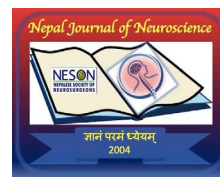


## Augmenting Cerebral Perfusion Via Bypass Technique in symptomatic intracranial atherosclerotic disease

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In Nepal, acute ischemic stroke (AIS) holds the sobering distinction of being the fifth leading cause of mortality and the third most prevalent source of disability. This underscores a pressing health concern that demands attention and proactive measures to address its impact on public well-being. Nepal is amidst a swift epidemiological shift, witnessing a surge in stroke and noncommunicable diseases due to rapid urbanization, sedentary lifestyles, and poor dietary habits. Urgent measures are essential to address this burgeoning public health challenge.<sup>1,2,3</sup>

Nepal has advanced in acute ischemic stroke (AIS) treatment, employing tissue plasminogen activator (tPA) and innovative interventions like mechanical thrombectomy (MT) for large vessel occlusion (LVO). This signifies significant progress in enhancing medical care for stroke patients.<sup>4</sup> Kathmandu, the bustling capital, serves as the hub for these operations. Yet, Intracranial Atherosclerotic Disease (ICAD) stands out as a prevalent culprit behind strokes. Among those with symptomatic ICAD, a substantial 40% grapple with recurrent cerebral ischemia within a mere two-year span. Ethnic groups of Asian and African descent exhibit a heightened susceptibility to Intracranial Atherosclerotic Disease (ICAD), a complex condition influenced by various factors, including genetic predisposition. Specifically, ICAD is associated with singular polymorphisms in several genes related to adiponectin, lipoprotein lipase, and angiotensin-converting enzymes.<sup>5</sup> ICAD can lead to in-situ thrombosis, hemodynamic insufficiency, small vascular blockages, or artery-to-artery embolism.

Presently, therapeutic avenues for ICAD involve sophisticated interventions such as endovascular stenting, bypass surgery, and the implementation of intensive medical management

(IMM). IMM, characterized by a robust strategy of dual antiplatelet therapy and meticulous risk factor optimization, stands as a cornerstone in addressing this complex condition. Our practice includes the execution of Direct Bypass procedures, a specialized technique offering flow replacement for intricate cerebral aneurysms or skull base tumors. Moreover, we utilize this approach for flow augmentation in cases of ischemia and Moya Moya illness. Noteworthy examples comprise the EC-IC Bypass for high-flow scenarios and STA-MCA Bypass (M3) for low-flow situations.

In 1967, Professor Mahmut Gazi Yasargil achieved a groundbreaking milestone by conducting the inaugural EC-IC bypass on a patient with MCA blockage and Marfan's disease. This landmark procedure marked the inception of cerebral revascularization, demonstrating Professor Yasargil's pioneering contributions to neurosurgical innovation.<sup>6</sup> The seminal EC-IC Bypass trial, conducted since 1985, has significantly impacted the landscape of bypass surgeries. This pivotal trial revealed that there was no discernible difference in overall outcomes between direct bypass and Intensive Medical Management (IMM) for cerebrovascular ischemic disease. As a result, it contributed to a notable decline in the frequency of bypass surgeries.<sup>7</sup>

Perfusion studies were alluded to as potentially advantageous for high-risk patients. However, a notable critique of the trial arose from the absence of hemodynamic assessments when selecting surgical candidates. This concern was effectively addressed in the Carotid Occlusion Surgery Study (COSS) trial, where The Oxygen Extraction Factor (OEF) was calculated through PET scans to discern hemodynamic cerebral ischemia. Despite the discernible enhancement of cerebral hemodynamics with bypass surgery, the PET scan results revealed no significant improvement compared to Intensive Medical Management (IMM). Notably, the COSS trial demonstrated that, although bypass surgery improved cerebral hemodynamics, it did not yield a discernible reduction in the risk of stroke recurrence over two years when compared to IMM.<sup>8</sup>

Subsequent findings from the prospective cohort study, the Japanese Extracranial Intracranial Bypass Trial (JET-2), shed light on the favorable prognosis for medically treated patients facing symptomatic major cerebral arterial occlusive diseases with mild hemodynamic compromise. The study highlighted that the recurrence rate of stroke in medically treated patients increased when the resting cerebral blood flow (CBF) was less than 80% of the normal value and cerebral vascular reserve (CVR) was less than 10%. In such cases, bypass surgery emerged as a likely beneficial intervention for patients with resting CBF < 80% or CVR < 10%.<sup>9</sup>

The application of an indirect bypass represents an alternative technique that fosters angiogenesis, offering

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collateral supply in the post-stenotic territory of Intracranial Atherosclerotic Disease (ICAD) lesions. However, this process of regaining collateral circulation poses a potential risk of stroke to the patient. Factors such as age, medical comorbidities (such as diabetes), and diminished endothelial progenitor cells can compromise angiogenesis during this critical phase.

The Encephaloduroarteriosynangiosis Revascularization Intracranial Arterial Stenosis (ERIAS) Phase 2 trial is presently underway, guided by the hypothesis that, in meticulously selected patients, it surpasses the outcomes achieved with Intensive Medical Management (IMM). This trial aims to contribute valuable insights into the effectiveness of ERIAS as a revascularization strategy for intracranial arterial stenosis.<sup>10</sup>

Several randomized clinical trials, such as the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) and Stenting versus Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS), have consistently showcased the superiority of Intensive Medical Management (IMM) when compared to endovascular procedures. These trials collectively underscore the robust efficacy of IMM in the context of ischemic stroke therapy and prevention of recurrent strokes in cases of intracranial stenosis.<sup>11,12</sup>

## Conclusion

In the upcoming decades, the prevalence of both ICAD and stroke is set to double with the aging global population. Notwithstanding current AHA guidelines advising against EC-IC bypass for ICAD, in carefully chosen cases where Intensive Medical Management (IMM) falls short in alleviating symptoms, the strategic recourse of rescue surgery whether through direct or indirect bypass presents itself as a prudent intervention.<sup>13</sup>

Delivering satisfactory outcomes in Intracranial Atherosclerotic Disease (ICAD) bypass procedures demands meticulous consideration of the affected cerebral angioarchitecture, hemodynamic parameters, and the suitability of both donor and recipient vessels. This comprehensive approach involves utilizing diagnostic tools such as SPECT with and without Diamox challenge to assess cerebral vascular reactivity (CVR), Quantitative MRA (QMRA) for non-invasive optimal vessel analysis (NOVA) to evaluate flow in the vascular territory, as well as MR Perfusion or CT Perfusion scans. These advanced imaging techniques collectively contribute to a nuanced understanding of the patient's vascular dynamics, informing a tailored and effective course of intervention.

Anticipation surrounds the forthcoming results of the ERIAS Phase 2 trial, eagerly awaited to discern whether Indirect Bypass could ameliorate the perioperative morbidities associated with Direct Bypass. This trial holds promise for refining our understanding of optimal revascularization strategies and their impact on patient outcomes.

To minimize perioperative morbidity, it is imperative to entrust the procedure to highly skilled and experienced surgeons operating in high-volume centers with specialized staff. In select centers in Nepal, a pioneering approach involves Augmenting Cerebral Perfusion Via Bypass

Technique for individuals with symptomatic intracranial atherosclerotic disease, particularly in stroke patients. This tailored and expert-led strategy signifies a noteworthy advancement in the pursuit of optimal patient outcomes.

Mastering the skills requisite for these procedures demands rigorous dry and wet lab practice, contributing to a protracted learning curve. In the realm of bypass surgery, the judicious selection of patients is pivotal, serving as the linchpin to substantiate its necessity and superiority over alternative options. Optimal decisions for swift and secure revascularization hinge on possessing a composed demeanor, a relaxed upper body, a steady hand, and a compassionate heart. The crux of a successful bypass procedure lies in the amalgamation of innovation, flexibility, and adaptability.

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