Emergency Neurological Life Support: Intracerebral Hemorrhage

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Abstract

Intracerebral hemorrhage (ICH) is a subset of stroke due to spontaneous bleeding within the parenchyma of the brain. It is potentially lethal, and often results in permanent neurological deficits and disability. Survival with a favorable outcome depends on ensuring an adequate airway, proper diagnosis, and early management of several specific issues such as blood pressure, coagulopathy reversal, and surgical hematoma evacuation for appropriate patients. ICH was chosen as an Emergency Neurological Life Support (ENLS) protocol because intervention within the first hours may improve outcome, and it is critical to have site-specific protocols to drive care quickly and efficiently. This module is meant to give a broad framework for the principles of diagnosis and emergent management of ICH, which can be adapted to reflect global and regional variations based on the local availability of diagnostic tools and treatments such as a specific reversal of coagulopathy or for management of hypertension.

Key words: Intracerebral Hemorrhage, Blood Pressure, Hematoma, Coagulopathy, Surgery, External Ventricular Drain

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1 Introduction

Intracerebral hemorrhage (ICH) results from spontaneous direct bleeding into the brain parenchyma. In the U.S., ICH accounts for 10–15% of all strokes, but it carries a disproportionately high risk of death or long-term disability. It is considered an acute neurological emergency because of the potential to treat or mitigate injury from the ICH and attenuate the risk of ongoing secondary brain injury.

The availability of treatments proven to benefit ICH patients has lagged behind that of ischemic stroke and aneurysmal subarachnoid hemorrhage, and this has resulted in variability in care that ranges from aggressive treatment to a nihilistic approach. Guidelines exist for the management of ICH, and the purpose of this ENLS protocol is to emphasize initial management, with the goal of optimizing recovery. Acknowledging that there is variability in the strength of evidence for treatment recommendations for certain interventions, aggressive initial care of the ICH patient is recommended, in accordance with existing guidelines.[1,2]

Management of the ICH patient during the initial "golden hour" emphasizes the following aspects:

1. Stabilization and frequent reassessment of the patient's airway, breathing, and circulation (ABCs)
2. Rapid and accurate diagnosis using neuroimaging
3. Concise clinical assessment regarding ICH characteristics and patient condition
4. Targeted assessment for potential early interventions including:
    a. Control of elevated blood pressure
    b. Correction of coagulopathy
    c. Need for early surgical intervention
5. Anticipation of specific patient care needs such as:
    a. Specific treatment aspects related to underlying ICH cause
    b. Risk for early clinical deterioration and hematoma expansion
    c. Need for EVD placement to treat hydrocephalus
    d. Patient disposition from the Emergency Department (ED)

2 Management Protocol

The ENLS suggested algorithm for the initial management of ICH is shown in Figure 1. Suggested items to complete within the first hour of evaluating a patient with ICH are shown in Table 1. After initial management of Airway, Breathing and Circulation, and the diagnosis of ICH is made, all five steps should be addressed simultaneously (history, BP control, hemostasis, surgery, and EVD) with specific management dictated by the patient's condition. Transfer to a neurocritical care unit (NCCU) which has physician and nursing expertise in management of ICH patients is recommended and is associated with improved outcomes.[2]

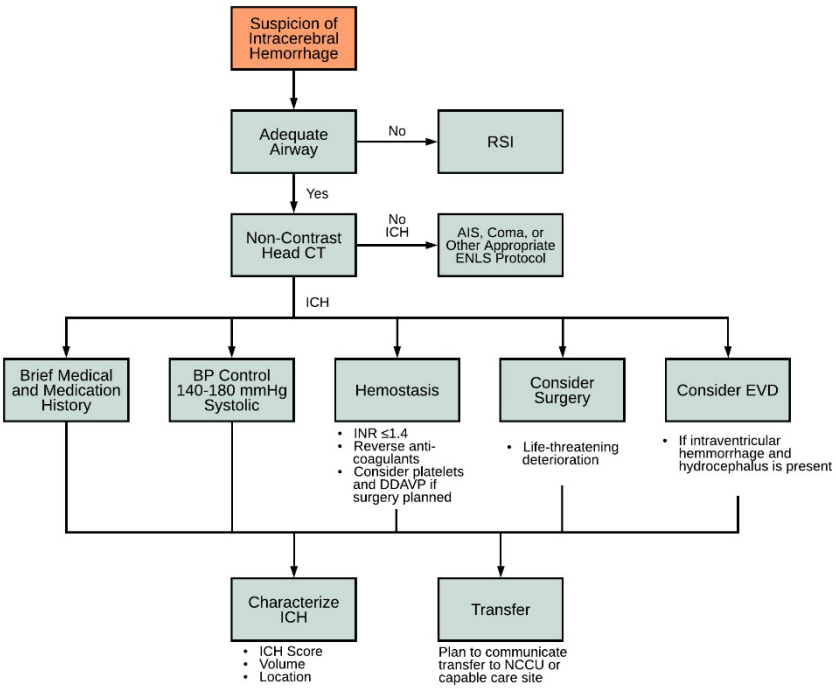

FIGURE 1

ENLS Intracerebral Hemorrhage Management Algorithm

TABLE 1

Intracerebral Hemorrhage Checklist for the First Hour

Intracerebral hemorrhage checklist for the first hour
Complete blood count with platelet count, PT, PTT, INR
CT head results: hematoma size, location, presence of intraventricular hemorrhage
Glasgow Coma Scale (GCS) score
Calculate ICH Score
Interventions:
Coagulopathy reversal (goal INR ≤ 1.4)
Blood pressure lowering (goal systolic 140-180 mmHg)
Surgical hematoma evacuation (if indicated)
Airway/ventilation management

3 Prehospital Consideration

The initial prehospital and ED resuscitation is similar across stroke subtypes, with rapid neuroimaging being essential to diagnosis. Because treatments for ICH and acute ischemic stroke are different, ICH-specific interventions are not provided until the diagnosis is made. Thus, prehospital care focuses on management of the ABCs, identification, and treatment of rapidly reversible causes of neurologic deficit (e.g., hypoglycemia), early notification and rapid transport to a designated stroke receiving hospital.

As with all emergency medical care, initial assessment of the ABCs is critical. Obtunded or comatose patients will need intubation for airway protection and/or adequate ventilation aimed at normocapnia. It is important to obtain a brief history on the onset of symptoms and when the patient was last seen normal. Prehospital providers should attempt to get a medical history and list of medications prescribed for the patient with specific attention to antiplatelet, anticoagulant and antihypertensive medications. Triage to an appropriate emergency facility for stroke management should be done promptly and expeditiously. Suggested sample "hand-off" language to the ED team by paramedics is included in Table 4.

4 Diagnosis

ICH may result from a variety of underlying etiologies. Rupture of a small arteriole(s) due to chronic hypertension accounts for approximately 60% of cases. Other common causes include cerebral amyloid angiopathy, coagulopathy due to antithrombotic and anticoagulant medications, sympathomimetic drugs such as cocaine, and underlying vascular anomalies such as arteriovenous malformations (AVMs) or cavernous malformations. Less common causes include cerebral vasculitis, Moya-Moya disease, and rupture of a saccular or mycotic aneurysm. Secondary hemorrhagic transformation of an arterial or venous infarct may also occur.

Most patients with acute ICH develop the sudden onset of a focal neurological abnormality. Without neuroimaging, ICH often cannot be reliably distinguished from an acute ischemic stroke. Headache, progressive neurological signs and symptoms, acute severe hypertension, and decreased level of consciousness occur more frequently in ICH than in ischemic stroke.

4.1 Neuroimaging

Non-contrast computed tomography (CT) is the most used modality given that it can be completed quickly, can be used for critically ill patients, and has a very high sensitivity and specificity for acute parenchymal hemorrhage. Due to varying appearance of blood over time, Magnetic Resonance Imaging (MRI) interpretation is more complex than CT, and its longer acquisition time combined with a limited ability to monitor patients at high risk of neurological deterioration during the study limits its use as a primary modality.[3,4]

4.2 Interpreting the CT Scan: Location, Volume, Spot Sign and the BAT score

ICH tends to occur in characteristic locations, with hypertensive ICH most frequently located in the basal ganglia, thalamus, pons (brainstem), and cerebellum. ICH due to cerebral amyloid angiopathy or AVM tends to have a lobar location. The origin of the hematoma is usually evident from the initial CT scan, and its location influences outcome and treatment (Figure 2).

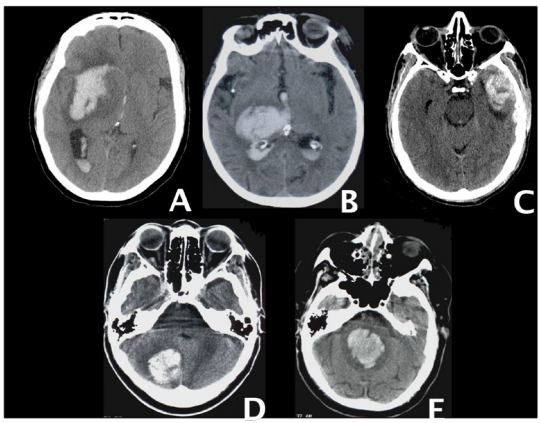

FIGURE 2

ICH due to chronic hypertension is usually due to rupture of small penetrating arterioles and typically occurs in the basal ganglia (A), thalamus (B), cerebellum (D),and pons (E). ICH from cerebral amyloid angiopathy and sympathomimetic drugs of abuse such as cocaine or methamphetamine often occurs in lobar regions such as the tempo- ral lobe (C). Supratentorial ICH would be considered as basal ganglia, thalamic, or lobar (A–C), whereas ICH originating in the cerebellum or pons would be considered infratentorial (D– E). A, B, and E also demonstrate IVH.

While ICH location is important, ICH hematoma volume is a stronger predictor of patient outcome. The ability to calculate hematoma volume quickly from the initial CT scan is an advantage in directing communication and treatment decisions. Automated CT software algorithms can be used to calculate hematoma volume. However, the manual ABC/2 formula is simple and reasonably accurate compared to computerized methods.[5] When using the ABC/2 method for calculating volume, the axial CT image is selected with the largest cross-sectional area of hemorrhage. Figure 3 demonstrates an example of calculating ICH volume by the ABC/2 method.

Many ICH patients (up to 40%) experience hematoma growth after initial presentation, and the ability to anticipate expansion is desirable, as expansion is associated with worse clinical outcome and these patients may benefit from even closer monitoring.[6]

Several retrospective reports have suggested that the use of intravenous contrast administration during the initial CT scan may identify extravasation into the hematoma and that this “spot sign” (contrast within the hematoma) is predictive of hematoma growth (Figure 4).[7–9]

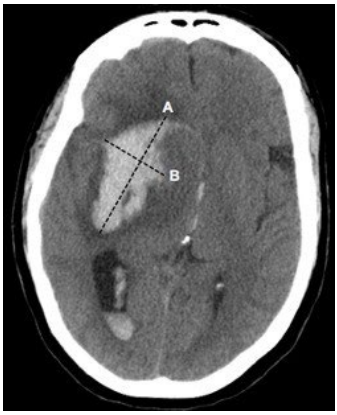

FIGURE 3

ABC/2 Method for Estimating ICH Hematoma Volume[5]

Right basal gan- glia intracerebral hemorrhage. The axial CT image with the largest cross-sectional area of hemorrhage is selected and is the reference slice. In this example, the largest diameter (A) is 6 cm, the largest diameter perpendicular to (A) on the same slice (B) is 3 cm, and hemorrhage is seen on 6slices of 0.5 cm (5 mm) thickness for a (C) of 3 cm (not shown). Note that for(C), if the hematoma area on a slice is approximately 25% to 75% of the hematoma area on the reference slice used to determine (A), then this slice is considered half a hemorrhage slice, and if the area is less than 25% of thereference slice, the slice is not considered a hemorrhage slice. Thus, the hematoma volume is (6 x 3 x 3)/2 = 27 mL. Alternately, (C) can be assessed by measuring the largest diameter, superior to inferior, that is seen on coronalor sagittal images. Multiply (A) times (B) times (C), then divide by 2 to obtain the hematoma volume.

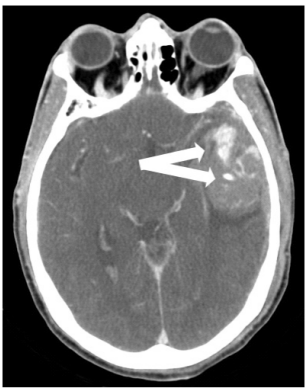

FIGURE 4

Contrast Extravasation("Spot Sign") in Acute ICH

In this post-contrast image obtained after administration of IV contrast during a "code stroke" CT (non- contrast head CT, CT angiogram, CT perfusion), contrast extravasation is present in this acute left temporal lobe ICH. This finding is commonly referred to as a "spot sign" (ar- rows) and is associated with increased risk of hematoma expansion.

Thus, the use of a "stroke CT" that includes non-contrast CT as well as CT angiography (and possibly CT perfusion and post-contrast images) may be considered in patients presenting with acute stroke (ischemic or ICH). In acute ICH, this can detect a "spot sign," as well as reveal an underlying vascular anomaly. Ongoing studies are seeking to use the "spot sign" as a way to identify those at risk for hemorrhage expansion and to determine if hemostatic agents may benefit these specific high-risk patients. However, CT angiography is not performed routinely in many centers, and recently the BAT score based on non-contrast CT has been reported to have a 50% sensitivity, 89% specificity, and 82% accuracy to predict hematoma expansion when the score is >3 (Table 2, Figure 5).[10]

TABLE 2
Individual Components of the BAT Score

Variable	Point
Blend Sign	
Present	1
Absent	0
Any Hypodensity	
Present	2
Absent	0
Time from onset to NCCT	
<2.5 h	2
≥2.5 h or unknown	0

NCCT Indicates noncontract computed tomography

The Blendsign is defined as a hypoattenuating area next to a hyperattenuating area of the hematoma, with sharp separation between the 2 regions and a density difference of at least 18 Hounsfield units.

Intrahematomahypodensity is defined as a hypodense region inside the hemorrhage with anyshape and dimension and lack of connection with the surrounding brainparenchyma.

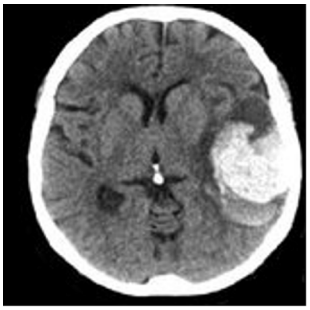

FIGURE 5

Non contrast head CT demonstrating blend sign. This non contrast CT was performed 1.5 hours after symptom onset and shows the presence of the blend sign (black arrow) which is defined as areas within the ICH of differing densities with a sharp separation between the regions and intrahematoma hypodensity (red arrow). The BAT score that is calculated fromthis CT is 5: 2 for time of onset, 1 for blend sign and 2 for hypodensity.

5 Management

Initial Patient Assessment and Primary Intervention: ABCs and the ICH Score

5.1 After Arrival in Hospital

Until the diagnosis of ICH is made from neuroimaging, overall airway and hemodynamic management proceeds in a common pathway with other stroke subtypes. However, immediately following the ICH diagnosis, disease-specific treatment can be instituted.

Airway management should be considered immediately after arrival. Thus, while "Airway" is listed under secondary treatment in the ENLS ICH algorithm (Figure 1), it is concurrent with the initial evaluation. In general, if an ICH patient is comatose, rapid sequence intubation (RSI) should be undertaken, with a goal of normoventilation (see the *ENLS Airway, Ventilation, and Sedation* protocol).

An initial clinical assessment of the patient's condition and stroke severity is essential for rapid treatment planning and communication among providers. Performance of a detailed neurological examination as permitted by time and clinical stability is recommended, but much information can be gleaned from a quick assessment using existing clinical grading scales. At a minimum, the initial evaluation should include assessment of pupillary reactivity, the Glasgow Coma Scale (GCS) and respiratory function, with an emphasis on assessing the adequacy of airway protective reflexes. The ICH Score is the most commonly used validated clinical grading scale for patients with ICH, combining elements related to patient demographics, clinical condition, and neuroimaging findings that are readily available at the time of hospital admission.[11,12] Several other useful clinical grading scales are also available.[13–15]

Table 3 demonstrates the components of the ICH score, with the full score being the sum of points given for each component. Each point increase in the ICH Score is associated with an increased risk of mortality and a decreased likelihood of good functional outcome. The ICH Score is best used as a communication tool among providers and with patients or family members regarding a patient's condition rather than as a tool to precisely prognosticate outcome. While it is tempting to utilize clinical grading scales to triage severely impaired patients toward less-aggressive intervention, this approach is not recommended. Rather, in general, initial aggressive therapy is recommended in order to avoid the potential for a self-fulfilling prophecy of poor outcome in the context of early care limitations.[1,16–19]

TABLE 3
The ICH Score [10]

Component	ICH Score
Glasgow Coma Scale	
3–4	2
5–12	1
13–15	0
ICH Volume (mL)	
> 30	1
< 30	0
Presence of IVH	
Yes	1
No	0
Infratentorial Origin of ICH	
Yes	1
No	0
Age (years)	
> 80	1
< 80	0
Total ICH Score	**0–6**

30-day Mortality: ICH score: 0 – 0%; 1- 13%; 2 – 26%; 3 – 72%; 4 – 97%; 5 – 100%

6 Primary Intervention: Blood Pressure, Coagulopathy, And Surgery

Following the diagnosis of ICH, immediate consideration should be given to the need for (a) acute control of elevated blood pressure, (b) correction of coagulopathy due to medications or underlying medical conditions, and (c) the need for urgent surgical hematoma evacuation or EVD placement. These are common themes that should form part of the initial ICH evaluation and treatment plan. Decisions regarding these interventions will influence the succeeding aspects of ICH care.

6.1 Blood Pressure Management

Elevated blood pressure is extremely common in patients with acute ICH. While it seems intuitive that elevated blood pressure may predispose to hematoma expansion due to increased bleeding or to elevated ICP from worsening edema, clinical studies have had conflicting results regarding the impact of acutely elevated blood pressure and the value of acutely lowering the blood pressure.[20,21] There has been a concern that acutely lowering blood pressure could lead to ischemic brain injury in the peri-hematoma region, but this risk has not been supported by recent studies.[22,23]

While blood pressure management has remained controversial, current approaches favor rapid lowering of moderately elevated blood pressures.[1,2] Two pilot randomized clinical trials, INTERACT and ATACH, suggested that acutely lowering systolic blood pressure (SBP) to below 140 mmHg is safe.[24,25] These were followed by pivotal phase III efficacy trials to test the impact of blood pressure lowering on clinical outcome. INTERACT2 randomized ICH patients presenting with a SBP between 150 and 200 mmHg to two different SBP thresholds: a standard threshold of < 180 mmHg and an intensive threshold of < 140 mmHg.[26] Patients in the intensive arm had modestly better outcomes with about 3% fewer patients having death or severe disability. Interestingly, there was no difference in hematoma expansion between groups. ATACH 2 had a similar design and attempted to test the two SBP thresholds of <180 and <140 mmHg. However, most patients in the aggressive blood pressure arm had a minimum SBP close to 120 mmHg, while most patients in the <180 arm had a minimum SBP near 140 mmHg.[27] ATACH 2 did not demonstrate a difference in outcome between treatment groups and a small increased risk of renal adverse events in the aggressive arm.

The 2015 American Heart Association/American Stroke Association (AHA/ASA) Guidelines for the Management of Intracerebral Hemorrhage recommends acutely lowering SBP to 140 mmHg in patients presenting with SBP between 150-220 mmHg. For those presenting with SBP >220 mmHg, it is reasonable to consider aggressive reduction in blood pressure. Thus, it appears reasonable to target a SBP between 140 and 180 mmHg with the specific threshold determined based on patient comorbidities and level of chronic hypertension. Although the clinical difference between these two SBP thresholds may be modest and debatable, none of the current guidelines recommend allowing blood pressure to remain extremely elevated without treatment.[1,2]

Basic principles of blood pressure lowering in ICH are that management should be

initiated immediately and a titratable agent should be used to ensure that the target value is reached quickly and with minimal potential for overshoot. Intravenous beta-blockers and calcium-channel blockers are the most commonly used medications for this indication in the ED and the intensive care unit (ICU). Because nitroprusside and nitroglycerin trigger cerebral vasodilation and thus can increase ICP, their use should be avoided.

A more detailed discussion of common anti-hypertensive medications utilized in neurologic emergencies can be found in the *ENLS Pharmacotherapy* chapter. Invasive arterial monitoring is not mandatory but will facilitate titration and improve safety of anti-hypertensive medication infusion.

6.2 Coagulopathy: Anticoagulants, Antiplatelet Agents, and Heparin

The use of antithrombotic medications for prevention and treatment of ischemic stroke, cardiovascular disease, and systemic venous thromboembolism is common and is increasing as the population ages. Antithrombotic medications are a risk factor for the occurrence of ICH, as well as for hematoma expansion if an ICH occurs. Given the range of antithrombotic medications, including warfarin, heparin, antiplatelet agents such as aspirin and clopidogrel, and newer agents such as dabigatran, rivaroxaban and apixaban, the specific risks and interventions to reverse coagulopathy vary. Additionally, coagulopathies may be due to underlying medical conditions, such as liver disease or hematologic malignancies. The second focus in ICH management is on correction of coagulopathy. As part of the initial evaluation of the ICH patient, a medical history and medication list should be obtained and, if possible, when the last dose was taken should be noted. Urgent laboratory tests should include a complete blood count (CBC) with platelet count, an international normalized ratio (INR), and a partial thromboplastin time (PTT).

Patients taking a vitamin K antagonist such as warfarin and whose INR is >1.4 should receive agents to normalize the INR to ≤1.4. For the purpose of emergent EVD placement, no INR threshold has been established, and an INR of ≤ 1.5 is generally considered safe.[28] Options have included the administration of fresh frozen plasma (FFP), vitamin K, prothrombin complex concentrates (PCC), and the hemostatic agent recombinant Factor VIIa (rFVIIa), although PCC is now the recommended approach.[29,30] The most important principle is to normalize the INR as soon as possible, ideally within minutes.

While FFP is widely used for reversing the effect of warfarin, it may not be optimal in other medical conditions. Fairly large volumes of FFP (10–15 ml/kg) are often required for full reversal of anticoagulation, and this places patients at risk for volume overload and pulmonary edema.[31] FFP, like other blood products, also carries a risk for transfusion related events and requires thawing after cross-matching by a blood bank.

PCCs contain much higher concentrations of clotting factors in smaller amounts of volume than FFP. These drugs can correct the INR within minutes, faster than FFP, and with fewer cardiopulmonary complications.[32]

The most recent Neurocritical Care Society (NCS) guidelines recommend weight-based dosing for PCC (or FFP only if PCC is not available) with the dose adjusted based on INR.[30] However, the specific dose may vary based on the PCC formulation used at a specific hospital. Current guidelines recommend the use of vitamin K 10 mg administered

intravenously by slow push, in conjunction with another more rapidly acting agent (e.g. PCC), as it typically takes hours after vitamin K administration for reversal of warfarin-induced coagulopathy, but it has a more long-lasting effect than PCC or FFP.[1,29–34]

While rFVIIa also quickly reverses an elevated INR, this may reflect a specific effect on the INR laboratory test and a clinically important coagulopathy may remain. rFVIIa has been shown to decrease hematoma growth in non-coagulopathic ICH patients, but this did not translate into improved clinical outcome.[35] Thus, rFVIIa is not recommended for use in ICH patients with or without warfarin-related coagulopathy[1]; however, it is occasionally used in patients with coagulopathy related to liver failure.

Observational studies have varied regarding the impact of concurrent antiplatelet therapy on hematoma expansion and outcome for patients presenting with ICH.[36–39] The PATCH study was an open-label clinical trial testing the efficacy and safety of platelet transfusion in ICH patients taking antiplatelet agents.[40] Platelet transfusions did not improve outcome and were associated with a significant increase in risk of death and adverse events. Thus, platelet transfusion is not recommended for most patients with ICH on an antiplatelet agent.[30] Few patients in PATCH were on clopidogrel and those undergoing neurosurgical procedures were excluded. The most recent antithrombotic reversal guidelines from NCS recommend platelet transfusion for patients on antiplatelet medications who are undergoing a neurosurgical procedure.[30] They also recommend considering a single intravenous dose of 0.4 mcg/kg of DDAVP (desmopressin) in antiplatelet medication-related ICH.

Newer anticoagulants, such as direct thrombin inhibitors (e.g., dabigatran) or direct Xa inhibitors (e.g., rivaroxaban and apixaban) now have specific reversal agents available. Idarucizumab is a targeted monoclonal antibody that binds to the thrombin binding site of dabigatran.[41] It is approved for use and is recommended as the initial reversal agent for patients with ICH while on dabigatran.[30] Activated charcoal (50 gm) should also be given if ICH occurs within 2 hours of the most recent dabigatran dose. Less-recommended alternatives for reversal of direct thrombin inhibitors if idarucizumab is not available are the activated PCC FEIBA (factor VIII inhibitor bypassing activity) or 4-factor PCC; however, these approaches have not been formally tested and do not fully reverse dabigatran coagulopathy.[30,42,43] As of 2017, the FDA has approved Andexanet alfa for reversal of rivaroxaban and apixaban, based on ANNEXA-4 trial, the final report of which included 352 patients with active bleeding (227 with ICH).[44] The reduction in anti-Xa activity with administration of Andexanet alfa correlated with clinical hemostatic efficacy in patients with ICH. If this is not available, PCCs may have some effectiveness in reversing the effect of rivaroxaban and apixaban.[45] The current recommended approach is to use Andexanet alfa, but clinical trials of its efficacy are ongoing, and at present many hospitals have elected to not include it in their formularies. Note that the half-life of the reversal agents may be shorter than the Xa inhibitors, and if available, anti-Xa activity should be monitored to determine if an additional dose of Andexanet alfa is needed. If this is not available, use FEIBA or 4-factor PCC with the addition of oral charcoal to retard absorption if the last dose of direct Xa inhibitor was within 2 hours.[30] Additional laboratory tests, such as endogenous thrombin potential and thrombin clotting time, may have some value in assessing the activity of these newer anticoagulant agents. Vitamin K is of no value and

FFP is of unclear utility. Currently there is no approved reversal agent for edoxaban and betrixaban. Detailed information on reversal of warfarin, direct thrombin inhibitors, and factor –Xa inhibitors can be found in the *ENLS Pharmacotherapy* module.

Unfractionated heparin binds to and activates antithrombin III, thus inactivating thrombin and favoring thrombolysis. The reversal agent for heparin is protamine sulfate, administered 1 mg for every 100 units of heparin received in the prior two hours, with a maximum dose of 50 mg.[46] Given the short half-life of heparin, reversal is likely unnecessary if the last dose was received greater than four hours prior to ICH onset. Protamine sulfate can also be used in the same dose in an attempt to reverse the effect of low molecular weight heparin that was given within the prior eight hours. However, this reversal may be incomplete.

6.3 Neurosurgical Interventions

Though most patients with acute ICH do not require surgery for removal of the hematoma, it is worthwhile to address the option of surgery immediately after ICH diagnosis. The effects of surgical evacuation were addressed in the Surgical Trial in Intracerebral Hemorrhage (STICH) that found early surgical evacuation of a supratentorial ICH was not harmful, but there was no difference in long-term mortality or functional outcome.[47] Because the subgroup of patients in STICH with lobar ICH within 1 cm of the cortical surface may have benefited from surgical evacuation, the STICH II clinical trial was undertaken for this group of patients.[48] However, STICH II did not demonstrate a significant benefit to early hematoma evacuation in these patients either. The recently completed MISTIE-III trial (minimally invasive stereotactic hematoma evacuation with tPA instillation) showed that the technique is safe and effective in reducing ICH volume faster than usual medical management; however, despite improved mortality, there was no statistically significant improvement in functional outcomes, unless the ICH volume was reduced to < 15 ml.[49] Minimally invasive endoscopic hematoma aspiration techniques are also being studied.[50–52] At present, routine removal of supratentorial hematoma cannot be endorsed, but it is still undertaken as a life-saving measure in selected patients, such as those who are deteriorating clinically and are considered good surgical candidates based on characteristics such as co-morbidities and age.

In contrast, several case series suggest that patients with cerebellar ICH > 3 cm in diameter or with compression of the brain stem or hydrocephalus may benefit from surgical hematoma evacuation.[53,54] There has not been a randomized trial of cerebellar hematoma evacuation analogous to STICH, but it is not clear there is clinical equipoise to justify such a trial.

Current AHA/ASA ICH guidelines recommend that patients with cerebellar hemorrhage who are deteriorating neurologically or have brainstem compression should undergo surgical removal of the hemorrhage as soon as possible. Initial treatment of these patients with ventricular drainage alone rather than surgical evacuation is not recommended.[1] Supratentorial hematoma evacuation or decompressive hemicraniectomy might be considered as a life-saving measure in deteriorating patients. Correction of coagulopathy is critical in patients undergoing surgical hematoma evacuation. Spontaneous ICH may

extend into the ventricles (secondary intraventricular hemorrhage), while primary intraventricular hemorrhage (IVH) can also occur without a parenchymal component. When present, intraventricular clot frequently obstructs CSF flow leading to hydrocephalus that, if left untreated, will result in secondary brain injury and life-threatening ICP elevation. All patients with IVH should be monitored closely for developing hydrocephalus. When present, hydrocephalus is treated by placement of an EVD to facilitate CSF diversion. In the CLEAR III trial, patients with hydrocephalus due to IVH with or without an intraparenchymal hemorrhage up to 30cc were treated with intraventricular alteplase versus placebo to facilitate hematoma resolution. Despite a mortality benefit, there was no difference in the primary outcome of 6-month functional status. Consequently, at present there is not a clear role for scheduled alteplase to treat IVH-associated hydrocephalus, but prompt diagnosis of hydrocephalus followed by EVD placement remains an important life-saving intervention. Of note, perhaps due to the lack of direct parenchymal brain injury, patients with primary IVH likely have significantly better long-term outcomes than secondary IVH, as suggested in a recent secondary analysis of the CLEAR III.

7 Secondary Intervention: Hospital Admission, ICP Management, And Seizures

Ideally, patients with acute ICH should be admitted to an ICU based on the need for close monitoring of neurological and hemodynamic condition and the risk for early deterioration from hematoma expansion, cerebral edema, hydrocephalus, or airway compromise. Admission to a neuro critical care unit has been associated with improved outcomes compared with admission to a non-NCCU.[55] Acknowledging that certain patients will require transfer between hospitals for neurologic intensive care management, neurosurgical intervention, or neurointerventional capabilities, all aspects of ICH primary intervention can and should take place without delay in the initial presenting hospital.

Specifically, correction of coagulopathy with appropriate agents, blood pressure control, and treatment of acute seizures should be initiated in the ED of the presenting hospital and not deferred until after transfer. It is critical that the above-discussed aspects of acute ICH evaluation and treatment are initiated at the time of original diagnosis and that transitions in care are smooth from ED to ICU (or operating room, interventional radiology, or comprehensive stroke center).

While this ENLS ICH protocol is principally concerned with the initial evaluation and treatment period, it is important to anticipate the health care needs of the following 24–72 hours as part of care planning. The first 24 hours are critical for blood pressure management, identification of seizures, ICP management, and maintaining a secure airway. Avoidance of fever, hyperglycemia/hypoglycemia, and hypoxia are also important, as these may impact outcomes.[1,56,57] In addition, patients with ICH are at increased risk for the developing venous thromboembolism (VTE); current guidelines recommend use of intermittent pneumatic compression devices at hospital admission, as well as initiation of prophylaxis-dose unfractionated or low-molecular weight heparin within 1–4 days following onset (assuming cessation of bleeding).[1,58]

The incidence and impact of elevated ICP in ICH has received limited study, but it is an important factor in some cases, particularly when hydrocephalus is present.[59–62] In the IVH patients enrolled in the CLEAR III trial, 72.8% had at least one ICP reading greater than 20 mm Hg, while 33.3% had a reading greater than 30 mm Hg. A greater proportion of time spent with an ICP above 18 mm Hg or CPP below 70 mm Hg was associated with worse neurological outcomes. Current guidelines for ICP monitoring in ICH follow the approach in severe traumatic brain injury (TBI), but because they represent distinct entities, TBI-specific recommendations should be extrapolated cautiously to ICH, which is itself a heterogeneous disease. It is also prudent to note that, in many instances, local pressure gradients from an expanding hematoma can result in severe brain compression and cerebral herniation that may not be initially reflected in global ICP measurements.

While seizures may occur in ICH patients, their incidence and impact on outcome have varied across studies.[63,64] In a single study, prophylactic anticonvulsants reduced seizure occurrence in lobar ICH [64]. However, two recent studies found worse functional outcomes in patients routinely given prophylactic anticonvulsants (primarily phenytoin).[65,66] While comatose ICH patients may have a high risk (approximately 20%) of non-convulsive seizures, the impact of prophylactic anticonvulsants on their occurrence is also unclear.[67,68] Current guidelines do not recommend routine use of prophylactic anticonvulsants[1], though some practitioners still use a short course in patients with lobar ICH and those undergoing surgical hematoma evacuation. Newer antiseizure agents such as levetiracetam are now more commonly used for prophylaxis. Although antiseizure agents have been suspected to be associated with worse outcome after ICH, data from the ERICH study did not support this contention as levetiracetam use was not associated with poor outcome at 3 months.[69] Clinical seizures should be treated, and continuous EEG monitoring should be performed in patients with inadequately explained decreased level of consciousness.

A checklist for the acute management of the ICH patient according to the principles of ENLS is presented in Table 4. This could be used as a checklist for proceeding throughout the domains of care from prehospital, to ED, to disposition in the euro critical care unit, OR, or interfacility transfer and can be shared across medical providers as this care proceeds. Note that frequent reassessment of ABCs and clinical neurological status is a key component throughout the care pathway as is revisiting the effectiveness of initial interventions such as blood pressure lowering and coagulopathy reversal in rapidly achieving the desired targets.

Table 4
Standardized ICH Management

Prehospital Care
□ ABCs
□ Fingerstick glucose, peripheral IV
□ Determine time of onset and circumstances
□ Perform prehospital stroke screen
□ Brief medical history and medication list
□ Triage to stroke center
□ Perform prehospital notification of stroke patient
ED Care
□ Emergent triage to high acuity area
□ Perform primary assessment – ABCs
□ Perform focused neurologic exam (GCS, NIHSS)
□ Obtain baseline screening labs (CBC and platelet count, electrolytes, INR and PTT, glucose)
□ Obtain cerebrovascular imaging as soon as possible (non-con CT, stroke CT/CTA/CTP, or MRI)
□ Obtain medical history and medication list
After Confirmation of ICH
□ Reassess ABCs (consider intubation if comatose, GCS < 9)
□ Initiate blood pressure intervention (target SBP 140-180 mmHg)
□ Quantify ICH volume (ABC/2 calculation)
□ Perform ICH Score (0–6)
□ Begin correction of anticoagulation as required (goal INR < 1.4)
□ Consult neurosurgery for potential hematoma evacuation or ICP monitor placement
In-hospital Setting
□ Continue to reassess ABCs
□ Continue neurologic reassessment
□ ICP monitor and/or ventriculostomy for treatment of elevated ICP or hydrocephalus
□ Continue management of blood pressure
□ Place arterial blood pressure catheter as needed
□ Place central venous catheter as needed
□ Urine toxicology screen (if not already done)
□ Foley catheter (needed for most ICH patients early)
□ Feeding tube (goal to begin feeding within first day)
□ DVT prophylaxis with sequential compression devices (consider heparin/LWMH after ICH stability between days 1-4)
□ Recheck INR and PTT if patient was coagulopathic and received reversal agents
□ No anticonvulsant prophylaxis; treat clinical seizures; continuous EEG if level of consciousness impaired out of proportion to ICH or IVH
□ Consider need for repeat head CT
□ Consider need for catheter cerebral angiography for etiology of ICH

8 Nursing Considerations

Nursing responsibilities in emergency care of ICH patients are focused on monitoring and careful titration of BP to meet goals. The primary nurse recognizes and alerts appropriate members of the emergency team with changes in cardiac rhythm, oxygenation, mental and neurological status (e.g., pupillary changes), hemodynamics and ICP/CPP in a timely fashion. Because they are trusted healthcare providers who have very frequent interactions with patients and families, nursing staff typically also plays an important role in providing education about ICH treatment and secondary prevention. Lastly, activation and coordination of acute care pathways to ensure safe transport of patients from one level of care to the other is vital and best managed by the primary nurse.

9 Pediatric Considerations

The etiology of pediatric ICH is vastly different than that in adults because chronic hypertension and therapeutic anticoagulation are less prevalent. ICH is seen much less frequently in pediatric patients. However, children do present with life threatening ICH most frequently due to vascular malformations though bleeding disorders, vasculitis, sickle cell disease, or infection may also cause ICH.[70] While less than 2% of cerebral aneurysms are found in pediatric patients, as many as 24% of children with intracranial aneurysms may have ICH at the time of their initial presentation.[71] Hemorrhagic transformation after ischemic stroke can occur, particularly because recognition of stroke in children lags behind that in adults. ICH as a result of hemorrhagic disease of the newborn was virtually eradicated by routine vitamin K administration after birth but can be seen in cases of parental refusal or in regions of the world where vitamin K is not routinely administered. Trauma-related ICH can require emergent intervention, and while isolated ICH is uncommon compared to SDH in young children who have been abused, these children often present without disclosure of trauma. Other important etiologies of significant pediatric ICH are oncologic and include bleeding of brain tumors (the most common solid tumor of childhood), and ICH as a result of combined thrombocytopenia and vascular sludging from hyperleukocytosis in acute leukemic blast crisis.

A priori knowledge of your facility's capabilities and identification of and early referral to a center with expertise and comfort with neuro critically ill children with acute hemorrhagic stroke is paramount. Optimal outcomes may be related to interventions in the first hours, and children are at risk for etiologies that require a variety of pediatric subspecialty care. As an example, a child with leukemic blast crisis may require emergent white cell reduction with pheresis and chemotherapy in addition to management of ICH and this will usually require transfer to a larger pediatric referral center.

Children should be admitted to a pediatric intensive care unit or where available, a pediatric neuro-intensive care unit with close monitoring of the neurological exam. Management of ICH in pediatric patients is addressed in the 2019 AHA/ASA statement on the Management of Stroke in Neonates and Children.[72] Goals of treatment for children with

ICH, like adults, are stabilizing the patient and protecting the brain from secondary injury. For children with significant ICH, the same emergent care principles described earlier in this chapter apply regarding the need for establishment of the airway and providing adequate oxygenation and maintaining blood pressure (see pediatric section in *ENLS Airway, Ventilation and Sedation*). Normothermia and normoglycemia are recommended. Due to the high incidence of vascular lesions in children, vessel imaging will be necessary, and patients may eventually require digital subtraction angiography.

Children are at high risk for increased ICP as they have less age-related brain volume loss and therefore less compliance and less space in the cranial vault compared with adults.[72] Guidelines suggest that children, therefore, may experience more benefit from surgical intervention for ICH compared with adults.[72] Careful attention should be given to the identification of ICH in need of emergent surgical evacuation, and decompression including large lobar and posterior fossa hemorrhages. Children are also at risk for hematoma expansion occurring in almost one third of patients receiving two CT scans within 48 hours.[70] Close monitoring is required to detect and treat clinically significant progression, just as in adults.

Seizures have been reported as the presenting symptom in pediatric ICH in 36% of patients with 9% in status epilepticus.[70] As in adults, seizures should be treated. Continuous EEG monitoring to evaluate for electrographic seizures and status epilepticus in children with ICH and altered mental status is recommended in a recent consensus statement for cEEG in critically ill adults and children.[72] It is unclear whether prophylactic anti-convulsant agents should be started in children who have not experienced seizures.[72]

In pediatric patients with acute ICH the role of targeted BP management is unknown. Avoidance of hypotension and maintenance of adequate CPP is essential. Hypotension in pediatric patients is defined as SBP below the 5^{th} percentile for age (SBP 5^{th} percentile = 70 mmHg + age in years X 2). There are no established parameters for treatment of hypertension in pediatric patients with ICH, but a SBP target of 140-180 mmHg may be reasonable in older children. Blood pressure goals for younger children with ICH and hypertension are best established in consultation with subspecialists experienced in pediatric neurocritical care. For controlled reduction in blood pressure, nicardipine is well tolerated in pediatric patients. The recommended starting dose is 0.5 mcg/kg/min, titrated by 0.5 mcg/kg/min every 15 minutes to a maximum of 5 mcg/kg/min. In older children (adult weight), similar dosing and titration as that for adults is followed. Hydralazine is also an option with a recommended starting an intravenous dose of 0.1 to 0.2 mg/kg/dose every 4 to 6 hours with a maximum dose of 10 to 20 mg for children and adolescents. For young infants, the maximum dose will be lower. Esmolol and labetolol are reasonable alternatives and generally well tolerated. It should be noted that beta-blockers in young children should be avoided, particularly during the first hours of resuscitation, as cardiac output in this age group is heart rate dependent and artificially low heart rate can complicate identification of increased ICP in addition to lowering blood pressure. Developmentally, infants have higher baseline vagal tone and are prone to bradycardia from a variety of stimuli. Infants also have a high glucose utilization rate and are more at risk for hypoglycemia that can occur with beta-blockers.

If receiving therapeutic anticoagulation at the time of ICH, anticoagulation is typically held if possible and coagulation abnormality may require immediate correction.[72] Finally, pediatric patients with ICH may present with coagulation abnormalities that require careful evaluation and treatment to prevent hematoma expansion and facilitate surgical therapy.

10 Considerations In Pregnancy

ICH is a rare event during pregnancy but one that can lead to significant maternal morbidity and mortality and a substantial risk to the unborn child.[73] Most cases occur late in pregnancy or in the post-partum period.

A combination of physiological factors contributes to this increased risk, but hypertensive disorders of pregnancy are most implicated. The combination of hypertension, endothelial changes and dysregulated vascular tone that occurs in eclampsia predisposes to cerebral edema and ICH, and there is significant overlap between eclampsia and the posterior reversible encephalopathic syndrome and reversible cerebral vasoconstriction syndrome. Similarly, a hypercoagulable state during pregnancy that is associated with increased frequency of cerebral venous sinus thrombosis can present with venous congestion and ICH.[73]

The diagnosis and treatment of ICH in pregnancy should generally follow the standard guideline recommendations for ICH.[73] Due to the perceived risk to the fetus of ionizing radiation, there is sometimes reluctance to obtain a CT scan. However, CT imaging can usually be obtained much more quickly than MRI and more accurately identifies acute hemorrhage. The shielded radiation dose to the fetus is relatively low, whereas delayed diagnosis of an ICH can lead to profound adverse maternal and fetal consequences.

Hypertension, if present, must be controlled. Labetalol and nicardipine are the recommended first-line antihypertensive agents in ICH, and their use is appropriate in pregnancy, while ACE-inhibitors and ARBs should be avoided. Intravenous magnesium infusion and prompt delivery is indicated for both pre-eclampsia and eclampsia. Venous sinus thrombosis should be treated with anticoagulation, even in the setting of associated ICH. Unfractionated and low-molecular weight heparins are generally used, as warfarin is contraindicated in pregnancy. In general, obstetrics or maternal-fetal medicine consultation is indicated to assist with the often-complex decision-making regarding risks and benefits of various medical and surgical interventions for pregnancy-associated ICH.

11 TRANSPORT CONSIDERATIONS

This section addresses patient transport e.g., from ED to radiology suite, ED to ICU, or interhospital transport. Before the patient is transported, the responsible physician should assess the condition of the patient to determine the necessary personnel and equipment needed. Patients with borderline airways should be intubated before transport.

1. Personnel: In addition to a transporter, this should include an experienced nurse/physician/critical care transport paramedic who can manage the patient's ABCs.

2. Equipment: A transport monitor that can display blood pressure (noninvasive or invasive), ECG, pulse oximetry with supplemental oxygen and/or ventilator as indicated. If an EVD is in place, it should be clearly stated whether the drain should be clamped or open, and if open, what level it should be set at.

3. Drugs: Basic medications for blood pressure control/support, sedation, analgesia and osmotic agents (e.g., mannitol or hypertonic saline as needed).

12 Communication

When communicating to an accepting or referring physician about a patient with ICH, consider including the key elements listed in Table 5.

TABLE 5

Intracerebral Hemorrhage Communication/Hand-off

Communication – Prehospital to Emergency Department (before diagnosis of ICH)
□Airway status – patent airway/supraglottic device/endotracheal tube
□ Breathing – respiratory status
□ Blood pressure and pulse
□ Age/gender
□ GCS, pupils
□ Signs and Symptoms
□ Last known normal
□ Brief relevant medical history – previous stroke, blood thinners, bleeding
□ Current medications
Sample Emergency Medical Services call
"This is Medic 1 with a stroke alert - 85-year-old male, acute right hemiparesis, on aspirin 81 mg. Last known normal at 13:00. Vital signs stable. Estimated Time of Arrival, 30 min."
Communication – Hand off after ICH diagnosis has been made
□ Age
□ GCS, pupil exam
□ Hematoma volume and location
□ Other CT findings (intraventricular hemorrhage, hydrocephalus, spot sign)
□ ICH Score
□ Airway status
□ Blood Pressure, target, and treatment initiated

Continued on next page

Table 5 continued

- □ Coagulation parameters (INR, PT, PTT, platelet count, WBC, Hgb) and reversal treatment if any
- □ Medications given
- □ Plan for surgery if any

Sample Sign-Off Narrative

"I am signing out a 62-year-old man with known hypertension and atrial fibrillation who is presumed to be on warfarin."
"He was found at home this morning at 9 AM by his wife who last saw him normal at 7 AM.
He was talking to emergency medical services and had left-sided weakness, GCS in the field was 13, and BP was 170/100 mm Hg."
"On arrival to the emergency department here, he was the same, we obtained labs and sent him for a head CT."
"CT completed at 10 AM showed a 20 ml right thalamic ICH with mild IVH, but no hydrocephalus.
There is about 4 mm of right-to-left midline shift. CTA/CTP showed no AVM or aneurysm, but there is a positive spot sign."
"When he returned to the ED, he was sleepier, with a GCS of 9, and his left-sided weakness was worse.
So he has an ICH Score of 2. His labs came back with an INR of 1.9."
"We intubated him using rocuronium and etomidate. PCC infusion of 2250 IU (estimated weight 90 kg; dose of 25 IU/kg)
is going in now. He also had 10 mg of intravenous vitamin K."
"Neurosurgery has been called, and they are on their way to see him. He is in emergency department Resuscitation Room 1,
intubated and sedated now on propofol at 60 mcg/kg/min and fentanyl 50 mcg/hr. His BP is 140/85 mm Hg with no other treatment."
"They are ready to take him in Bed 2 in the neurocritical care unit in five minutes. Nursing is also calling report."

Clinical Pearls

□ Hematoma expansion occurs within the first 6-12 hours in up to 40% of patients. This can lead to neurological deterioration and airway compromise and should be anticipated.

□ The "spot sign" on contrast CT/CTA and the "BAT" score on non-contrast CT can help to identify patients at high risk of hematoma expansion.

□ The ABC/2 method can be quickly used to measure hematoma volume on a CT scan.

□ The ICH score is best used as a communication tool between providers rather than to predict neurological outcome.

□ Admission to a neurological critical care unit with physician and nursing expertise in ICH is associated with improved ICH outcomes.

□ Current recommendations are to lower BP to SBP between 140 mm Hg – 180 mm Hg with the specific target determined by patient related factors.

□ Urgent coagulopathy reversal should be done to minimize ICH expansion. Specific reversal agents are available for all oral anticoagulants.

□ The role of open craniotomy is limited to cerebellar hematoma with brainstem compression and as a life saving measure in selected patients with supratentorial ICH.

□ Current recommendations do not endorse routine prophylactic use of antiseizure medication for all patients with ICH.

□ A patient who has a level of consciousness out of proportion to imaging findings should be investigated for subclinical seizures.

13 Starred References

#1. *Latest guideline on the management of all aspects of spontaneous intracerebral hemorrhage with comprehensive review of the literature and evidence for the recommendations.*

#10. Potential use of the routine CT scan and BAT score to predict hematoma expansion.

#11. The most frequently used scale to grade and standardize the severity of ICH.

#26. INTERACT 2-*Multi-center trial that demonstrates the feasibility and safety of acute lowering of blood pressure in ICH.*

#27. ATACH 2- *Another multi-center trial that demonstrates the feasibility and safety of acute lowering of blood pressure in ICH.*

#41. This study establishes the efficacy of reversal of effects of dabigatran with idarucizumab.

#44. *This study establishes the clinical efficacy of Andexanet for the reversal of rivaroxaban or apixaban induced coagulopathy.*

#72 Latest guideline on the management of childhood stroke including ICH, based on expert consensus considerations for clinical practice. Ferriero, DM et al 2019

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