Aetiology	Number of cases	Uni/bilateral	Symptoms
Phatourous and McConachie (1998)	Brainstem cavernoma	1	Left	
Tsui *et al*. (1999)	Brainstem cavernoma	1	Bilateral	Palatal tremor
Harter and Davis (2004)	Brainstem cavernoma	1	Left	
Sanchez *et al*. (2013)	Brainstem cavernoma	2	1-Right, 1-Left	
Carvalho *et al*. (2016)	Brainstem cavernoma	1	Left	Palatal tremor
Wein *et al*. (2015)	Brainstem cavernoma	1	Right	
Vyas *et al*. (2013)	Brainstem cavernoma	1	Bilateral	
Santos *et al*. (2015)	Brainstem cavernoma	1	Left	Cerebellar speech
Santos *et al*. (2015)	Traumatic brain injury	1	Bilateral	
Asal *et al*. (2012)	Brainstem cavernoma	1	Bilateral	Ataxia
Macht *et al*. (2009)	Brainstem cavernoma	1	Right	Intentional tremor
Koska *et al*. (2014)	Brainstem cavernoma	1	Right	Limb ataxia
Menendez *et al*. (2014)	Brainstem cavernoma	1	Right	Limb ataxia
Crosbie *et al*. (2013)	Brainstem cavernoma	1	Left	Palatal tremor
Walker *et al*.(2007)	Brainstem cavernoma	1	Right	Holmes tremor
Rosenblum *et al*.(2018)	Brainstem cavernoma	1	Left	Ataxia
Yoshi *et al*. (2018)	Brainstem cavernoma	1	Bilateral	
Howard *et al*. (2019)	Brainstem cavernoma	1	Left	Ataxia
Kim *et al*. (2014)	Cerebral haemorrhage	1	Bilateral	Holmes tremor
Martins *et al*. (2016)	Cerebral haemorrhage	1	Right	Hemi-dystonic movements
Sarawagi and Murugesan (2015)	Cerebral haemorrhage	1	Right	Dysathria
Araujo *et al*. (2015)	Cerebral haemorrhage	1	Left	Palatal tremor
Guo *et al*. (2015)	Cerebral haemorrhage	1	Right	Palatal tremor
Suner *et al*. (2017)	Cerebral haemorrhage	1	Bilateral	Palatal tremor , pendular nystagmus
Lim and Lim (2009)	Cerebral haemorrhage	1	Bilateral	Palatal tremor , pendular nystagmus
Uchino *et al*. (1993)	Cerebral haemorrhage	6	3-Right , 3-Left	
Yokota *et al*. (1989)	Cerebral haemorrhage	1	Bilateral	Palatal tremors
Hirono *et al*. (1990)	Cerebral haemorrhage	2	1-Right , 1-Left	Palatal tremors
Revel *et al*. (1991)	Cerebral haemorrhage	1	Right	Palatal tremors
Salamon-muayama *et al*. (1999)	Cerebral haemorrhage	1	Left	Dentatorubral tremor
Alstadhaug *et al*. (2007)	Cerebral haemorrhage	1	Left	Occulopalatal tremor
Rieder *et al*. (2003)	Cerebral haemorrhage	1	Bilateral	Holmes tremor
Chhetri *et al*. (2014)	Cerebral haemorrhage	1	Right	Holmes tremor
Xia *et al*. (2018)	Cerebral haemorrhage	1	Right	
Bruno and Wooten *et al*. (2012)	Cerebral infarction	1	Right	Dysathria
Gerace *et al*. (2006)	Cerebral infarction	1	Bilateral	
Conforto *et al*. (2005)	Cerebral infarction	1	Bilateral	Cerebellar syndrome
Inhoue *et al*. (2014)	Cerebral infarction	1	Bilateral	
Dubinsky *et al*. (1991)	Cerebral infarction	1	Bilateral	Palatal tremors
Pierot *et al*. (1992)	Cerebral infarction	1		
Zhou *et al*. (2017)	Cerebral infarction	1	Bilateral	Palatal tremors
Mossuto-Agatiello (2006)	Cerebral infarction	5	5-Bilateral	1-ataxia, 2- palatal tremors
Sen *et al*. (2014)	Cerebral infarction	1	Bilateral	Tremor
Vekatesh *et al*. (2017)	Cerebral infarction	1	Bilateral	Palatal tremors
Sanverdi *et al*. (2012)	Medulloblastoma excision	3	Bilateral	
Nowak *et al*. (2014)	Medulloblastoma excision	1	Bilateral	Cerebellar mutism
MFM *et al*. (2018)	Medulloblastoma excision	1	Right	Ataxia
Hirano *et al*. (2015)	Tumour resection	7	4-Bilateral, 3-Right	4-nystagmus , 3-ataxia
Sato *et al*. (2019)	Tumour resection	2	Bilateral	Palatal tremors
Ash and srinivasan (2008)	Tumour resection	1	Left	Swallowing difficulty

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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