Intracranial Hemorrhage: Diagnosis and Management

William David Freeman, MD\textsuperscript{a,b,*}, Maria I. Aguilar, MD\textsuperscript{c}

Intracranial hemorrhage (ICH) is defined as bleeding within the intracranial vault. ICH subtypes are further defined by the anatomic site of the bleeding (Fig. 1). Intraparenchymal hemorrhage (IPH) is defined as bleeding within the brain parenchyma, which can be spontaneous or posttraumatic. Subarachnoid hemorrhage (SAH) signifies blood within the subarachnoid space and is commonly from a ruptured intracranial aneurysm (aneurysmal SAH) or trauma. Subdural hematoma (SDH) indicates bleeding underneath the dural membrane, whereas epidural hematoma (EDH) indicates bleeding exterior to the dura. Intraventricular hemorrhage (IVH) indicates blood within the ventricular system, which normally contains cerebrospinal fluid. This article reviews the approach to the diagnosis and general management of ICH, followed by a focused discussion of specialized ICH subtype management for IPH, SAH, SDH, EDH, and IVH.

DIAGNOSIS OF ICH

ICH is diagnosed through a combination of history, physical examination, and, most commonly, noncontrast CT examination of the brain\textsuperscript{1–3} which discloses the anatomic bleeding location. The approach to ICH diagnosis should begin with a detailed history.
if available. If the patient cannot provide the history because of unconsciousness or altered mental state, a witness or other historian should be interviewed. Important historical clues include time and activity of onset if sudden deficits appeared, or loss of consciousness, fall, or presence or absence of seizure at onset. If the patient was “found down,” and unresponsive by a witness, a description of the scene is often useful. Other historical information that should be collected includes medications, such as antithrombotic agents or anticoagulants; medical and surgical history; allergies; family history; and social history such as drug or alcohol use.

Laboratory values that should be checked in patients with ICH include a complete blood cell count, electrolytes, blood urea nitrogen, and creatinine (Box 1). Serum glucose is reasonable to screen for hypoglycemia. A 12-lead electrocardiogram is useful to screen for arrhythmias, heart block, or myocardial ischemic changes. Coagulation parameters, including prothrombin time, activated partial thromboplastin time, and international normalized ratio (INR) are particularly useful in patients taking warfarin or heparin anticoagulation. Patients suspected of having sepsis and disseminated intravascular coagulation may have abnormal coagulation function tests, thrombocytopenia, leukocytosis/leucopenia, and additional fibrinogen and fibrin split products, and D-dimer levels should be checked. A pregnancy test is reasonable to perform in women of childbearing age before radiographs or CT scans are considered. A drug screen may be useful in patients with hypertensive IPH from amphetamines or cocaine, or in those found unresponsive from barbiturate or opiate overdose with secondary traumatic ICH.

A stat noncontrast head CT can provide clues regarding the primary cause of ICH if the history is unclear. Table 1 provides differential diagnoses for patients with ICH based on the initial history and CT findings. Traumatic ICH may have a telltale or characteristic “coup–countercoup” (eg, left occipital head injury creates right frontal contusion) ICH pattern that is caused by acceleration-deceleration forces of the brain tissue.
against a hard skull interior or surface edges, such as the dura matter. In severe traumatic brain injury, diffuse hemorrhage from shearing of the brain across several bony intracranial landmarks, tearing of bridging veins, cortical hemorrhage or contusions, and possibly skull fractures may occur (Fig. 2A–F).

**Traumatic ICH**

Patients with significant head and neck trauma or who are suspected of having this trauma should have the cervical spine immobilized until cleared by a neurosurgeon. Patients with trauma or evidence of bruising around the eyes (“raccoon eyes”) should be examined carefully for a cerebrospinal fluid leak from the nose. Similarly, patients with bruising around the posterior ear or mastoid (“battle sign”) should have careful inspection for a cerebrospinal fluid leak around the external auditory canal. If the cranial CT bone windows show a skull fracture (eg, Fig. 2B) or base of skull fracture, consultation with a neurosurgeon or otolaryngologist may be necessary. Patients with unstable facial fractures or base of skull fractures should have caution applied with any instrumentation to the nose (eg, nasogastric tubes) unless approved or placed by a specialist. Patients with cervical spine trauma should have the neck immobilized until cleared by the neurosurgeon, and doll’s eyes (oculocephalic) responses deferred because of risk of cervical manipulation until then. If oculovestibular responses need to be tested in these patients, cold water calorics can be used instead. Patients with cervical spine trauma should still be tested within these limitations for spinal cord injury.

Neurosurgical consultation is advised when a mass effect, ongoing herniation, or obstructive hydrocephalus is present. Each ICH subtype is discussed further in the following sections. Patients with ICH are typically admitted to the intensive care unit (ICU) for frequent hemodynamic and neurologic monitoring.

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**Box 1**

**Recommended tests in patients with acute ICH**

<table>
<thead>
<tr>
<th>Radiology</th>
<th>Electrocardiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stat noncontrast head CT</td>
<td></td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td></td>
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</tbody>
</table>

**Laboratory**

- Complete blood cell count with platelet count
- Prothrombin time with INR
- Activated partial thromboplastin time
- Serum glucose
- Electrolytes
- Blood urea nitrogen and creatinine
- Pregnancy test in women of childbearing age
- Drugs of abuse screen (eg, opiates, barbiturates, benzodiazepines, cocaine, amphetamine)
- Troponin (or creatine kinase isoenzymes [CK-MB] if renal impairment)

*Data from Refs. 1–3*
<table>
<thead>
<tr>
<th>Cause</th>
<th>Clues to Diagnosis</th>
<th>Initial CT Findings</th>
<th>Additional/Useful Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive IPH</td>
<td>History of hypertension, cardiomegaly on electrocardiogram, left ventricular hypertrophy</td>
<td>Basal ganglia/deep IPH</td>
<td>MRI with gradient echo with deep hemosiderin changes</td>
</tr>
<tr>
<td>Traumatic ICH</td>
<td>Facial or other bodily trauma signs or history</td>
<td>Cortical, coup, or contrecoup pattern of ICH, traumatic SAH pattern</td>
<td>MRI showing diffuse gradient echo changes consistent with diffuse axonal injury, or diffusion tensor imaging</td>
</tr>
<tr>
<td>Cerebral amyloid angiopathy</td>
<td>History of cognitive decline or prior IPH</td>
<td>Lobar IPH/SAH, may occur with anticoagulation④</td>
<td>MRI with gradient echo changes in the cortical-subcortical locations Present in up to 15% of patients older than 70 years</td>
</tr>
<tr>
<td>AVM</td>
<td>Headache, seizure, focal deficit</td>
<td>IPH ± IVH, or SAH, calcification on CT</td>
<td>CT angiogram or DSA</td>
</tr>
<tr>
<td>Cavernous angioma</td>
<td>Headache, seizure, focal deficit</td>
<td>IPH ± IVH, or SAH, calcification on CT if chronic</td>
<td>MRI with “bloom artifact” on gradient echo consistent with areas of older microhemorrhage (hemosiderin)</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>Thunderclap headache, stupor/coma, meningismus, focal deficit</td>
<td>Characteristic SAH pattern</td>
<td>CTA and/or DSA showing intracranial aneurysm</td>
</tr>
<tr>
<td>CVT/SST</td>
<td>Thrombotic history</td>
<td>Cortical infarct or hemorrhage, sometimes bilateral; delta sign or cord sign</td>
<td>CTV, MRV, or DSA showing cortical vein thrombus, sagittal sinus thrombosis, other dural sinus thrombosis</td>
</tr>
<tr>
<td>Condition</td>
<td>Symptoms</td>
<td>Imaging Features</td>
<td>Additional Information</td>
</tr>
<tr>
<td>---------------------------------</td>
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<tr>
<td>Hemorrhagic tumor</td>
<td>Metastatic tumor history or newly diagnosed; weight loss</td>
<td>Vasogenic edema surrounding hemorrhage seen on CT</td>
<td>MRI with contrast shows ring-enhancing tumor and hemorrhage; body imaging may reveal other metastatic lesions</td>
</tr>
<tr>
<td>SDH</td>
<td>Fall or trauma typical, or minor trauma in the setting of anticoagulation</td>
<td>CT shows convexity hematoma, beyond suture lines</td>
<td>MRI may reveal chronic subdural hematomas or hygromas that are small or contralateral</td>
</tr>
<tr>
<td>EDH</td>
<td>Trauma to the temporal head region</td>
<td>Lens-shaped hematoma respecting suture lines</td>
<td>Repeat CT may be useful if abrupt neurologic deterioration occurs for surgery</td>
</tr>
<tr>
<td>Pituitary (hemorrhagic) apoplexy</td>
<td>Headache, obtundation, cranial nerve (III, IV, VI), shock</td>
<td>Initial CT may appear negative unless attention paid to sella, sometimes faint SAH around the sella</td>
<td>MRI with contrast, with emphasis on sella turcica/pituitary gland Pituitary apoplexy can also be infarction, which can later hemorrhage</td>
</tr>
<tr>
<td>Hemorrhagic Infarct</td>
<td>Clinical history of sudden stroke deficit, sometimes with major improvement; seizure from recanalization of occluded vessel</td>
<td>Cortical arterial territory with hemorrhagic infarct pattern (hemorrhage is around rim of vascular margins or gyri and sulci)</td>
<td>MRI with gradient echo showing hemosiderin around cortical infarct margins, MRA sometimes shows recanalized arterial segment (hemorrhage is from reperfusion injury)</td>
</tr>
</tbody>
</table>

**Abbreviations:** AVM, arteriovenous malformation; BPH, epidural hematoma; CAA, cerebral amyloid angiopathy; CTA, CT angiogram; CTV, CT venogram; CVT, cerebral vein thrombosis; DSA, digital subtraction angiogram; MRA, magnetic resonance angiogram; MRV, magnetic resonance venogram; SST, sagittal sinus thrombosis.
GENERAL MANAGEMENT OF ICH

After ICH is diagnosed, patients should be triaged according to level of consciousness, using tools such as the Glasgow Coma Scale (GCS) or other similar scale, and screened for airway protection and impending respiratory failure (Table 2). Patients with ICH in a coma (GCS <8) are at risk for aspirating upper-airway or gastrointestinal contents into the lungs, leading to aspiration pneumonia or acute respiratory distress syndrome. If a patient with ICH is not protecting their airway (eg, GCS <8, no gag response, or in respiratory failure from another cause, such as pulmonary contusion or chronic obstructive pulmonary disease), rapid sequence intubation (RSI) protocol is suggested. RSI protocol is essentially preoxygenation, Sellick maneuver

Fig. 2. Traumatic ICH in an 80-year-old woman with a witnessed fall at home. The family member stated that she fell straight backward and head hit her head on the floor, which made a sound like “a watermelon hit the ground.” The patient arrived in the emergency department with a GCS of E1M2V1 (intubated) with intact pupillary, corneal, and cough brainstem reflexes. (A) Bitemporal hemorrhagic parenchymal contusions with SAH, right occipital cephalohematoma, with underlying right occipital lobe hypodense cerebral edema, left temporal lobe convexity SDH, and left tentorial SDH (upper left). (B) Nondisplaced right occipital bone fracture relative to Fig. 1A (upper middle). (C) Bifrontal (medial frontal, olfactory region) hemorrhagic parenchymal contusions with subarachnoid blood, right middle cerebral artery region SAH, which is small in comparison to most true aneurysmal SAH and in fact traumatic in origin (upper right). Left greater than right tentorial subdural hemorrhage is seen, consistent with acceleration-deceleration injury to the right occipital head region, and left convexity subdural hemorrhage. (D) Bifrontal hemorrhagic contusions (cortical parenchymal) and SAH (right sylvian fissure), and subdural hemorrhage (bihemispheric convexities and bifalcine) (bottom left). (E) Bifrontal hemorrhagic contusions, right greater than left, subdural hemorrhage left hemispheric convexity, and posterior falx cerebri (bottom middle). (F) CT scan 6 hours after images shown in Fig. 1A–D (bottom right), status postplacement of right external ventricular drain with IVH and enlarging left hemispheric convexity-acute SDH.
(pressure applied to the larynx to compress the esophagus to prevent reflux of gastrointestinal contents into the lungs during intubation), and premedication with drugs that blunt the sympathetic response to laryngoscopy and intubation that could cause an unsafe rise in intracranial pressure.6 These RSI drugs include intravenous lidocaine and muscle relaxants. If cervical trauma is known or suspected, these patients may need fiberoptic intubation because of immobilization of the cervical spine in a cervical collar by a skilled airway provider. Patients who are alert or drowsy (eg, GCS 12–14) but have intact airway protective reflexes (gag, cough) with no signs of impending respiratory failure should be monitored for neurologic deterioration and subsequent airway compromise and admitted to an ICU. If a patient with ICH deteriorates to a comatose state (GCS ≤8), similar airway management should be implemented. Stuporous (eg, GCS 9–11) patients with ICH should be monitored closely for airway and respiratory compromise, and discretion used regarding intubation depending on the complete clinical scenario.

Blood pressure assessment and management should occur during the initial evaluation of patients with ICH (see Table 2), and whether the patient has raised intracranial pressure and will need neurosurgical intervention such as placement of an intracranial pressure monitor should be determined. Raising the patient’s head of bed to 30° to 45° and ensuring the patient’s neck is straight in midline and without constricting tape around the neck if intubated can help optimize intracranial pressure through optimizing jugular venous outflow. Elevating the head of bed also reduces the risk of aspiration pneumonia.

The initial approach to acute blood pressure management is shown in Table 3. Blood pressure should be tailored to each patient’s blood pressure history and their particular ICH subtype (see Table 3). For most patients with ICH without intracranial pressure concerns, maintaining a mean arterial pressure of 60 to 65 mm Hg is the minimum.2,3,5 If an intracranial pressure monitor is placed for raised intracranial pressure, then cerebral perfusion pressure should be maintained around a minimum of approximately 65 mm Hg.2,3,5 Patients with chronic hypertension have rightward shifted cerebral autoregulation and may be accustomed to a higher baseline mean arterial pressure than normotensive patients. Oral antihypertensive medications are

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**Table 2**

<table>
<thead>
<tr>
<th>Letter</th>
<th>Management</th>
<th>Level of Evidence (AHA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Airway: GCS &lt;8: consider intubation with RSI protocol</td>
<td>Class I</td>
</tr>
<tr>
<td>B</td>
<td>Blood pressure control (see Box 2)</td>
<td>Class II</td>
</tr>
<tr>
<td>C</td>
<td>CPP (control ICP if elevated): HOB elevation 30°–45°</td>
<td>Class II</td>
</tr>
<tr>
<td>D</td>
<td>DVT prevention with pneumatic compression devices until bleeding stops, then consider subcutaneous UFH or LMWH</td>
<td>Class II</td>
</tr>
<tr>
<td>E</td>
<td>Early mobilization</td>
<td>Class I</td>
</tr>
<tr>
<td>F</td>
<td>Fever (core temperature &gt;38.0°C–38.3°C)</td>
<td>Class I</td>
</tr>
<tr>
<td>G</td>
<td>Glucose target &gt;140–185 mg/dL, use insulin, Avoid hypoglycemia</td>
<td>Class I</td>
</tr>
</tbody>
</table>

Abbreviations: AHA, American Heart Association; CPP, cerebral perfusion pressure; DVT, deep vein thrombosis; GCS, Glasgow Coma Scale; HOB, head of bed; ICP, intracranial pressure; LMWH, low-molecular-weight heparin; RSI, rapid sequence intubation; UFH, unfractionated heparin.

Data from Refs.1–3,5,6
typically held during the first 24 hours, and short-acting agents such as labetolol, hydralazine, enalprilat, nicardipine, or esmolol drips are used as needed to control mean arterial pressure/cerebral perfusion pressure within specified targets (see Table 3). However, caution is advised regarding holding β-blockers and clonidine in patients with known coronary disease, because of the risk for β-blocker withdrawal and rebound hypertension, respectively. In these patients, sometimes holding or halving the dose with ICU-level blood pressure monitoring is required for making informed decision about these medications. IPH and SAH blood pressures are discussed later.

Other management issues for patients with ICH include central nervous system (CNS) complications and non-CNS organ complications (Boxes 2 and 3). ICH growth is a significant concern and present in up to one-third of patients with IPH within 24 hours, and is associated with neurologic deterioration. Patients with traumatic ICH may also have hemorrhagic expansion because of ongoing bleeding sources, such as torn bridging veins in SDH or cortical contusions (see Fig. 2F). EDH and aneurysmal SAH are particularly concerning because they represent arterial bleeding sources at a higher pressure than venous bleeding sources and can have rapid and dramatic deterioration. Patients with ICH on anticoagulants such as warfarin or antiplatelet

### Table 3

<table>
<thead>
<tr>
<th>ICH</th>
<th>Initial Blood Pressure Management</th>
<th>Additional Notes</th>
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</thead>
<tbody>
<tr>
<td>IPH</td>
<td>Reduce SBP if &gt;180 mm Hg or MAP &gt;130 mm Hg using short-acting agents</td>
<td>Correct any underlying coagulopathy stat If IVH (especially high-grade) present, increased odds of hydrocephalus and possible need of ventriculostomy, ICP monitoring</td>
</tr>
<tr>
<td></td>
<td>If raised ICP suspected, ask for neurosurgical placement of ICP monitor or EVD, maintain CPP &gt;60 mm Hg</td>
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<tr>
<td></td>
<td>Monitor neurologic examination q15 min until stable and gradually de-escalate monitoring per local ICU protocol</td>
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<tr>
<td>aSAH</td>
<td>Reduce SBP if &gt;160 mm Hg or MAP &gt;130 mm Hg using short-acting agents</td>
<td>Secure aneurysm to prevent rebleeding if possible</td>
</tr>
<tr>
<td></td>
<td>If raised ICP suspected, ask for neurosurgical placement of ICP monitor or EVD, maintain CPP &gt;60 mm Hg</td>
<td>Monitor for vasospasm and allow permissive hypertension (eg, up to 160 mm Hg SBP) if safe (aneurysm secure), especially during vasospasm peak window</td>
</tr>
<tr>
<td></td>
<td>Monitor neurologic examination q15 min until stable and gradually de-escalate monitoring per local ICU protocol</td>
<td>Maintain normal volume status (euvolemia) until vasospasm occurs then initiate HHH for secured aSAH</td>
</tr>
<tr>
<td>t-ICH</td>
<td>If raised ICP suspected, ask for neurosurgical placement of ICP monitor or EVD, maintain MAP/CPP &gt;60–65 mm Hg</td>
<td>Neurosurgical evaluation if surgical operable lesion or condition is identified</td>
</tr>
<tr>
<td></td>
<td>Monitor neurologic examination q15 min until stable and gradually de-escalate monitoring per local ICU protocol</td>
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</table>

**Abbreviations:** aSAH, aneurysmal SAH; CPP, cerebral perfusion pressure (CPP = MAP - ICP); EVD, external ventricular drain; HHH, hypervolemic, hypertensive, hemodilution; ICP, intracranial pressure; MAP, mean arterial pressure; SBP, systolic blood pressure; t-ICH, traumatic ICH (eg, traumatic SAH, SDH, or EDH).

Data from Refs.1–3,5,6
agents such as aspirin or clopidogrel are also at risk for significant ICH expansion, especially if the hemostatic deficit is not reversed. Reversal of anticoagulants in the setting of ICH is recommended. Patients with mechanical heart valves and those at high risk for embolism pose a short-term embolic risk, which must be weighed against the risk of ICH expansion, herniation, and death. Restarting anticoagulants

<table>
<thead>
<tr>
<th>Box 2</th>
<th>CNS and non-CNS organ complications of ICH</th>
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</thead>
<tbody>
<tr>
<td><strong>CNS complications</strong></td>
<td></td>
</tr>
<tr>
<td>• ICH growth and herniation</td>
<td></td>
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<tr>
<td>• IVH extension and hydrocephalus</td>
<td></td>
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<tr>
<td>• Raised intracranial pressure</td>
<td></td>
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<tr>
<td>• Cerebral edema</td>
<td></td>
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<tr>
<td>• Autonomic dysfunction: Cushing reflex from raised intracranial pressure, paroxysmal autonomic instability activity (with or without dystonia)</td>
<td></td>
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<tr>
<td>• Seizures: convulsive or nonconvulsive seizures or status epilepticus</td>
<td></td>
</tr>
<tr>
<td>• Neurologic deficits: hemiparesis, ataxia, coma, sensory loss, cognitive deficits, brainstem deficits</td>
<td></td>
</tr>
<tr>
<td><strong>Non-CNS organ complications of ICH</strong></td>
<td></td>
</tr>
<tr>
<td>• Cardiac: troponin leak, acute myocardial infarction from underlying coronary disease, electrocardiogram changes (QTc prolongation, ST- or T-wave changes, U waves, arrhythmias)</td>
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</tr>
<tr>
<td>• Pulmonary: aspiration pneumonia, CNS breathing patterns (eg, ataxic [Biot], cluster, Cheyne-Stokes, hyperventilation, pneumotaxic), respiratory failure, acute respiratory distress syndrome, neurogenic pulmonary edema</td>
<td></td>
</tr>
<tr>
<td>• Gastrointestinal: Cushing ulcer and gastrointestinal hemorrhage, ileus, gastroparesis</td>
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<tr>
<td>• Neuroendocrine: hyponatremia, syndrome of inappropriate antidiuretic hormone release, cerebral salt wasting, relative adrenal insufficiency from central hypothalamic dysautoregulation</td>
<td></td>
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<tr>
<td>• Hematologic: deep vein thrombosis and pulmonary embolism</td>
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<tr>
<td>• Skin: decubitus</td>
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</table>


<table>
<thead>
<tr>
<th>Box 3</th>
<th>Antiepileptic drug prophylaxis for patients with ICH</th>
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<tr>
<td>• Patients with severe traumatic brain injury (GCS ≤8): 7 days (not after unless seizure occurs)</td>
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<tr>
<td>• Witnessed seizure or status epilepticus during hospitalization (or nonconvulsive seizure on electroencephalogram): duration varies according to clinical situation</td>
<td></td>
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<tr>
<td>• Lobar IPH: optional</td>
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</table>

*Data from* Refs. 1–3, 5
after the acute phase of ICH is outside the scope of this article. Antithrombotic reversal, however, is discussed later.

Treatment of Raised Intracranial Pressure (Intracranial Hypertension)

Methods to control raised intracranial pressure include head of bed elevation (30°–45°), mannitol (0.25–1 g/kg intravenously as needed), intravenous furosemide, transient hyperventilation, and sedation and paralysis. Ventriculostomy placement is suggested to drain cerebrospinal fluid from symptomatic obstructive hydrocephalus in patients with IPH with IVH extension, or patients with hydrocephalus from aneurysmal SAH. Use of hypertonic saline (HTS) either as a 3% or 23.4% infusion in 15- to 30-mL boluses is increasing as a treatment option for reducing intracranial pressure. Recent studies show HTS may be as effective as mannitol for reducing intracranial pressure and with similar safety in brain-injured patients. Hypertonic (3%) saline/acetate was studied in 27 patients with cerebral edema and raised intracranial pressure, 8 of whom had spontaneous IPH. HTS infusion raised serum sodium concentrations to 145 to 155 mmol/L and reduced intracranial pressure in patients with traumatic brain injury and postoperative brain edema but not in patients with IPH or cerebral infarction. Suarez and colleagues also retrospectively studied 20 patients (1 with basal ganglia IPH) with intracranial hypertension refractory to standard intracranial pressure management, including mannitol (1 g/kg), who were treated with 30 mL intravenous boluses of 23.4% saline (8008 mOsm/L). Approximately 80% of these patients experienced a decrease in intracranial pressure by at least 50% of the pretreatment value in 20 to 30 minutes. In a dog model of IPH, HTS (3% and 23.4%) was equally as effective as 1 g/kg of mannitol in reducing intracranial pressure. A longer duration of effect was also noted with HTS compared with mannitol.

Overall, considerable debate remains regarding whether one agent (HTS or mannitol) is superior to the other. Theoretical considerations exist about mannitol extravasating across a leaky blood-brain barrier and worsening brain edema and intracranial pressure because mannitol’s reflection coefficient (ie, ability to dissolve into injured brain tissue and back) is 0.9 compared with 1.0 for HTS. These theoretical considerations have not been seen in clinical practice per se, although mannitol should be used with caution in patients with end-stage renal disease who are dialysis-dependent, unless dialysis is planned after treatment, because it is renally excreted and works via an osmotic diuretic mechanism. Another important consideration is the ability to give mannitol via a peripheral intravenous line rather than as a 3% or 23.4% infusion, which should be given via a central venous catheter or equivalent given the high tonicity and risk of peripheral venous thrombophlebitis. Mannitol also may crystallize in the bag, which can be offset by the use of a crystalline filter on the intravenous tubing system.

If hypertonic/hyperosmolar agents such as mannitol or HTS are used to control intracranial pressure, frequent measurement of plasma osmolality and/or serum sodium is suggested (eg, serum sodium every 4–6 hours). If sodium exceeds 150 to 155 mmol/L, holding these agents is advised until these values trend back toward a more normal range (eg, 145 mmol/L). Management of fluid balance and type of total fluids in these patients is extremely important. Avoidance of intravenous free water (D5W) or hypotonic fluids (eg, 1/2 normal saline) is advised because a leaky blood-brain barrier typically exists in some form in patients with ICH, and can pass into injured brain and worsen cerebral edema and intracranial pressure. If patients become severely hypernatremic (eg, serum sodium>160 mmol/L), careful and slow correction is advised to avoid rebound intracranial hypertension and cerebral edema. Enteral free
water is absorbed more slowly and can be administered via a nasogastric tube while monitoring serum sodium.

If intracranial pressure remains refractory to hyperosmolar/hypertonic agents (osmotherapy), other options include sedation, neuromuscular blockade, barbiturate-induced coma, and transient hyperventilation (partial pressure of carbon dioxide, 30–35 mm Hg) until discussion with the neurosurgeon regarding whether a role exists for structural management, such as craniotomy or decompressive craniectomy. Hypothermia is also effective for cerebral edema irrespective of cause when used in a mild to moderate range (i.e., 32°C–24°C). However, questions data regarding outcomes and safety remain.

**Treatment of Seizures**

For patients with severe traumatic brain injury with ICH with a GCS score of 8 or less, the Brain Trauma Organization recommends antiepileptic drug (AED) prophylaxis against seizures for 7 days, such as with phenytoin. This recommendation is because these patients have a higher incidence of seizures in the first week, but therapy beyond 7 days has not been proven to be efficacious. AEDs should be given in patients who have experienced a witnessed seizure for a duration, as deemed appropriate by the treating physician. Otherwise, AED prophylaxis is not routinely advised unless a seizure occurs. If a seizure occurs, most physicians treat patients acutely with intravenous lorazepam and follow with a loading dose infusion of fos-phenytoin or phenytoin (15–20 mg/kg) along with daily maintenance dosing to prevent seizure recurrence. If no further seizures occur after 1 month, AED therapy can be discontinued. Prolonged AED therapy is considered on a case-by-case basis. Nonconvulsive seizure and nonconvulsive status epilepticus occur in 10% to 20% of patients with ICH in the neurological ICU, and are difficult to detect clinically unless motor manifestations are seen. Some neurological ICUs use continuous electroencephalography monitoring to improve detection of nonconvulsive seizure and nonconvulsive status epilepticus.

**Gastrointestinal Stress Ulcer Prophylaxis and Nutrition**

Patients with ICH are at risk for Cushing (stress) ulcers and gastrointestinal hemorrhage. Stress ulcer prophylaxis is recommended with either enteral or intravenous H₂-block ing agents, such as famotidine or ranitidine. Proton pump inhibitors such as omeprazole may be used if H₂-blocking agents are not available during hospitalization. Nutrition should be started if the patient is cleared from an aspiration risk standpoint. However, if the patient is unable to take in food by mouth safely and is at risk for aspiration, nutrition is typically started within the first week of hospitalization via an enteral feeding tube, unless a contraindication exists, such as bowel obstruction or perforated viscus, with intravenous fluid support provided temporarily. Enteral feeding is preferable over intravenous total parenteral nutrition.

**Temperature, Fever, and Shivering**

Normothermia is defined as 98.6°F (37°C). Fever (temperature, ≥38°C) in brain-injured patients worsens clinical outcomes compared with those without fever. Fever increases the body’s basal metabolic rate and raises the cerebral metabolic rate of oxygen (CMRO₂), which creates a relative catabolic state. A febrile (temperature, ≥38°C –38.3°C) patient with ICH should be examined for a source of infection and, when clinically appropriate, undergo laboratory and microbiological testing of invasive lines, central lines, and urinary Foley tubes. If an external ventricular drain (EVD) is present, cerebrospinal fluid analysis and culture should be considered. A chest
radiograph may be helpful to confirm pulmonary infection, especially in patients on mechanical ventilation. Other occult sources of infection include sinusitis, acalculous cholecystitis, and some medications. Fever of neurologic origin is considered a diagnosis of exclusion but is common after stroke, especially hemorrhagic stroke (eg, subarachnoid or intraventricular blood). Fever may also be from the systemic inflammatory response syndrome associated with critical illness.

Febrile patients with ICH should receive acetaminophen assuming no contraindication is present, such as hepatic impairment. For patients with ICH and fever that is refractory to acetaminophen and has no infectious cause, thermoregulatory interventions may be necessary, such as use of a cooling blanket or cooling devices to obtain normothermia (ie, 37°C). In one study, patients treated with a cooling pad device had a 75% reduction in fever and more time normothermic compared with those treated with a conventional cooling blanket, but the pad caused more shivering than the blanket. Other interventions include infusion of cool fluids or, in mechanically ventilated patients, increasing sedative-analgesic medication (eg, propofol, fentanyl). Reported side effects from cooling include vasoconstriction (particularly extremities), adrenergic hyperactivation, and postoperative myocardial events.

Shivering is an autonomic reflex response to cooling to cause thermogenesis and raise body temperature, which also raises the basal metabolic rate and CMRO₂ similar to fever. Shivering can be difficult to control in patients not under general anesthesia, and may require multimodal treatment. Drugs such as thiopental and fentanyl reduce CMRO₂ and may also reduce shivering. Meperidine is a good antishiver medication, and can be combined with a dexmedetomidine infusion or buspirone enterally for additive or synergistic effects in lowering the shiver threshold. Meperidine, however, can cause sedation and CNS toxicity (eg, seizures) and should be used with caution. In intubated, mechanically ventilated patients with ICH, refractory fever, shiver, and raised intracranial pressure, treatment may require a combination of acetaminophen, a cooling device, adequate sedation, and neuromuscular blocking agents as a last resort.

**Management of ICH on Antithrombotics**

The most common coagulopathic ICH encountered is associated with warfarin or coumarins, given their widespread use. Warfarin-related spontaneous ICH (WICH) occurs in only 7 to 10,000 patients annually or approximately every one in five cases of spontaneous ICH. WICH are thought to be larger and continue to grow after 24 hours compared with spontaneous ICH in patients not taking anticoagulants. One-month mortality is approximately 50% in patients with WICH compared with approximately 40% in patients not undergoing anticoagulation therapy. The intensity of anticoagulation (eg, INR) also contributes to hematoma expansion and worse outcomes. Therefore patients with symptomatic WICH with an INR greater than 1.3 should undergo emergent anticoagulation reversal, which was reviewed in recent guidelines and summarized in Table 4. Other antithrombotic agents may be associated with ICH, and reversal of these agents is also addressed in Table 4. A more detailed discussion on management of coagulopathic ICH is outside the scope of this article, but has been provided elsewhere.

**IPH**

Spontaneous IPH is twice as common as SAH but is equally as deadly, with a 1-month mortality of 40%. The incidence of spontaneous IPH is between 37,000 and 50,000 patients per year in the United States. IPH is a medical emergency
that requires emergent evaluation and management for optimal patient survival. Risk factors for IPH include increasing age, especially older than 85 years; hypertension; INR intensity greater than 3.5; cerebral amyloid angiopathy; renal failure; and prior stroke (hemorrhagic or ischemic). Neuroimaging factors predictive of IPH include leukoaraiosis, evidence of recent or prior stroke (ischemic or hemorrhagic), and the presence of cerebral microbleeds.40–43

IPH location and pattern of bleeding are important clues to the underlying disease (see Table 1). Anatomically speaking, IPH generally occurs in either a deep or a lobar location. Deep IPH (Fig. 3) include the caudate, thalamus, putamen, globus pallidus (basal ganglia or ganglionic ICH), internal capsule, and other deep white matter loci. In contrast, lobar IPH (Fig. 4) is defined as bleeding within the cortical-subcortical cerebral hemisphere. Lobar IPH is attributed to cerebral amyloid angiopathy in approximately one-third of patients.44 Advancing age is an important risk factor for IPH occurring at all locations. Other causes of nontraumatic IPH include bleeding from arteriovenous malformations, aneurysms, cavernous angiomas, moyamoya disease, venous sinus thrombosis, venous angiomas, neoplasm, abscess, drug use (eg, cocaine), and, rarely, vasculitis (see Table 1).18

Chronic hypertension causes pathologic changes within cerebral blood vessels called lipohyalinosis, a process affecting small penetrating arteries or arterioles 50 to 200 μm in diameter, especially at branch points, and contributing to the formation of microaneurysms that can hemorrhage, as originally described by Charcot and Bouchard and subsequent investigators.45–47 Hypertension has a 0.5 attributable risk for

<table>
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<th>Table 4</th>
<th>Treatment for antithrombotic-associated intracranial bleeding</th>
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<td>Antithrombotic Agent</td>
<td>Treatment</td>
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| Warfarin | Discontinue warfarin  
Give 10 mg of intravenous vitamin K\(^a\) slowly over 30 minutes\(^{29–32}\)  
Give PCC or rFVIIa over FFP if available\(^2\)  
If PCC and rFVIIa are unavailable, give approximately 15 mL/kg of FFP\(^{2,33–35}\)  
Check coagulation parameters frequently after treatment (eg, PT/PTT Q6 h × 24 h) then daily until anticoagulation is reversed |
| Tissue plasminogen activator (t-PA) | Intravenous platelet transfusion (“sixpack,” or one single-donor unit)  
Cryoprecipitate that contains factor VIII to rapidly correct the systemic fibrinolytic state created by t-PA |
| Antiplatelet (aspirin, clopidogrel) | Unknown  
DDAVP or platelet transfusion |
| Dabigatran | Unknown antidote\(^{36–39}\)  
Discontinue dabigatran  
Hydrate (renally excreted) |
| Heparin | Protamine, 1 mg per 100 U heparin\(^{1,2}\) |

Abbreviations: DDAVP, 1-deamino-8-D-arginine vasopressin; FFP, fresh frozen plasma; PCC, prothrombin complex concentrate; rFVIIa, recombinant factor VIIa.

\(^a\) Intravenous vitamin K carries an approximate 3/10,000 risk of anaphylaxis and uncertain risk (possibly rare) of anaphylactoid reaction.\(^{30,31}\)

Data from Refs.\(^1,2,29–35\)
deep IPH, suggesting that hypertension causes approximately half of the cases of deep (nonlobar) IPHs, which means the other half are from other causes. Recent MRI with gradient echo sequencing has shown microhemorrhages (Fig. 5) in similar locations to these vessels.

Fig. 3. Deep IPH (deep or ganglionic IPH) within the right basal ganglia below the right caudate nucleus from a ruptured penetrating blood vessel caused by chronic uncontrolled hypertension (eg, Charcot-Bouchard microaneurysm).

Fig. 4. Lobar IPH. Noncontrast cranial CT scan showing a right cortical-subcortical (lobar) hematoma and orientation in sagittal plane (upper left).
Cerebral amyloid angiopathy (CAA) is increasingly recognized as a disorder leading to spontaneous IPH. CAA is caused by amyloid protein deposition within the walls of blood vessels in cortical-subcortical locations. Amyloid-laden blood vessels are fragile and prone to bleed. CAA affects leptomeningeal blood vessels covering the surface of the brain (ie, pial blood vessels), which can cause spontaneous cortical SAH and superficial siderosis. Patients with CAA may also experience recurrent transient ischemic attack (TIA)–like spells from microhemorrhage deposits or superficial siderosis. These microhemorrhages are seen on MRI with gradient echo in up to 15% of patients older than 70 years. These asymptomatic microhemorrhages also may predict future larger IPH (macrohemorrhage) events.

Clinical Presentation and Medical Management of Patients with IPH

Patients with IPH present with sudden onset of alteration of consciousness, vomiting, headache, or focal neurologic deficits. The extent of neurologic deficits depends on the area of brain or brainstem affected. A patient may become unconsciousness or rapidly comatose because of massive IPH, elevated intracranial pressure, hydrocephalus, brainstem compression, nonconvulsive seizure, or postictal state. Because of the acuity and severity of presentation, most patients with IPH are brought to the emergency department for evaluation.

IPH is diagnosed using the same approach as described earlier for patients with ICH. Some centers use the National Institutes of Health (NIH) stroke scale in their initial, rapid neurologic examination, whereas others obtain a GCS score to gauge level of responsiveness and to measure possible neurologic deterioration. MRI has at least similar sensitivity for detecting ICH as CT. However, CT remains the preferred diagnostic test for detecting ICH and IPH at most hospitals because of its rapid acquisition time, widespread availability, and high sensitivity. Standard laboratory tests in the acute setting for patients with IPH are shown in Box 1. Cranial CT imaging in acute IPH typically shows a spherical or ellipsoid hyperdense (ie, bright or white)
accumulation of intraparenchymal blood (Fig. 6A). Extension of the hematoma into the ventricles is common (see Fig. 6B, C) and can cause dilated ventricles (hydrocephalus).

Patients with IPH should be admitted to an ICU for monitoring and management of airway, respiratory function, and blood pressure; avoidance of fever; and careful glucose and electrolyte regulation. Preventing certain medical complications during hospitalization is also crucial, including pneumonia, deep venous thrombosis, pulmonary embolism, and sacral and pressure ulcers (ie, decubitus). Specific management issues are subsequently discussed.

**Treatment of hypertension in IPH**

Current guidelines for acute IPH target an arterial systolic blood pressure (SBP) of greater than 180 mm Hg or mean arterial pressure greater than 130 to 150 mm Hg (see Table 3).\(^1,^2\) When raised intracranial pressure is suspected, placement of an intracranial pressure monitor is suggested and an SBP greater than 180 should be treated with either intermittent or continuous antihypertensive medications, while maintaining a cerebral perfusion pressure of at least 60 mm Hg. For patients without raised intracranial pressure, SBP greater than 180 mm Hg should be treated to lower it to approximately 160 mm Hg, or to a mean arterial pressure of approximately 110 mm Hg. Considerable debate remains whether high or low arterial blood pressures contribute to intracerebral bleeding and hematoma expansion, and whether lower

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**Fig. 6.** Hypertensive deep IPH with IVH extension and contrast extravasation. (A) Left basal ganglia IPH with mass effect and midline shift from left to right, and IVH with the left frontal horn and third ventricle. (B) Higher slice cut with IPH, third-ventricle IVH, and left lateral ventricular IVH. (C) “Casted” left lateral ventricle from IPH extending into the ipsilateral ventricle. (D–F) The ‘spot sign’ (red arrows) described with contrast extravasation within the IPH. Whether this site of contrast leak represents the original arteriolar vessel bleeding source of the IPH, damaged blood-brain barrier with contrast leak, or secondary torn vessels injured during an expanding IPH remains unknown.
blood pressure may cause perihematomal ischemia. This controversy has led to a “chicken or the egg” analogy about whether the ICH is the cause of the acute hypertension response or is the effect as a physiologic response similar to Cushing reflex to maintain brain perfusion.

Recent data suggest the acute hypertensive response in patients with IPH typically declines approximately 2 mm Hg of mean arterial pressure per hour within 6 hours of acute IPH before reaching a plateau by 24 hours.\(^{50,51}\) Because blood pressure declines naturally after acute IPH, overaggressive treatment may be unwise, and short-acting intravenous medications such as labetalol, esmolol, and enalaprilat are typically administered.\(^1,2\) The particular antihypertensive agent chosen should be individualized based on hemodynamic parameters of the patient and other comorbidities (eg, tachycardia and hypertension may be treated with labetalol or esmolol, whereas isolated severe hypertension should be treated with hydralazine or nicardipine). Debate remains regarding whether rapid reduction in blood pressure after IPH would be injurious to perihematomal brain similar to large-vessel ischemic stroke models.

The completed phase II multicenter trials, Antihypertensive Treatment in Acute Cerebral Hemorrhage (ATACH) and the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT)\(^{51,52}\) suggest there may be a lower blood pressure threshold (eg, 140 mm Hg systolic) for antihypertensive treatment than current guidelines recommend. Currently, two large phase III trials are underway, ATACH II and INTERACT II, targeting lower systolic ranges of 120 to 140 mm Hg or less for SBP in IPH based on these trials’ previous data showing preliminary safety.

**Hematoma volume and growth**

IPH volume (cm\(^3\)) is a powerful predictor of 30-day mortality\(^{27}\) and can be easily calculated using the formula \(ABC/2\),\(^{53}\) where A and B are the largest perpendicular diameters of the hematoma in centimeters (cm), and C is the number of vertical CT slices multiplied by the slice thickness (cm) (Fig. 7). IPH growth (volume increase of at least

![Fig. 7. ABC/2 IPH hematoma calculation of hematoma volume. The visually largest CT slice with IPH hematoma is identified, then A and B are diameters of the IPH measured in centimeters. The number of vertical slices of IPH seen is defined as C. C is multiplied by slice thickness. For example, if A and B are both 3 cm, and C is three slices vertically with 5 mm per CT slice cut, then ABC/2 = (3 cm × 3 cm × (3 slices × 0.5 cm))/2 = 13.5/2 = 6.75 cm\(^3\)](image)
33%) occurs in approximately 38% of patients, with 26% of hematoma growth occurring between the baseline and 1-hour CT scan, and the remaining 12% of patients with IPH growth between the 1- and 20-hour CT scans.\textsuperscript{7} IPH growth is associated with clinical neurologic deterioration.\textsuperscript{7} Factors associated with hematoma growth include presentation within 6 hours of ictus, contrast extravasation (see Fig. 6D, E), antiplatelet or anticoagulant therapy, platelet count less than 100,000/\(\mu\)L, and liver disease.\textsuperscript{54–56} Patients taking antiplatelet agents (eg, aspirin, clopidogrel, ticlopidine) or warfarin must stop the medication. If the platelet count is less than 50,000/\(\mu\)L in the setting of acute IPH, platelet transfusion may be considered, although evidence-based data supporting this are lacking. Recent data by Naidech and colleagues\textsuperscript{57} show that patients with IPH who have impaired platelet function have a higher rate of subsequent IPH growth. This finding raises the question whether 1-deamino-8-D-arginine vasopressin (DDAVP) or platelet transfusion would help reduce IPH hematoma growth.

**Treatment to reduce IPH growth: blood pressure control and recombinant factor VIIa**

Because IPH volume correlates strongly with mortality, reducing hematoma growth and volume are logical targets for therapeutic intervention. It seems intuitive that hypertension could contribute to IPH growth, but limited data support a cause-and-effect relationship. Kazui and colleagues\textsuperscript{55} found that SBP greater than 200 mm Hg at admission correlated with hematoma expansion, but this relationship was not observed in two other studies.\textsuperscript{7,54} Additional studies have shown reduced hematoma enlargement in acute IPH when SBP was treated to 150 mm Hg or less.\textsuperscript{51,52,56} Two of these trials, ATACH\textsuperscript{51} and INTERACT,\textsuperscript{52} focused on safety and CT evidence of hematoma growth. The hope is that these phase III trials will answer specifically whether aggressive blood pressure control (eg, SBP between 120 and 140 mm Hg) reduces hematoma growth and improves clinical outcomes. Based on these ongoing trials, current guidelines (eg, from the American Heart Association [AHA])\textsuperscript{9} suggest treatment only if SBP is greater than 180 mm Hg, and assuming no increased intracranial pressure is suspected.

Mayer and colleagues\textsuperscript{58} studied the effect of hemostatic drug recombinant factor VIIa on slowing early hematoma growth. Recombinant factor VIIa (rFVIIa or Novoseven) is a cloned product of endogenous activated coagulation factor VII and only has a U.S. Food and Drug Administration (FDA) label indication for bleeding episodes in hemophiliac patients associated with factor inhibitors.\textsuperscript{59} In the phase II multicenter study by Mayer and colleagues,\textsuperscript{58} 399 patients with acute IPH were randomized to receive placebo or 40 \(\mu\)g/kg, 80 \(\mu\)g/kg, or 160 \(\mu\)g/kg of rFVIIa within 1 hour after IPH was diagnosed on baseline CT scan. The primary outcome of the study was to assess IPH growth at 24 hours. The study found a dose-dependent effect on reducing hematoma growth, with a mean increase of 29%, 16%, 14%, and 11% in the placebo, 40 \(\mu\)g/kg, 80 \(\mu\)g/kg, and 160 \(\mu\)g/kg dose arms, respectively (\(P = .01\)). Clinical outcomes were secondary measurements by the modified Rankin Scale (mRS). The mRS outcome measure was assessed at 90 days and showed that 69% of placebo-treated patients were either dead or severely disabled (modified Rankin Scale score 4–6), compared with 49% to 55% for the rFVIIa-treated patients (\(P = .004\)). Mortality at 90 days was 29% for placebo-treated patients compared with 18% in rFVIIa-treated patients. Thromboembolic events of myocardial infarction or ischemic stroke occurred in 7% of rFVIIa-treated patients compared with 2% of placebo-treated patients (\(P = .12\)). In more than 170,000 doses of rFVIIa administered to hemophiliac patients for whom the drug was originally manufactured, only 17 serious thromboembolic complications were reported\textsuperscript{54} as comparison. Hemophiliac patients
are typically younger with fewer vascular risk factors than patients with IPH in the rFVIIa study. Another important issue is the cost of rFVIIa, which is approximately $1020 to $1369 per 1.2-mg vial.60

In 2008, a subsequent phase III multicenter trial was reported61 for acute IPH using rFVIIa among 841 randomized patients. In this study, 268 patients received placebo, whereas the other 297 patients received either 20 μg/kg intravenously of rFVIIa (276 patients) or 80 μg/kg intravenously of rFVIIa within 4 hours after symptomatic stroke onset. The primary end point was poor outcome, defined as severe disability or death according to the modified Rankin scale 90 days after stroke onset. The mean increase in IPH volume at 24 hours was 26% in the placebo group, 18% in the 20-μg/kg rFVIIa group (P = .09), and 11% in the 80-μg/kg group (P<.001). IPH volume growth was reduced by 2.6 mL (95% CI, −0.3–5.5; P = .08) in the group receiving 20 μg/kg of rFVIIa, and 3.8 mL (95% CI, 0.9–6.7; P = .009) in the group receiving 80 μg/kg, compared with the placebo group. No significant difference was seen in the proportion of patients with poor clinical outcome (24% in the placebo group, 26% in the 20-μg/kg rFVIIa group, and 29% in 80-μg/kg group). The frequency of thromboembolic events was similar in the three groups, but the arterial events were more frequent in patients receiving 80 μg/kg of rFVIIa compared with the placebo group (9% vs 4%; P = .04). Therefore, rFVIIa seems to reduce IPH hematoma growth but did not improve survival or functional outcome. Based on this information, the FDA did not approve rFVIIa for a label indication for IPH. Based on these data, the authors do not recommend rFVIIa outside of a clinical trial.

**Perihematoma edema**

Three phases of perihematomal edema occur after IPH.62 The first phase occurs within hours and involves separation of clot and plasma (clot retraction). The second phase occurs over the next 2 days and involves plasma protein extravasation, activation of the coagulation cascade and complement, and an inflammatory process triggered by fibrin and thrombin. The third phase (after the third day) involves erythrocyte lysis and hemoglobin-mediated neuronal toxicity. Perihematoma edema volume increases up to 75% of the hematoma size in patients with hyperacute IPH, and strongly predicts functional outcome.63,64

**Surgical Management**

A meta-analysis of seven surgical trials for supratentorial IPH showed no benefit with surgery.65 The most recent and largest study, the Surgical Trial in Intracerebral Hemorrhage (STICH) trial was an international, prospective, randomized trial comparing early surgery (n = 503) and initial conservative management (n = 530) in 1033 patients with spontaneous supratentorial IPH for whom best treatment was deemed uncertain.66 The study end point was favorable clinical outcome, which was defined as good recovery or moderate disability on the Glasgow Outcome Scale. No significant difference was seen between groups, with favorable outcome achieved in 26% of patients randomized to early surgery compared with 24% of patients randomized to conservative treatment (P = .414). The authors concluded that early surgical evacuation of IPH showed no overall benefit compared with conservative medical therapy.

STICH had some limitations that should be noted. First, 73% of patients who underwent very early surgery (n = 339) did not undergo surgery until 12 hours from randomization, and only 16% (n = 74) underwent surgery within 12 hours of ictus. Most patients (>75%) underwent frank craniotomy with hematoma evacuation, but other less-invasive techniques were used, including minimally invasive methods such as endoscopic methods of hematoma evacuation.
Established indications for potential neurosurgical intervention are shown in Box 4, which include comatose patients with transtentorial herniation, those with significant IVH and hydrocephalus, and those with symptomatic cerebellar ICH (AHA).

**Newer surgical therapies**

Although the STICH trial suggested no benefit of surgical treatment in supratentorial IPH, several newer surgical methods are being reported. Nishihara and colleagues report use of novel transparent endoscopic tools for hematoma evacuation treated within 24 hours of IPH onset via a burr-hole approach in 82 patients. Vespa and colleagues report a pilot study of IPH evacuation using a frameless stereotactic aspiration and thrombolysis method using recombinant tissue plasminogen activator (rt-PA) in 28 patients with ICH, and found a 77% reduction in ICH volume after surgery. IPH volume was reduced, but no significant difference was seen in mortality between surgical (56%) and nonsurgical patients (59%) at 180 days. Murthy and colleagues performed decompressive craniectomy and IPH clot evacuation for large hemispheric IPH (volume>48 cm³) in 12 patients. Eleven (91.6%) patients survived to discharge, and 6 had good functional outcome (modified Rankin Scale score, 0–3). An NIH-sponsored safety study Minimally Invasive Surgery plus tPA for Intracerebral Hemorrhage Evacuation (MISTIE) is investigating minimally invasive surgery in combination with rt-PA for IPH removal.

**Prognosis After IPH**

Poor-prognostic variables in IPH include IPH volume greater than 30 cm³, age older than 80 years, infratentorial location, low presenting GCS score, and the presence of intraventricular blood. These variables were combined in a composite scale called the ICH score by Hemphill and colleagues to estimate 30-day mortality, and were derived from a multivariate regression analysis study of patients with IPH. Mortality increases with increasing ICH total score (ICH score of 0–6 ranges from 0%–100% mortality).

**SAH: DIAGNOSIS AND MANAGEMENT**

Aneurysmal SAH is typically characterized by an explosive or “thunderclap headache,” which is instantaneously maximal at onset. The headache of aneurysmal SAH is fairly distinct in patients who are able to provide history, but it is typically the “worst headache of one’s life” even among those with migraines and other headache disorders. Aneurysmal SAH headache should be considered in the evaluation of patients with a “worst or first” headache, but most headaches are instantaneously

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**Box 4**

**Indications for neurosurgical consultation or intervention in patients with IPH-IVH**

- GCS score of 8 or less with transtentorial herniation
- Significant IVH or hydrocephalus
- 3 cm or more of posterior fossa or symptomatic cerebellar ICH evacuation (ventricular cerebrospinal fluid drainage alone not recommended)

maximal in pain at onset. Patients with aneurysmal SAH may also have transient loss of consciousness from an acute spike in intracranial pressure and a drop in cerebral perfusion pressure (transient intracranial circulation arrest), or from acute diffuse vasospasm of the cerebral arteries. The longer duration of intracranial bleeding and lack of intracranial circulatory flow can lead to global cerebral edema, which can lead to refractory intracranial hypertension and death. Patients who have lesser forms of intracranial SAH bleeding and who survive to seek medical attention often present to an emergency department. A noncontrast head CT is warranted immediately. The CT scan in aneurysmal SAH typically shows a star-shaped pattern of intracranial bleeding around the basal cisterns, around the Circle of Willis vessels, and in front of the brainstem (Fig. 8A, B); sometimes IPH with SAH blood (see Fig. 8C); and, less commonly, subdural or epidural blood. Associated extension of SAH blood into ventricles may be present, leading to obstructive (noncommunicating) hydrocephalus or communicating hydrocephalus from occlusion of the arachnoid granulations. Both forms of hydrocephalus can lead to increased hydrostatic pressure within the brain and increased intracranial pressure, leading to depressed cerebral perfusion pressure and, if unchecked, eventual cessation of intracranial flow and brain death.

Patients should undergo a CT angiogram or diagnostic cerebral angiogram to identify the aneurysm as soon as possible. Once the location of the aneurysm is identified, the configuration and the aneurysm’s dome-to-neck ratio and other factors dictate treatment with either endovascular coiling (Fig. 9) with platinum coils or craniotomy with base clipping of the aneurysm.

Patients with aneurysmal SAH and symptomatic hydrocephalus should have an EVD placed to measure intracranial pressure and calculate cerebral perfusion pressure. The zero point of the EVD and the arterial line should be at the same level, which is at the foramen of Monro (approximately the level of the tragus at the ear) for accurate cerebral perfusion pressure calculation. Once the aneurysm is secure,
post–aneurysmal SAH management is typically predicated on maintaining euvolemia (or normal fluid balance state) and permissive hypertension to allow adequate cerebral perfusion. Immediate blood pressure goals are listed in Table 3. However, extreme hypertension (cerebral perfusion pressure, >120–130) in aneurysmal SAH beyond autoregulation is typically avoided.

**Vasospasm (Delayed Arterial Vessel Narrowing After Aneurysmal SAH)**

Aneurysmal SAH is unique in that the aneurysm rupture event begins a cascade of events intracranially that potentially cause delayed ischemic neurologic deficits. These deficits span an average 21 days post–aneurysmal SAH but peaks between days 7 and 14, with vasospasm risk being proportional to the amount of SAH blood seen on the initial CT scan (ie, Fisher Grade).\(^{74,75}\) Nimodipine enterally, 60 mg every 4 hours for 21 days, is the standard prophylactic medication for vasospasm prevention, and for making sure patients with aneurysmal SAH do not become dehydrated or volume-depleted. Detailed review of vasospasm management and hypervolemic hypertensive hemodilution therapy is outside the scope of this article, but is addressed elsewhere.\(^{76,77}\)

Patients with aneurysmal SAH can develop a host of CNS and non-CNS organ complications (see Box 2). Hyponatremia is common after aneurysmal SAH and may be from so-called cerebral salt wasting, which is a poorly understood natriuresis that occurs after aneurysmal SAH and other intracranial CNS disorders. Syndrome of inappropriate antidiuretic hormone hypersecretion may also occur. Other unique

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**Fig. 9.** Artistic representation of an intracranial aneurysm coiled with detachable platinum coils.
complications seen in aneurysmal SAH include takotsubo stress cardiomyopathy, which can be seen with troponin leak and cause left apical ballooning on echocardiogram. It represents a potentially reversible cardiomyopathy in terms of ejection fraction compared with coronary disease–based infarction of the myocardium. Takotsubo cardiomyopathy may complicate hypervolemic hypertensive hemodilution management because of heart failure and pulmonary edema.

**SDH AND EDH**

SDH or EDH are associated with a significant 30-day mortality of at least 40% to 60% (Fig. 10). SDH is typically caused by tearing of bridging veins between the brain and skull, either from trauma or sometimes spontaneously in elderly patients or those on anticoagulation. EDH, however, typically occurs from tearing of the middle meningeal artery from a blow to the temporal bone just above the zygomatic process, which represents a relative weak or thin spot on the human skull. A fracture or trauma to this area injures the middle meningeal artery and can cause arterial bleeding. The initial blow may cause transient loss of consciousness followed by a lucid interval, followed by a rapid neurologic deterioration from massive arterial bleeding and expansion of the EDH, herniation, and death. For both SDH and EDH, delay of operative intervention worsens outcomes. Indications for EDH surgery described by Bullock and colleagues and the Surgical Management of Traumatic Brain Injury Author Group state that an EDH greater than 30 cm³ should be surgically evacuated regardless of the patient’s GCS score, and that comatose patients with acute EDH (GCS<9) with anisocoria should undergo surgical evacuation as soon as possible. Patients with nonoperable, medically managed EDH are those with a GCS score greater than 8 without focal deficit, EDH volume less than 30 cm³, maximal EDH thickness less than 15 mm, and less than a 5-mm midline shift. These nonoperable patients require serial CT scanning and close neurologic observation in a neurosurgical center.

Other important complications to consider, particularly in patients with SDH, are seizures, especially those in nonconvulsive form, which may occur in up to 20% of patients with acute SDH. Cerebral or cortical edema also can occur with either, but cortical edema from SDH can cause TIA-like phenomena that are negative on MRI, and electroencephalogram should be considered. The authors have observed that sometimes patients with acute SDH experience a transient response to dexamethasone (eg, 4 mg intravenously every 6 hours) presumably from a forme fruste of cortical vasogenic edema, although little to no literature supports this.

**PRIMARY AND SECONDARY IVH AND HYDROCEPHALUS**

IVH results from either primary bleeding within the ventricle (primary IVH) or secondarily from ICH that expands into the ventricle (secondary IVH). The estimated incidence of IVH is 22,000 patients per year. Approximately one-third of IVHs are secondary, meaning bleeding from the parenchyma or another location leaked into the ventricle. Primary IVH is not as common as secondary IVH and is defined by blood only within the ventricles. The differential diagnosis of primary IVH includes aneurysm, arteriovenous malformation, trauma, coagulopathy, choroid plexus tumor, and ependymal lesion. Secondary IVH is caused by spontaneous IPH with IVH extension approximately half the time (see Fig. 6A–C) and aneurysm 10% to 30% of the time (Fig. 8C). Traumatic IVH should be considered when the history or findings support trauma (see Fig. 2F).

The pathophysiology of IVH is in causing obstruction of the cerebrospinal fluid flow by blockage of the ventricular pathways (obstructive or noncommunicating...
Fig. 10. SDH and EDH shown in artistic diagrams and on CT. SDHs look crescentic, like a crescent moon, and do not respect cranial suture lines because SDH are below the dura mater (subdural). EDHs, however, are lens-shaped and typically respect cranial suture lines because they are above the dura.
hydrocephalus) or of the tiny arachnoid granulations that normally drain cerebrospinal fluid into the draining veins from the head into the jugular venous sinuses (ie, communicating or nonobstructive hydrocephalus). IVH also causes localized inflammation, which can cause neurologic dysfunction and localized irritation of the surrounding brain tissue. Both types of hydrocephalus lead to an increase in hydrostatic pressure and increased intracranial pressure, which lowers cerebral perfusion pressure defined by the difference between the mean arterial pressure and the intracranial pressure (eg, cerebral perfusion pressure = mean arterial pressure – intracranial pressure). Hydrocephalus can be acute or delayed and lead to cognitive deficits, spasticity, incontinence, and gait dysfunction.

Standard treatment for IVH with acute obstructive hydrocephalus includes placement of a cerebrospinal fluid drain via external ventriculostomy. The volume of IVH is an independent predictor of mortality similar to IPH volume, and is up to 40% to 80% by 1 month. A study of urokinase placed in the ventricles of patients with IVH via ventriculostomy expedited clot resolution within the ventricles, and may improve 30-day mortality. However, rebleeding into the ventricles with urokinase treatment occurred in approximately 6% of patients. Some institutions are using rt-PA off-label in efforts to expedite IVH clot resolution. A large, multicenter, prospective phase III trial (clot lysis: evaluating accelerated resolution [CLEAR] IVH) is investigating the optimal dose of intraventricular rt-PA to expedite removal of IVH. The results of this pivotal trial will help determine whether this becomes an FDA-approved (label indication) drug for patients with IVH. Medical management of patients with IVH includes raising the head of bed, optimizing cerebral perfusion pressure (via an intracranial pressure monitor), and osmotherapy as needed.

SUMMARY

ICH is a neurologic emergency because of its high 1-month mortality, and may require neurosurgical intervention. Patients with ICH should be triaged rapidly and efficiently based on airway and respiratory function and level of consciousness. Patient history and noncontrast CT often yield clues to assist in diagnosing the underlying cause of the ICH. Specialized management of each ICH subtype depends on correct diagnosis. Indications for surgical intervention include a GCS score of 8 or less in potentially salvageable patients with either traumatic ICH or IPH with herniation (although deep IPH surgery has not been proven superior to optimal medical management), comatose patients with SDH or EDH with anisocoria, those with an EDH volume greater than 30 cm³, and those with symptomatic cerebellar IPH with mass effect or hydrocephalus. Medical and critical care management of patients with ICH, including optimizing cerebral perfusion pressure, oxygenation, and metabolic status (avoidance of fever and optimal nutrition), and preventing infections, deep vein thrombosis, and decubitus and gastrointestinal stress ulcers, will improve the chances of survival in patients with ICH.

REFERENCES


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