Chapter 439 | Intracerebral Hemorrhage

KEY CLINICAL POINTS

1. Intracerebral hemorrhage (ICH) accounts for approximately 10% of all strokes and 35–45% of patients die within the first month.
2. Target systolic blood pressure (SBP) for spontaneous ICH is 130–150 mmHg to avoid unintended hypoperfusion, based on INTERACT2 and ATACH2 trials.
3. The 'spot sign' on CT angiography represents ongoing bleeding and is associated with increased risk of hematoma expansion, increased mortality, and lower likelihood of favorable functional outcome.
4. Rapid reversal of coagulopathy is critical: Prothrombin complex concentrates (PCCs) for Vitamin K antagonists, Idarucizumab for dabigatran, and andexanet alfa for oral factor Xa inhibitors.
5. The ENRICH trial demonstrated that surgical removal of lobar hematomas within 24 hours of onset in selected patients (hematoma volume 30–80 mL; GCS 5–14) was beneficial compared with medical management alone.
6. Cerebral amyloid angiopathy (CAA) is the most common cause of lobar hemorrhage in the elderly; it is associated with ApoE ε2 and ε4 allelic variations and amyloid-beta deposits.
7. Putamen hemorrhage presents with contralateral hemiparesis as the sentinel sign; thalamic hemorrhage presents with prominent sensory deficit and aphasia.
8. Pontine hemorrhage typically presents with deep coma, quadriplegia, and pinpoint (1 mm) pupils that react to light.
9. Cerebellar hemorrhages usually develop over several hours and are characterized by occipital headache, repeated vomiting, and ataxia of gait.
10. The STICH trial found no benefit in early surgery for supratentorial ICH, though analysis was complicated by 26% of patients in the medical group ultimately having surgery for deterioration.

FIGURES IN THIS CHAPTER

1. DEFINITION & OVERVIEW

- Intracerebral hemorrhage (ICH) is a form of stroke.

• Harrison's defines this as: spontaneous hemorrhage directly into the brain parenchyma.

• ICH will be considered along with intracranial vascular anomalies such as arteriovenous malformations (AVMs) of the brain.

• Other categories of intracranial hemorrhage include bleeding into subarachnoid, subdural, or epidural spaces, usually caused by trauma, and subarachnoid hemorrhage due to trauma or the rupture of an intracranial aneurysm.

• ICH accounts for approximately 10% of all strokes.

• Approximately 35–45% of patients die within the first month.

• Incidence rates are particularly high in Asian and Black patient groups.

• Advanced age, heavy alcohol use, and low-dose aspirin use in those without symptomatic cardiovascular disease increase ICH risk.

• Cocaine or methamphetamine use is one of the most important causes in the young.

1.1 Epidemiology

• ICH accounts for ~10% of all strokes.

• ~35–45% of patients die within the first month.

• Incidence rates are particularly high in Asian and Black patient groups.

• Risk factors include advanced age, heavy alcohol use, and low-dose aspirin use in those without symptomatic cardiovascular disease.

• Cocaine or methamphetamine use is one of the most important causes in the young.

1.2 Classification

• Primary ICH: Spontaneous hemorrhage directly into the brain parenchyma.

• Secondary ICH: Includes bleeding into subarachnoid, subdural, or epidural spaces (usually trauma), and subarachnoid hemorrhage due to trauma or rupture of an intracranial aneurysm.

• ICH is defined as spontaneous hemorrhage directly into the brain parenchyma.

• ICH is considered along with intracranial vascular anomalies such as arteriovenous malformations (AVMs).

• Other categories include bleeding into subarachnoid, subdural, or epidural spaces, usually caused by trauma.

2. ETIOLOGY & PATHOPHYSIOLOGY

• Hypertension is the leading cause of primary ICH.

• Hypertensive ICH usually results from spontaneous rupture of a small penetrating artery deep in the brain.

• The most common sites are the basal ganglia (especially the putamen), thalamus, cerebellum, and pons.

• The small arteries in these areas seem most prone to hypertension-induced vascular injury.

• When hemorrhages occur in other brain areas or in nonhypertensive patients, greater consideration should be given to other causes such as hemorrhagic disorders, neoplasms, vascular malformations, vasculitis, and CAA.

• Cerebral amyloid angiopathy (CAA) is a disease of the elderly in which arteriolar degeneration occurs and amyloid is deposited in the walls of the cerebral arteries.

• CAA causes both single and recurrent lobar hemorrhages and is probably the most common cause of lobar hemorrhage in the elderly.

• It accounts for some intracranial hemorrhages associated with IV thrombolysis given for myocardial infarction.

• The ε2 and ε4 allelic variations of the apolipoprotein E gene are associated with increased risk of recurrent lobar hemorrhage and may therefore be markers of amyloid angiopathy.

• Cocaine and methamphetamine are frequent causes of stroke in young (age <45 years) patients.

• ICH, ischemic stroke, and subarachnoid hemorrhage (SAH) are all associated with stimulant use.

• Angiographic findings vary from completely normal arteries to large-vessel occlusion or stenosis, vasospasm, or changes consistent with vasculopathy.

• The mechanism of sympathomimetic-related stroke is not known, but cocaine enhances sympathetic activity causing acute, sometimes severe, hypertension, and this may lead to hemorrhage.

• Slightly more than one-half of stimulant-related intracranial hemorrhages are intracerebral and the rest are subarachnoid.

• In cases of SAH, a saccular aneurysm is usually identified.

• Presumably, acute hypertension causes aneurysmal rupture.

• Hemorrhage into a brain tumor may be the first manifestation of neoplasm.

• Choriocarcinoma, malignant melanoma, renal cell carcinoma, and thyroid, lung, and hepatocellular carcinoma are among the most common metastatic tumors associated with ICH.

• Pilocytic astrocytoma and glioblastoma multiforme in adults and medulloblastoma in children may also have areas of ICH.

• Vasculitis, usually polyarteritis nodosa or lupus erythematosus, can produce hemorrhage in any region of the central nervous system.

• Nearly one-half of patients with primary intraventricular hemorrhage have identifiable bleeding sources seen using conventional angiography.

• Moyamoya disease, mainly an occlusive arterial disease that causes ischemic symptoms, may on occasion produce ICH.

• Hemorrhages into the spinal cord are usually the result of an AVM, cavernous malformation, or metastatic tumor.

• Epidural spinal hemorrhage produces a rapidly evolving syndrome of spinal cord or nerve root compression.

• Sepsis can cause small petechial hemorrhages throughout the cerebral white matter.

Table 1 Table 439-1 Causes of Intracerebral Hemorrhage (ICH)

CAUSE	LOCATION	COMMENTS
Primary ICH	Cerebral amyloid angiopathy	Lobar; Degenerative disease of intracranial vessels; associated with dementia, rare in patients <60 years
Coagulopathy	Any	Risk for hematoma expansion
Drug	Any, lobar, subarachnoid	Cocaine, amphetamine
Hypertension	Putamen, globus pallidus, thalamus, cerebellar hemisphere, pons	Chronic hypertension produces hemorrhage from small (~30–100 μm) vessels in these regions
Secondary ICH	Aneurysm	Subarachnoid, intraparenchymal, rarely subdural; Mycotic and nonmycotic forms of aneurysms

CAUSE	LOCATION	COMMENTS
Arteriovenous malformation	Lobar, intraventricular, subarachnoid	Risk is ~2–4% per year for bleeding if previously unruptured
Capillary telangiectasias	Usually brainstem	Rare cause of hemorrhage
Cavernous angioma	Intraparenchymal	Multiple cavernous angioma linked to mutations in KRIT1, CCM2, and PDCD10 genes
Dural arteriovenous fistula	Lobar, subarachnoid	Produces bleeding from venous hypertension
Dural sinus thrombosis	Along sagittal sinus, posterior temporal/inferior parietal	Sagittal sinus thrombosis can cause hemispheric parasagittal hemorrhage with edema; vein of Labbé occlusion from transverse sinus occlusion produces posterior temporal and/or inferior parietal hemorrhage
Metastatic or primary brain tumors	Lobar	Lung, choriocarcinoma, melanoma, renal cell carcinoma, thyroid, hepatocellular carcinoma, and pilocytic astrocytoma are more commonly associated with bleeding complications
Transformation	Basal ganglion, subcortical regions, lobar	Occurs in a significant proportion of prior ischemic subcortical regions, lobar infarction commonly in large hemispheric infarctions; is symptomatic in 3–9% of patients undergoing acute intervention

2.1 Hypertensive ICH

- Usually results from spontaneous rupture of a small penetrating artery deep in the brain.
- Most common sites: basal ganglia (especially putamen), thalamus, cerebellum, and pons.
- Small arteries in these areas seem most prone to hypertension-induced vascular injury.
- Hemorrhage may be small, or a large clot may form and compress adjacent tissue, causing herniation and death.
- Blood may also dissect into the ventricular space, which substantially increases morbidity and may cause hydrocephalus.

2.2 Cerebral Amyloid Angiopathy (CAA)

- Disease of the elderly in which arteriolar degeneration occurs and amyloid is deposited in the walls of the cerebral arteries.
- Causes both single and recurrent lobar hemorrhages.
- Probably the most common cause of lobar hemorrhage in the elderly.
- Accounts for some intracranial hemorrhages associated with IV thrombolysis given for myocardial infarction.
- Suspected in patients who present with multiple hemorrhages (and infarcts) over several months or years.
- Seen in patients with 'microbleeds' in the cortex, seen on brain MRI sequences sensitive for hemosiderin.

• Definitively diagnosed by pathologic demonstration of Congo red staining of amyloid in cerebral vessels.

• ε2 and ε4 allelic variations of the apolipoprotein E gene are associated with increased risk of recurrent lobar hemorrhage.

• Positron emission tomography imaging can image amyloid-beta deposits in CAA using specific antibody labels.

• Cerebral biopsy is the most definitive method of diagnosis.

• Evidence of inflammation on lumbar puncture should prompt consideration of CAA-associated vasculitis as an underlying cause.

• Oral glucocorticoids may be beneficial for CAA-associated vasculitis.

• Noninflammatory CAA has no specific treatment.

• Oral anticoagulants are typically avoided.

2.3 Vascular Anomalies

• True AVMs are shunts between the arterial and venous systems.

• May present with headache, seizures, and intracranial hemorrhage.

• Consist of a tangle of abnormal vessels across the cortical surface or deep within the brain substance.

• Vary in size from a small blemish a few millimeters in diameter to a large mass of tortuous channels.

• Blood vessels forming the tangle interposed between arteries and veins are usually abnormally thin and histologically resemble both arteries and veins.

• Most AVMs are congenital, but cases of acquired lesions have been reported.

• Bleeding, headache, and seizures are most common between the ages of 10 and 30, occasionally as late as the fifties.

• AVMs are more frequent in men.

• Familial AVM may be a part of the autosomal dominant syndrome of hereditary hemorrhagic telangiectasia (Osler-Rendu-Weber) syndrome due to mutations in either endoglin or activin receptor-like kinase 1.

• Both involved in transforming growth factor (TGF) signaling and angiogenesis.

3. CLINICAL FEATURES

• ICH generally presents as the abrupt onset of a focal neurologic deficit.

• Seizures are uncommon on presentation but may occur in 6–15% of patients within the first 3 days.

• Although clinical symptoms may be maximal at onset, more commonly, the focal deficit worsens over 30–90 min and is associated with a diminishing level of consciousness and signs of increased ICP such as headache and vomiting.

• The putamen is the most common site for hypertensive hemorrhage, and the adjacent internal capsule is usually damaged.

• Contralateral hemiparesis is therefore the sentinel sign.

• When mild, the face sags on one side over 5–30 min, speech becomes slurred, the arm and leg gradually weaken, and the eyes deviate away from the side of the hemiparesis.

• The paralysis may worsen until the affected limbs become flaccid or extend rigidly.

• When hemorrhages are large, drowsiness gives way to stupor as signs of upper brainstem compression appear.

• Coma ensues, accompanied by deep, irregular, or intermittent respiration, a dilated and fixed ipsilateral pupil, and decerebrate rigidity.

• Edema in adjacent brain tissue may cause progressive deterioration over 24–96 h.

• Thalamic hemorrhages may also produce a contralateral hemiplegia or hemiparesis from pressure on, or dissection into, the adjacent internal capsule.

• A prominent sensory deficit involving all modalities is usually present.

• Aphasia, often with preserved verbal repetition, may occur after hemorrhage into the dominant thalamus.

• Constructional apraxia or mutism occurs in some cases of nondominant hemorrhage.

• There may also be a homonymous visual field defect.

• Thalamic hemorrhages cause several typical ocular disturbances by extension inferiorly into the upper midbrain.

• These include deviation of the eyes downward and inward so that they appear to be looking at the nose.

• Unequal pupils with absence of light reaction, skew deviation with the eye opposite the hemorrhage displaced downward and medially, ipsilateral Horner's syndrome, absence of convergence, paralysis of vertical gaze, and retraction nystagmus.

• Patients may later develop a chronic, contralateral pain syndrome (Déjérine-Roussy syndrome).

• In pontine hemorrhages, deep coma with quadriplegia often occurs over a few minutes.

• Typically, there is prominent decerebrate rigidity and 'pinpoint' (1 mm) pupils that react to light.

• There is impairment of reflex horizontal eye movements evoked by head turning (doll's-head or oculocephalic maneuver) or by irrigation of the ears with ice water.

• Hyperpnea, severe hypertension, and hyperhidrosis are common.

• Most patients with deep coma from pontine hemorrhage ultimately die or develop a locked-in state, but small hemorrhages are compatible with survival and significant recovery.

• Lobar hemorrhages usually present with symptoms related to the specific site of origin.

• The major neurologic deficit with an occipital hemorrhage is hemianopsia.

• With a left temporal hemorrhage, aphasia and confusion.

• With a parietal hemorrhage, hemisensory loss.

• With a frontal hemorrhage, arm weakness.

• Large hemorrhages may be associated with stupor or coma if they compress the thalamus or midbrain.

• Most patients with lobar hemorrhages have focal headaches, and more than one-half vomit or are drowsy.

• Seizures may occur.

• Cerebellar hemorrhages usually develop over several hours and are characterized by occipital headache, repeated vomiting, and ataxia of gait.

• In mild cases, there may be no other neurologic signs except for gait ataxia.

• Dizziness or vertigo may be prominent.

• There is often paresis of conjugate lateral gaze toward the side of the hemorrhage, forced deviation of the eyes to the opposite side, or an ipsilateral sixth nerve palsy.

• Less frequent ocular signs include blepharospasm, involuntary closure of one eye, ocular bobbing, and skew deviation.

• Dysarthria and dysphagia may occur.

• As the hours pass, the patient often becomes stuporous and then comatose from brainstem compression or obstructive hydrocephalus.

• Immediate surgical evacuation before severe brainstem compression occurs may be lifesaving.

• Hydrocephalus from fourth ventricle compression can be relieved by external ventricular drainage.

• However, in this situation, definitive hematoma evacuation is recommended rather than treatment with ventricular drainage alone.

• If the deep cerebellar nuclei are spared, full recovery is common.

• Hypertensive encephalopathy is a complication of malignant hypertension.

• In this acute syndrome, severe hypertension is associated with headache, nausea, vomiting, convulsions, confusion, stupor, and coma.

• Focal or lateralizing neurologic signs, either transitory or permanent, may occur but are infrequent and therefore suggest some other vascular disease (hemorrhage, embolism, or atherosclerotic thrombosis).

• There may be retinal hemorrhages, exudates, papilledema (hypertensive retinopathy), and evidence of renal and cardiac disease.

• MRI brain imaging shows a pattern of typically posterior (occipital > frontal) brain edema.

• The hypertension may be essential or due to chronic renal disease, acute glomerulonephritis, acute toxemia of pregnancy, pheochromocytoma, or other causes.

• Lowering the blood pressure reverses the process, but stroke can occur, especially if blood pressure is lowered too rapidly.

• Neuropathologic examination reveals multifocal to diffuse cerebral edema and hemorrhages of various sizes from petechial to massive.

• Microscopically, there is necrosis of arterioles, minute cerebral infarcts, and hemorrhages.

• The terms hypertensive encephalopathy and posterior reversible encephalopathy syndrome should be reserved for this syndrome and not for chronic recurrent headaches, dizziness, recurrent transient ischemic attacks, or small strokes that often occur in association with high blood pressure.

• Distinguishing hypertensive encephalopathy with ICH from hypertensive encephalopathy is important since aggressive lowering of SBP to 130–150 mmHg acutely is often considered in hypertensive ICH, but less aggressive measures should be used in hypertensive encephalopathy.

• Having no alteration in mental status or other prodrome prior to the ICH favors hypertensive ICH as the disease.

• Primary intraventricular hemorrhage is rare and should prompt investigation for an underlying vascular anomaly.

• Sometimes bleeding begins within the periventricular substance of the brain and dissects into the ventricular system without leaving signs of intraparenchymal hemorrhage.

• Alternatively, bleeding can arise from periependymal veins.

• Vasculitis, usually polyarteritis nodosa or lupus erythematosus, can produce hemorrhage in any region of the central nervous system.

• Nearly one-half of patients with primary intraventricular hemorrhage have identifiable bleeding sources seen using conventional angiography.

• Sepsis can cause small petechial hemorrhages throughout the cerebral white matter.

• Moyamoya disease, mainly an occlusive arterial disease that causes ischemic symptoms, may on occasion produce ICH.

• Hemorrhages into the spinal cord are usually the result of an AVM, cavernous malformation, or metastatic tumor.

• Epidural spinal hemorrhage produces a rapidly evolving syndrome of spinal cord or nerve root compression.

• Spinal hemorrhages usually present with sudden back pain and some manifestation of myelopathy.

3.1 Hypertensive ICH Manifestations

• Putamen: Contralateral hemiparesis (sentinel sign).

• Thalamus: Prominent sensory deficit, aphasia, ocular disturbances.

• Pons: Deep coma, quadriplegia, pinpoint pupils.

• Cerebellum: Headache, vomiting, ataxia.

• Lobar: Headache, vomiting, seizures.

3.2 Other Causes Manifestations

• CAA: Multiple hemorrhages, microbleeds.

• Drugs: Cocaine, methamphetamine.

• Trauma: Intraparenchymal (especially temporal and inferior frontal lobes) and into subarachnoid, subdural, and epidural spaces.

• Anticoagulant therapy: Lobar or subdural.

• Tumors: Choriocarcinoma, malignant melanoma, renal cell carcinoma, thyroid, lung, hepatocellular carcinoma, pilocytic astrocytoma, glioblastoma multiforme, medulloblastoma.

4. DIFFERENTIAL DIAGNOSIS

• Hypertensive encephalopathy vs ICH: Having no alteration in mental status or other prodrome prior to the ICH favors hypertensive ICH as the disease.

• Aggressive lowering of SBP to 130–150 mmHg acutely is often considered in hypertensive ICH, but less aggressive measures should be used in hypertensive encephalopathy.

• Focal or lateralizing neurologic signs, either transitory or permanent, may occur but are infrequent and therefore suggest some other vascular disease (hemorrhage, embolism, or atherosclerotic thrombosis).

• Retinal hemorrhages, exudates, papilledema (hypertensive retinopathy), and evidence of renal and cardiac disease suggest hypertensive encephalopathy.

• MRI brain imaging shows a pattern of typically posterior (occipital > frontal) brain edema.

• Primary intraventricular hemorrhage is rare and should prompt investigation for an underlying vascular anomaly.

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4.1 Mimics

• Hypertensive encephalopathy.

• Ischemic stroke with hemorrhagic transformation.

• Vasculitis.

• Sepsis.

• Moyamoya disease.

5. INVESTIGATIONS & DIAGNOSIS

• Intracranial hemorrhage is often identified on noncontrast computed tomography (CT) imaging of the head during the acute evaluation of stroke.

• Because CT is more widely available and may be logistically easier to perform than magnetic resonance imaging (MRI), CT imaging is generally the preferred method for acute stroke evaluation.

• The location of the hemorrhage narrows the differential diagnosis to a few entities.

• CT imaging reliably detects acute focal hemorrhages in the supratentorial space.

• Rarely, very small pontine or medullary hemorrhages may not be well delineated because of motion and bone-induced artifact that obscure structures in the posterior fossa.

• After the first 2 weeks, x-ray attenuation values of clotted blood diminish until they become isodense with surrounding brain.

• Mass effect and edema may remain.

• In some cases, a surrounding rim of contrast enhancement appears after 2–4 weeks and may persist for months.

• MRI, although more sensitive for delineating posterior fossa lesions, is generally not necessary for primary diagnosis.

• MR angiography (MRA), CT angiography (CTA), and conventional x-ray angiography are used when the cause of intracranial hemorrhage is uncertain, particularly if the patient is young or not hypertensive and the hematoma is not in one of the usual sites for hypertensive hemorrhage.

• CTA or postcontrast CT imaging may reveal one or more small areas of enhancement within a hematoma.

• This 'spot sign' is thought to represent ongoing bleeding.

• The presence of a spot sign is associated with an increased risk of hematoma expansion, increased mortality, and lower likelihood of favorable functional outcome.

• Because patients typically have focal neurologic signs and obtundation and often show signs of increased ICP, a lumbar puncture is generally unnecessary and should usually be avoided because it may induce cerebral herniation.

• Patients should have routine blood chemistries and hematologic studies.

• Specific attention to the platelet count, prothrombin time, partial thromboplastin time, and international normalized ratio is important to identify coagulopathy.

• Skin and mucous membrane bleeding may be evident and offers a diagnostic clue.

Table 2 Table 439-2 The Intracerebral Hemorrhage Score

CLINICAL OR IMAGING FACTOR	POINT SCORE		
Age	<80 years: 0	≥80 years: 1	
Hematoma Volume	<30 cc: 0	≥30 cc: 1	
Intraventricular Hemorrhage Present	No: 0	Yes: 1	
Infratentorial Origin of Hemorrhage	No: 0	Yes: 1	
Glasgow Coma Scale Score	13–15: 0	5–12: 1	3–4: 2
Total Score	0–6 Sum of each category above		

5.1 Imaging Modalities

• CT: Preferred for acute stroke evaluation.

• MRI: More sensitive for posterior fossa lesions.

• CTA/MRA: Used when cause is uncertain, particularly if patient is young or not hypertensive.

• Spot sign: CTA or postcontrast CT imaging may reveal one or more small areas of enhancement within a hematoma.

5.2 Laboratory Evaluation

• Routine blood chemistries and hematologic studies.

• Platelet count.

• Prothrombin time.

• Partial thromboplastin time.

• International normalized ratio (INR).

• Skin and mucous membrane bleeding may be evident and offers a diagnostic clue.

6. MANAGEMENT & TREATMENT

• Close attention should be paid to airway management because deterioration in the level of consciousness is common and often progressive.

• The initial blood pressure should be maintained until the results of the CT scan are reviewed and demonstrate ICH.

• A higher blood pressure may promote hematoma expansion, but it remains unclear if lowering of blood pressure reduces hematoma growth.

• Recent clinical trials have shown that systolic blood pressure (SBP) can be safely lowered acutely and rapidly to <140 mmHg in patients with spontaneous ICH whose initial SBP was 150–220 mmHg.

• The INTERACT2 trial was a large phase 3 clinical trial to address the effect of acute blood pressure lowering on ICH functional outcome.

• INTERACT2 randomized patients with spontaneous ICH within 6 h of onset and a baseline SBP of 150–220 mmHg to two different SBP targets (<140 and <180 mmHg).

• In those with the target SBP <140 mmHg, 52% had an outcome of death or major disability at 90 days compared with 55.6% of those with a target SBP <180 mmHg (p = .06).

• There was a significant shift to improved outcomes in the lower blood pressure arm, whereas both groups had a similar mortality.

• ATACH2 was a similarly designed clinical trial that assessed the same blood pressure targets but demonstrated no difference in outcome between groups.

• However, aggressive blood pressure lowering did increase renal adverse events.

• Current U.S. and European guidelines emphasize that blood pressure lowering to a target SBP is likely safe and possibly beneficial.

• While the specific optimal target remains a point of debate, the most recent American Heart Association/American Stroke Association guidelines for the management of spontaneous ICH endorse achieving and maintaining a target SBP of 130–150 mmHg in these patients to avoid unintended hypoperfusion.

• It is unclear whether these clinical trial results apply to patients who have higher SBP on presentation or who are deeply comatose with possible elevated intracranial pressure (ICP).

• In patients who have ICP monitors in place, maintaining the cerebral perfusion pressure (mean arterial pressure [MAP] minus ICP) of 60 to ≥70 mmHg is reasonable.

• Blood pressure should be lowered using IV drugs with less cerebral vasodilating action such as nicardipine, clevidipine, labetalol, or esmolol.

• Patients with radiographic evidence of hydrocephalus or cerebellar ICH with depressed mental status should undergo urgent neurosurgical evaluation.

• These patients require close monitoring because they can deteriorate rapidly.

• Based on the clinical examination and CT findings, further imaging studies may be necessary, including MRI or conventional x-ray angiography.

• Stuporous or comatose patients with clinical and imaging signs of herniation can be presumptively treated for elevated ICP with tracheal intubation and sedation, administration of osmotic diuretics such as mannitol or hypertonic saline, and elevation of the head of the bed while surgical consultation is obtained.

• Rapid reversal of coagulopathy ideally within 1 h of presentation and consideration of surgical evacuation of the hematoma are two other principal aspects of initial emergency management.

• Any identified coagulopathy should be corrected as soon as possible.

• For patients taking vitamin K antagonists (VKAs), rapid correction of coagulopathy can be achieved by infusing prothrombin complex concentrates (PCCs), which can be administered quickly, with vitamin K administered concurrently.

• Fresh frozen plasma (FFP) is an alternative, but since it requires larger fluid volumes and longer time to achieve adequate reversal than PCC, it is not recommended if PCC is available.

• Idarucizumab is a monoclonal antibody to dabigatran, and the administration of two doses reverses the anticoagulation effect of dabigatran quickly.

• The oral Xa inhibitors apixaban and rivaroxaban can be reversed with andexanet alfa.

• PCC may partially reverse the effects of oral factor Xa inhibitors and are reasonable to administer if andexanet alfa is not available.

• When ICH is associated with thrombocytopenia (platelet count <50,000/μL), transfusion of fresh platelets is indicated.

• A clinical trial of platelet transfusions in patients with ICH and without thrombocytopenia who were taking antiplatelet drugs showed no benefit and possible harm.

• Hematomas may expand for several hours following the initial hemorrhage, even in patients without coagulopathy.

• The precise mechanism is unclear.

• A phase 3 trial of treatment with recombinant factor VIIa reduced hematoma expansion; however, clinical outcomes were not improved, so use of this drug is not recommended.

• The administration of tranexamic acid was not found to alter outcome in a large randomized trial.

• Blood pressure lowering has been considered due to the theoretical risk of acutely elevated blood pressure on hematoma expansion, although clinical trials did not find a difference in hematoma expansion between the SBP targets of 140–180 mmHg.

• In deep hemorrhages that involve the basal ganglia, more intensive blood pressure lowering reduced hematoma expansion but had no effect on functional outcome.

• Initial clinical trials of evacuation of supratentorial hematomas, primarily via standard craniotomy, did not demonstrate clear benefit.

• However, recent focus on minimally-invasive surgical techniques holds promise.

• The International Surgical Trial in Intracerebral Haemorrhage (STICH) randomized patients with supratentorial ICH to either early surgical evacuation or initial medical management.

• No benefit was found in the early surgery arm, although analysis was complicated by the fact that 26% of patients in the initial medical management group ultimately had surgery for neurologic deterioration.

• The follow-up study, STICH-II, found that craniotomy and hematoma evacuation within 24 h of lobar supratentorial hemorrhage did not improve overall outcome but might have a role in select severely

affected patients.

• However, many centers still consider surgery for patients deemed salvageable and who are experiencing progressive neurologic deterioration due to herniation.

• Surgical techniques continue to evolve.

• In a clinical trial of minimally invasive hematoma evacuation using instillation of the thrombolytic agent alteplase into the clot, mortality was decreased but there was not an improvement in functional outcome.

• In 2024, the first randomized trial demonstrating improvement in functional outcome after surgical hematoma evacuation was published.

• The Early MiNimally-invasive Removal of IntraCerebral Hemorrhage (ENRICH) trial found that surgical removal of lobar hematomas within 24 hours of onset in selected patients (hematoma volume 30–80 mL; Glasgow Coma Score 5–14; pre-ICH functionally independent) was beneficial compared with medical management alone.

• Several clinical trials testing other minimally invasive surgical hematoma evacuation techniques are ongoing.

• For cerebellar hemorrhages in patients with decreased level of consciousness or obstructive hydrocephalus, a neurosurgeon should be consulted immediately to assist with the evaluation.

• If the patient is alert without focal brainstem signs and the hematoma is small, surgical removal is usually unnecessary.

• Patients with hematomas >1 cm in diameter require careful observation for signs of impaired consciousness, progressive hydrocephalus, and precipitous respiratory failure.

• Hydrocephalus due to cerebellar hematoma generally requires surgical evacuation and should usually not be treated solely with ventricular drainage.

• Tissue surrounding hematomas is displaced and compressed but not necessarily infarcted.

• Hence, major functional improvement often occurs as the hematoma is reabsorbed and the adjacent tissue regains its function over several months following acute injury.

• Careful management of the patient during the acute phase of the hemorrhage can lead to considerable recovery.

• Bundles of care that incorporate multiple interventions may provide more value in the management of ICH patients than separating out different singular interventions.

• A hospital in the United Kingdom found that an ICH care bundle consisting of coagulopathy reversal, blood pressure lowering, and neurosurgical referral decreased patient mortality when implemented as a quality assurance project.

• In the INTERACT-3 randomized clinical trial performed in low- to middle-income countries, a bundle of care that included vitamin K coagulopathy reversal, acute blood pressure lowering, glucose control, and temperature control was associated with improved functional outcome and fewer adverse events.

• Surprisingly, ICP is often normal even with large ICHs.

• However, if the hematoma causes marked midline shift of structures with consequent obtundation, coma, or hydrocephalus, osmotic agents can be instituted in preparation for placement of a ventriculostomy or parenchymal ICP monitor.

• Once ICP is recorded, CSF drainage (if available), osmotic therapy, and blood pressure management can be tailored to maintain cerebral perfusion pressure (MAP minus ICP) of 60 to ≥70 mmHg.

• For example, if ICP is found to be high, CSF can be drained from the ventricular space and osmotic therapy continued.

• Persistent or progressive elevation in ICP may prompt surgical evacuation of the clot.

• Alternately, if ICP is normal, interventions such as osmotic therapy may be tapered.

• Because hyperventilation may produce ischemia due to cerebral vasoconstriction, induced hyperventilation should be limited to acute resuscitation of the patient with presumptive high ICP and eliminated once osmotic therapy or surgical treatments have been instituted.

• Glucocorticoids are not recommended for the treatment of intracerebral hemorrhage.

• Hypertension is the leading cause of primary ICH.

• Prevention is aimed at reducing chronic hypertension, eliminating excessive alcohol use, and discontinuing use of illicit drugs such as cocaine and amphetamines.

• Oral anticoagulant medications should generally be avoided in patients with high-risk features for CAA, but antiplatelet agents may be administered if there is an indication based on atherosclerotic vascular disease.

• Ongoing studies are investigating the risk-benefit ratio of reinitiation of anticoagulation in patients with recent ICH who have atrial fibrillation.

6.1 Acute Management

• Airway management: Close attention should be paid to airway management because deterioration in the level of consciousness is common and often progressive.

• Blood pressure management: Initial blood pressure should be maintained until CT scan is reviewed.

• Target SBP: 130–150 mmHg (AHA/ASA guidelines).

• IV drugs: Nicardipine, clevidipine, labetalol, or esmolol.

• ICP management: Mannitol, hypertonic saline, intubation, sedation.

• Coagulopathy reversal: PCC for VKAs, Idarucizumab for dabigatran, Andexanet alfa for Xa inhibitors.

• Platelet transfusion: Indicated if platelet count <50,000/µL.

6.2 Surgical Management

• STICH Trial: No benefit in early surgery for supratentorial ICH.

• ENRICH Trial: Surgical removal of lobar hematomas within 24 hours beneficial in selected patients.

• Cerebellar Hemorrhage: Surgical evacuation if hydrocephalus or decreased consciousness.

• Minimally invasive techniques: Evacuation using instillation of thrombolytic agent alteplase.

• Surgical evacuation: Considered for patients deemed salvageable and experiencing progressive neurologic deterioration due to herniation.

6.3 ICP Management

• ICP is often normal even with large ICHs.

• If hematoma causes marked midline shift with obtundation, coma, or hydrocephalus, osmotic agents can be instituted.

• CSF drainage, osmotic therapy, and blood pressure management tailored to maintain cerebral perfusion pressure (MAP minus ICP) of 60 to ≥70 mmHg.

• Hyperventilation: Limited to acute resuscitation of the patient with presumptive high ICP.

• Glucocorticoids: Not recommended.

7. PROGNOSIS & COMPLICATIONS

• Approximately 40% of patients with a hypertensive ICH die.

• But survivors can have a good to complete recovery.

• The ICH Score is a validated clinical grading scale that is useful for stratification of mortality risk and clinical outcome.

• However, a specific ICH clinical grading scale should not be used to precisely prognosticate outcome because of the concern of creating a self-fulfilling prophecy of poor outcome if early aggressive care is withheld.

• Tissue surrounding hematomas is displaced and compressed but not necessarily infarcted.

• Hence, major functional improvement often occurs as the hematoma is reabsorbed and the adjacent tissue regains its function over several months following acute injury.

• Careful management of the patient during the acute phase of the hemorrhage can lead to considerable recovery.

• Bundles of care that incorporate multiple interventions may provide more value in the management of ICH patients than separating out different singular interventions.

• In the INTERACT-3 randomized clinical trial performed in low- to middle-income countries, a bundle of care that included vitamin K coagulopathy reversal, acute blood pressure lowering, glucose control, and temperature control was associated with improved functional outcome and fewer adverse events.

7.1 Mortality and Recovery

• Approximately 40% of patients with a hypertensive ICH die.

• Survivors can have a good to complete recovery.

• Major functional improvement often occurs as the hematoma is reabsorbed and the adjacent tissue regains its function over several months following acute injury.

7.2 Prognostic Scoring

• The ICH Score is a validated clinical grading scale that is useful for stratification of mortality risk and clinical outcome.

• However, a specific ICH clinical grading scale should not be used to precisely prognosticate outcome because of the concern of creating a self-fulfilling prophecy of poor outcome if early aggressive care is withheld.

8. SPECIAL CONSIDERATIONS

• Oral anticoagulant medications should generally be avoided in patients with high-risk features for CAA.

• Antiplatelet agents may be administered if there is an indication based on atherosclerotic vascular disease.

• Ongoing studies are investigating the risk-benefit ratio of reinitiation of anticoagulation in patients with recent ICH who have atrial fibrillation.

• Intracranial stenting of intracranial atherosclerosis was found to be dramatically harmful compared to aspirin in the Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial.

• This trial enrolled newly symptomatic TIA or minor stroke patients with associated 70–99% intracranial stenosis to primary stenting with a self-expanding stent or to medical management.

• Both groups received clopidogrel, aspirin, statin, and aggressive control of blood pressure.

• The endpoint of stroke or death occurred in 14.7% of the stented group and 5.8% of the medically treated groups (p = .002).

• This low rate of second stroke was significantly lower than in the WASID trial and suggests that aggressive medical management had a marked influence on secondary stroke risk.

• A concomitant study of balloon-expandable stenting was halted early at 125 patients because of the negative outcome.

• The International Carotid Stenting Study (ICSS) randomized symptomatic patients to stents versus endarterectomy and found a different result.

• At 120 days, the incidence of stroke, MI, or death was 8.5% in the stenting group versus 5.2% in the endarterectomy group (p = .006).

• At median follow-up of 5 years, these differences were no longer significant except a small increase in nondisabling stroke in the stenting group but no change in the average disability.

• In meta-analysis, carotid endarterectomy (CEA) is less morbid in older patients (aged ≥70) than is stenting.

• Recently, transcarotid artery revascularization (TCAR), which involves the reversal of blood flow during an angioplasty and stenting procedure, has been offered as an alternative to transfemoral carotid artery stenting or when CEA presents high risks.

• Investigation is ongoing in asymptomatic patients to compare medical therapy to stenting and CEA.

• This will likely answer how well medical patients do with more modern medical therapy (statins, close blood pressure control, and lifestyle modification).

• Extracranial-to-intracranial (EC-IC) bypass surgery has been proven ineffective for atherosclerotic stenoses that are inaccessible on conventional CEA.

• In patients with recent stroke, an associated carotid occlusion, and evidence of inadequate perfusion of the brain as measured with positron emission tomography, no benefit from EC-IC bypass was found in a trial stopped for futility.

• Dural Sinus Thrombosis: Limited evidence exists to support short-term use of anticoagulants, regardless of the presence of intracranial hemorrhage, for venous infarction following sinus thrombosis.

• The long-term outcome for most patients, even those with intracerebral hemorrhage, is excellent.

8.1 Anticoagulation

• Oral anticoagulant medications should generally be avoided in patients with high-risk features for CAA.

• Antiplatelet agents may be administered if there is an indication based on atherosclerotic vascular disease.

• Ongoing studies are investigating the risk-benefit ratio of reinitiation of anticoagulation in patients with recent ICH who have atrial fibrillation.

8.2 Vascular Interventions

• SAMMPRIS Trial: Intracranial stenting of intracranial atherosclerosis was found to be dramatically harmful compared to aspirin.

• ICSS Trial: Carotid endarterectomy (CEA) is less morbid in older patients (aged ≥70) than is stenting.

• TCAR: Transcarotid artery revascularization offered as an alternative to transfemoral carotid artery stenting or when CEA presents high risks.

• EC-IC Bypass: Proven ineffective for atherosclerotic stenoses that are inaccessible on conventional CEA.

9. KEY PEARLS & CLINICAL TRAPS

• The 'spot sign' on CTA represents ongoing bleeding and is associated with increased risk of hematoma expansion, increased mortality, and lower likelihood of favorable functional outcome.

• Target SBP of 130–150 mmHg is endorsed by AHA/ASA guidelines to avoid unintended hypoperfusion.

• Rapid reversal of coagulopathy is critical: PCC for VKAs, Idarucizumab for dabigatran, Andexanet alfa for Xa inhibitors.

• ENRICH trial: Surgical removal of lobar hematomas within 24 hours of onset in selected patients was beneficial compared with medical management alone.

• STICH trial: No benefit in early surgery for supratentorial ICH, though analysis was complicated by 26% of patients in the medical group ultimately having surgery for deterioration.

• Putamen hemorrhage: Contralateral hemiparesis is the sentinel sign.

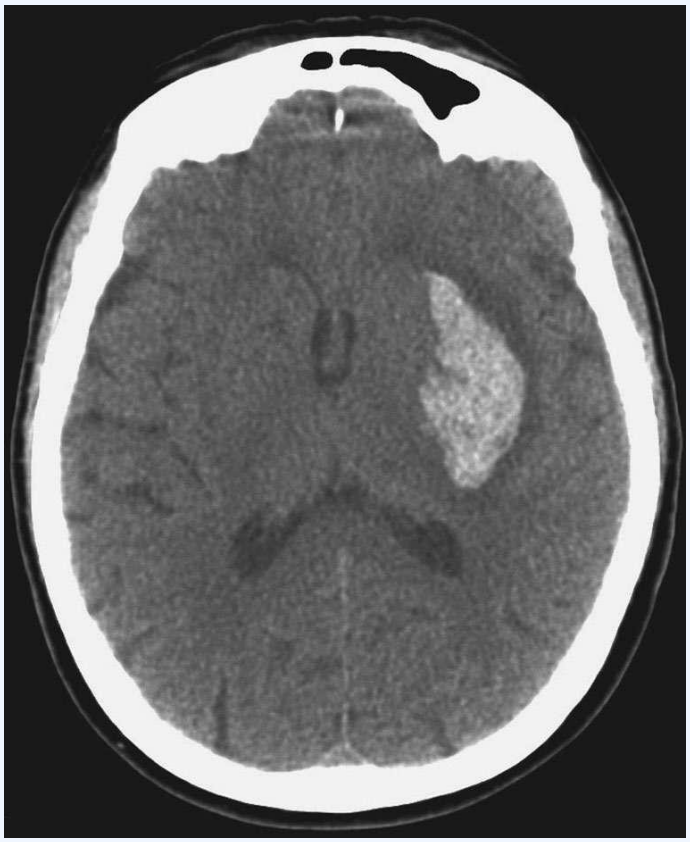
• Pons hemorrhage: Pinpoint (1 mm) pupils that react to light, deep coma, quadriplegia.

• Cerebellar hemorrhage: Occipital headache, repeated vomiting, ataxia; surgical evacuation if hydrocephalus.

• CAA: Most common cause of lobar hemorrhage in the elderly; associated with ApoE ε2 and ε4 allelic variations.

• Hypertensive encephalopathy vs ICH: Having no alteration in mental status or other prodrome prior to the ICH favors hypertensive ICH as the disease.

FIGURES & ILLUSTRATIONS — FROM HARRISON'S



Harrison's 22e · Figure 1

FIGURE 439-1 Hypertensive intracerebral hemorrhage. Transaxial noncontrast computed tomography scan through the region of the basal ganglia reveals a hematoma involving the left putamen in a patient with rapidly progressive onset of right hemiparesis. — Figure 439-1 Hypertensive intracerebral hemorrhage. Transaxial noncontrast computed tomography scan through the region of the basal ganglia reveals a hematoma involving the left putamen in a patient with rapidly progressive onset of right hemiparesis.