

Resource-Limited ENLS Intracerebral Hemorrhage

Epidemiology: While underdevelopment of surveillance and reporting systems in many low- and middle-income countries (LMICs) obscures the true global burden on intracerebral hemorrhage (ICH), it is known to account for a significantly greater proportion of the total stroke burden in LMICs compared to high-income countries (HICs).¹⁻⁴ Whereas ICH accounts for roughly 15% of all strokes in the United States, it has been reported to account for over half the stroke burden in some LMICs. The causes of this epidemiologic disparity are incompletely understood, but poor population-level control of hypertension resulting in a greater burden of cerebral small vessel disease in LMICs is likely a key driver.^{5–7} In light of these trends, the prior probability of ICH in patients in LMICs presenting with acute stroke of unknown type is greater in LMICs than in HICs, though distinguishing confidently between these stroke subtypes is difficult on clinical grounds alone.⁸ Patients with ICH may be more likely to present with headache, decreased level of consciousness, nausea/vomiting, and rapidly progressive neurologic deficits, though there is no proven clinical assessment tool to definitively differentiate these two stroke subtypes without a CT scan.⁹

<u>Pre-hospital care and patient transport:</u> Patients with acute onset of neurologic deficits should be promptly transported to the highest available level of care. In most LMICs, prehospital care and emergency medical services are underdeveloped or unavailable. All feasible efforts should be made to stabilize the patient's airway in field by clearing oral secretions and elevating the head of the bed. If the patient presents to a peripheral hospital or health care facility, the patient should undergo a rapid evaluation to assess airway, breathing, circulation, and signs of elevated intracranial pressure (ICP;see ENLS module on *Intracranial Hypertension and Herniation*). IV access should be established, and if there is concern for elevated ICP, an empiric dose of mannitol 1g/kg should be given if it is available. Once all feasible acute stabilization interventions have been performed, the patient should be transferred to the highest available level of care, ideally a referral hospital equipped with neurology and neurosurgery expertise and an intensive care unit capable of mechanical ventilation and external ventricular drain (EVD) management.

Acute blood pressure management in the absence of CT scan: Because distinguishing between ischemic and hemorrhagic stroke is often impossible on clinical grounds alone, early stabilization efforts should aim to balance the competing priorities to minimize risk of hematoma expansion (in the case of ICH) and maximize cerebral perfusion for tissue at risk (in the case of ischemic stroke). A systolic blood pressure (SBP) goal of <180mmHg and a mean arterial pressure (MAP) goal of <65mm/hg are reasonable when faced with diagnostic uncertainty before CT scan is performed.⁸ These goals can adjusted at the clinician's discretion to avoid overly rapid drops in blood pressure for patients who present with extreme hypertension (i.e. SBP >240mmHg). A key priority in acute stroke care is to avoid large swings in blood pressure. Titratable antihypertensive infusions are unavailable in most resource-limited settings, and close serial blood pressure monitoring is essential to detect dangerous BP fluctuations in real time, particularly in patients receiving bolus dose antihypertensives. CT scan should be obtained as early as possible, though delays may occur in many settings due to heavy scanner demand and out-of-pocket patient costs.

<u>Other considerations in resource-limited settings:</u> Beyond blood pressure control, reversal of coagulopathies is a key component of acute ICH care. Coagulation studies including, PT, PT-INR, PTT, and fibrinogen should be ordered for all patients (as available), and the results should be closely followed up to guide hematologic



resuscitation efforts. Prothrombin complex concentrate (PCC) is unavailable in many LMICs, but fresh frozen plasma (FFP) and vitamin K are available in many settings for reversal of warfarin-associated coagulopathies. Platelets should not be routinely administered for spontaneous ICH in patients on anti-platelet medications, but can be administered for patients requiring surgery to aid in surgical hemostasis. A clear line of communication between the emergency department and blood bank is essential to maintain clinicians' awareness of blood product availability for resuscitation of coagulopathies.

When clinical evidence of elevated ICP is present (depressed level of consciousness, pupil asymmetry, nausea/vomiting), the patient should be promptly intubated and positioned afterward with head of bed at 30 degrees. If CT reveals evidence of intraventricular hemorrhage or CSF outflow obstruction causing hydrocephalus, an EVD should be placed if this is available. Most resource-limited settings lack the capacity for ICP measurement or titrated drainage parameters from EVDs, and clinicians should follow institutional protocols for EVD management aimed at reversing hydrocephalus, allowing time for restoration of CSF outflow, avoiding overdrainage, and minimizing risk of infection. Non-invasive methods for monitoring ICP elevation in resource-limited settings are still being validated but may include hourly pupil exams and serial funduscopic exams. Because of the widespread lack of hypertonic saline worldwide, mannitol is likely to be the mainstay of medical ICP management in most resource-limited settings. Heavy sedation should be avoided if possible, in order to preserve the patient's neurologic exam, though intubated patients may require some sedation for comfort and safety. Mild hyperventilation can serve as a temporizing measure, though should be used with caution in settings where arterial blood gas monitoring is unavailable.

Options for surgical management of ICH are likely to be confined to decompressive hemicraniectomy to treat ICP crisis refractory to medical management. Shared decision-making between the provider team and patient's family in this circumstance should account for the potential for survival, the surgical and ICU capabilities of the local institution, and an understanding of the patient's goals of care.





References

1. Prust ML, Forman R, Ovbiagele B. Addressing disparities in the global epidemiology of stroke. *Nature reviews. Neurology.* 2024.

2. Li X, Zhang L, Wolfe CDA, Wang Y. Incidence and Long-Term Survival of Spontaneous Intracerebral Hemorrhage Over Time: A Systematic Review and Meta-Analysis. *Frontiers in Neurology*. 2022;13:171.

3. Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *The Lancet. Neurology*. 2009;8(4):345–354.

4. 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.

5. Yusuf S, Islam S, Chow CK, Rangarajan S, Dagenais G, Diaz R, Gupta R, Kelishadi R, Iqbal R, Avezum A, Kruger A, Kutty R, Lanas F, Liu L, Wei L, et al. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): A prospective epidemiological survey. *The Lancet*. 2011;378(9798):1231–1243.

6. Khatib R, McKee M, Shannon H, Chow C, Rangarajan S, Teo K, Wei L, Mony P, Mohan V, Gupta R, Kumar R, Vijayakumar K, Lear SA, Diaz R, Avezum A, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. *The Lancet*. 2016;387(10013):61–69.

7. Zhou B, Carrillo-Larco RM, Danaei G, Riley LM, Paciorek CJ, Stevens GA, Gregg EW, Bennett JE, Solomon B, Singleton RK, Sophiea MK, Iurilli MLC, Lhoste VPF, Cowan MJ, Savin S, et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet*. 2021;398(10304):957–980.

8. 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).

9. 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.