

Resource-Limited ENLS Acute Ischemic Stroke

General considerations: Resource gaps in many low- and middle-income countries (LMICs) and other resource-limited settings preclude adherence to many of the evidence-based strategies for acute stroke management developed in high-income settings.¹ Key resource limitations that may impact acute stroke care include timely access to CT imaging, thrombolysis, and endovascular thrombectomy. Delays in neuroimaging prevent early differentiation between ischemic stroke and intracerebral hemorrhage (ICH),² creating uncertainty around indications for antiplatelet therapy and optimal blood pressure management. Because thrombolytic and endovascular therapy rely on the timely deployment of a broad range of human and material resources that are undeveloped or unavailable in many LMIC settings, these acute interventions remain out of reach for many populations worldwide.³ Optimal acute stroke care in resource-limited settings must therefore prioritize early stabilization of the patient's airway, breathing, and circulation, mitigation of common hospital-acquired complications, and interdisciplinary care to support rehabilitation in the subacute phase of the disease course. Protocolized stroke unit-based care has been shown to significantly improve stroke outcomes in LMICs without significant increases in cost or resource utilization.^{4,5}

<u>Acute stroke management in the absence of CT:</u> In many healthcare settings worldwide, CT is unavailable for acute decision-making due to low scanner availability in LMICs, concentration of imaging resources in urban centers, and out-of-pocket costs to patients that must be furnished before imaging.⁶ Antiplatelet therapy is known to lower risk for recurrent ischemic stroke acutely, but may worsen risk of hemorrhage expansion in the event of an ICH. A decision analysis investigating the use of aspirin for acute stroke of unknown etiology found that empiric aspirin in the absence of CT imaging improved rates of survival and recurrent stroke, even in countries where ICH accounts for as much as 60% of the overall stroke burden.⁷ If early CT is available and rules out a hemorrhagic etiology, aspirin should be started immediately. If CT is delayed and the patient remains clinically stable without worsening of their NIH stroke scale (NIHSS) or Glasgow Coma Scale (GCS) scores over the first 24 hours of admission, aspirin should be started empirically though should be carefully considered on a case-by-case basis. If one or more clinical indicators suggestive of ICH is present (headache, vomiting, rapidly progressive neurologic deficits, coma, concern for increase intracranial pressure, or hypertensive emergency), it is reasonable to withhold aspirin at the clinician's discretion until imaging can be performed.

Goals for blood pressure management differ between acute ischemic stroke and ICH, as cerebral ischemia theoretically favors higher blood pressure for penumbral nourishment and cerebral hemorrhage theoretically favors lower blood pressure to minimize risk of hematoma expansion. The optimal blood pressure after ICH has never been definitively established^{8,9}. A recent trial of blood pressure lowering below 140mmHg for patients with ICH in several LMICs demonstrated a functional outcome benefit of tighter blood pressure control, though this intervention was coupled with a protocolized care bundle that makes it difficult to isolate the effect of blood pressure control *per se.*¹⁰ There is evidence to suggest that minimizing early blood pressure variability improves outcomes from ICH. Taken together, the available evidence suggests that an empiric blood pressure goal of <180mmHg for stroke of unknown etiology with CT imaging is safe, balances the physiologic considerations of ischemic and hemorrhagic strokes, and likely reduces large fluctuations in blood pressure for patients presenting with extreme hypertension.¹



Protocolized stroke care: Because disease-modifying acute stroke interventions are generally unavailable in resource-limited settings, an emphasis on preventing and managing hospital-acquired complications and physiologic derangements is paramount to optimize stroke outcomes. Aspiration pneumonia is common complication of acute stroke in LMICs,¹¹ and early priority should be given to dysphagia screening to identify the need for non-enteral feeding. Patients with evidence of aspiration pneumonia (cough, tachypnea, fever, leukocytosis, abnormal chest X-ray) should be treated promptly with antibiotics and supplemental oxygen, and their airway stability should be reassessed. Hypovolemia appears to worsen outcomes from acute stroke and patients' daily fluid balance should be monitored closely to identify need for intravenous fluid resuscitation. Fever is known to increase risk for secondary brain injury and should be treated aggressively with antipyretics and chilled saline as available along with assessment for an underlying infectious source. Detection of complications in real time requires careful standardized nursing care for regular neurologic assessments and vital sign checks.



References

1. Prust ML, Saylor D, Zimba S, Sarfo FS, Shrestha GS, Berkowitz A, Vora N. Inpatient Management of Acute Stroke of Unknown Type in Resource-Limited Settings. *Stroke*. 2022;53(3).

2. Runchey S, McGee S. Does this patient have a hemorrhagic stroke?: clinical findings distinguishing hemorrhagic stroke from ischemic stroke. *JAMA*. 2010;303(22):2280–2286.

3. Prust M, Mbonde A, Rubinos C, Shrestha G, Komolafe M, Saylor D, Mangat H. Providing Neurocritical Care in Resource-Limited Settings: Challenges and Opportunities. *Neurocritical Care*. 2022;37(2):583–592.

4. Langhorne P. Organised inpatient (stroke unit) care for stroke. *Cochrane Database of Systematic Reviews*. 2013;2013(9):CD000197.

5. Langhorne P, de Villiers L, Pandian JD. Applicability of stroke-unit care to low-income and middle-income countries. *The Lancet Neurology*. 2012;11(4):341–348.

6. McLane H, Berkowitz A, Patenaude B, McKenzie E, Wolper E, Wahlster S, Fink G, Mateen F. Availability, accessibility, and affordability of neurodiagnostic tests in 37 countries. *Neurology*. 2015;85(18):1614–1622.

7. Berkowitz AL, Westover MB, Bianchi MT, Chou SHY. Aspirin for acute stroke of unknown etiology in resource-limited settings A decision analysis. *Neurology*. 2014;83(9):787–793.



8. Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, Moy CS, Silbergleit R, Steiner T, Suarez JI, Toyoda K, Wang Y, Yamamoto H, Yoon B-W. Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage. *New England Journal of Medicine*. 2016;375(11):1033–1043.

9. Anderson CS, Heeley E, Huang Y, Wang J, Stapf C, Delcourt C, Lindley R, Robinson T, Lavados P, Neal B, Hata J, Arima H, Parsons M, Li Y, Wang J, et al. Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage. *New England Journal of Medicine*. 2013;368(25):2355–2365.

10. Ma L, Hu X, Song L, Chen X, Ouyang M, Billot L, Li Q, Malavera A, Li X, Muñoz-Venturelli P, de Silva A, Thang NH, Wahab KW, Pandian JD, Wasay M, et al. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial. *Lancet (London, England)*. 2023;402(10395):27–40.

11. Prust ML, Nutakki A, Habanyama G, Chishimba L, Chomba M, Mataa M, Yumbe K, Zimba S, Gottesman RF, Bahouth MN, Saylor DR. Aspiration Pneumonia in Adults Hospitalized With Stroke at a Large Academic Hospital in Zambia. *Neurology: Clinical Practice*. 2021;11(6):e840–e847.