Intracerebral hemorrhage (ICH)

July 22, 2020 by Josh Farkas

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pathophysiology
Hematoma expansion
- Up to a third of patients experience an increase in hematoma size following the initial hemorrhage.
- When it occurs, this generally happens within the first 6 hours (yet it can occur within ~48 hours in coagulopathic patients).
- Cytotoxic edema surrounding the hematoma worsens over a period of days, before improving.
- Intracranial pressure may increase due to the mass effect of the hemorrhage, as well as blood accumulation in the ventricles (if the hematoma extends into the ventricles).

**differential diagnosis & causes**

**hypertensive intraparenchymal hemorrhage**
- Location: Most often basal ganglia, thalamus, internal capsule, pons and cerebellum.
- Epidemiology:
  - Most common cause of intracranial hemorrhage.
  - Risk factors include age, hypertension, and diabetes.

**cerebral amyloid angiopathy**
- Location: Usually lobar, sometimes with subarachnoid extension or finger-like projections of the hemorrhage (image below).
- Epidemiology:
  - This is the most common cause of lobar hemorrhage in normotensive elderly.
  - It is often provoked by anticoagulation or thrombolysis.

**vascular malformations**
- Types include:
  - Arteriovenous malformation (AVM).
  - Cavernous malformation.
  - Dural arteriovenous fistula.
  - Berry aneurysm rupture (can cause a combination of subarachnoid plus intraparenchymal hemorrhage).
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- Mycotic aneurysm (may result from endocarditis or bacteremia).
- Treatment implication: Vascular malformations often require surgical resection and/or embolization by interventional radiology to avoid re-bleeding.

**malignancy**
- Primary CNS tumor.

**ischemic stroke with hemorrhagic conversion**
- Epidemiology: More common for larger infarctions (as may occur due to atrial fibrillation).
- Three types (in order of increasing severity):
  - Petechial hemorrhages – very small hemorrhages.
  - Type 1 parenchymal hematoma: <30% of ischemic territory involved, with minimal mass effect.
  - Type 2 parenchymal hematoma: >30% of ischemic territory involved, with mass effect.

**venous sinus thrombosis with secondary hemorrhage**
- Epidemiology: Risk factors include hypercoagulability, dehydration, pregnancy, parameningeal infection, lupus, inflammatory bowel disease, and thyroid disease. This accounts for 5% of parenchymal hemorrhage in younger patients.
- Treatment implication: Transvenous thrombectomy and/or anticoagulation may be needed.

**less common causes**
- Trauma
  - Location: Usually inferior frontal location and anterior tip of the temporal lobe.
- Vasculitis
  - Epidemiology: Usually caused by polyarteritis nodosa or lupus, but may also occur with ANCA vasculitis, rheumatoid arthritis, sarcoidosis, drug-induced vasculitis, or Henoch-Schonlein purpura.
- Moyamoya disease
  - Hemorrhage is typically in the basal ganglia.

**noncontrast CT scan**

Noncontrast CT scan is the standard diagnostic test to rapidly evaluate for intracranial hemorrhage.

**hematoma volume**
- Hematoma volume may be estimated as the multiple of the diameters divided by two (ABC/2, see below).
- Volume >60 ml suggests a worse prognosis (more below (#prognostication)).
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“black hole” sign on nonenhanced CT scan

- Defined as a relatively hypo-attenuated area within a hematoma and not connected with adjacent brain tissue.
- Predicts hematoma growth with 32% sensitivity and 94% specificity.
- Shown below (top, second panel from the left), along with other potential markers of hematoma growth. ([28289239](https://pubmed.ncbi.nlm.nih.gov/28289239/))

serial CT scan?

- Hematoma expansion will often occur within 6 hours (or longer in anticoagulated patients).
- In patients without an accessible neurologic examination (e.g., due to sedation), consider a repeat CT scan in 4-6 hours. If hydrocephalus develops, this may be an indication for external ventricular drain placement (more on this below (#neurosurgical_interventions)).

evaluation for an underlying etiology

when to suspect an underlying vascular intracranial pathology 😊

- Identification of underlying vascular pathology is potentially important, as many of these lesions require specific therapy.
- Factors which increase the likelihood of an underlying vascular pathology include:
  - (1) Imaging findings on noncontrast CT scan
    - Hematoma located outside of the typical location for a hypertensive hemorrhage.
    - Fluid level within the hematoma (bottom right panel of the above figure).
    - Isolated intraventricular hemorrhage.
- Calcified or dilated vessels.
- Abnormal parenchyma surrounding the hematoma (e.g., more edema than might be expected).

- (2) Epidemiological findings
  - Younger age
  - Female sex
  - No history of hypertension
  - No coagulopathy

CT angiography (+/- CT venography)
- This is the front-line test to evaluate for an underlying cause of ICH due to speed and safety (especially for causes which require more immediate management).
  - CT angiography may be useful to detect an underlying aneurysm or vascular malformation.
  - CT venography may be useful to diagnose venous sinus thrombosis.
  - Both CT angiography and venography may be performed together (CTAV).

- Prognostication of the risk of hematoma expansion
  - This isn't the reason for obtaining CT angiography, but it may be helpful nonetheless.
  - The spot sign reveals leakage of contrast into the hematoma (predicting expansion with 51% sensitivity and 85% specificity).
  - Please note that contrast dye is not nephrotoxic. Appropriate imaging should not be deferred due to renal dysfunction.

MRI
- This generally isn't performed immediately, due to logistic constraints.
- MRI may be superior for detecting certain underlying pathologies:
  - Tumor
  - Ischemic stroke with hemorrhagic transformation
  - Amyloid angiopathy with multiple occult cerebral micro-bleeds
  - Underlying hypertensive microangiopathy (may be suggested by white matter lesions and small lacunar strokes)
- MR angiography can image the vessels, so this may be considered as well (especially if a CT angiography hasn't been performed).

invasive angiography (a.k.a. digital subtraction angiography)
- This is the definitive study to evaluate for aneurysm, arteriovenous malformation, or vasculitis.
- This is indicated if there is a high suspicion for vascular abnormality (e.g., ruptured aneurysm).
- Angiography can be both diagnostic and therapeutic (if an aneurysm or arteriovenous malformation is discovered, some may be embolized immediately).

[https://emcrit.org/ibcc/ICH/](https://emcrit.org/ibcc/ICH/)
airway management

- Intubation may be required for airway protection. However two thirds of patients won't require intubation.[31092052](https://pubmed.ncbi.nlm.nih.gov/31092052/)
- There are no validated or well-defined criteria for intubation – this is a clinical judgement based on examination and trajectory.
- Care is required to avoid stimulation[https://emcrit.org/emcrit/neurocritical-care-intubation/] and hypertension, which could worsen intracranial pressure elevation.

anticoagulation reversal

- Assess coagulation thoroughly (including both laboratory tests and medication review).
- Platelet function
  - Thrombocytopenia should be treated, to maintain a platelet count > 100,000 if possible.
  - There is no benefit in platelet transfusion for patients who had been treated with aspirin or anti-platelet agents (PATCH trial).[27178479](https://pubmed.ncbi.nlm.nih.gov/27178479/)
- Therapeutic anticoagulation (e.g., warfarin, NOACs) should be aggressively reversed.
- For more, see the chapter on anticoagulation reversal[https://emcrit.org/ibcc/anticoagulant-reversal/].

blood pressure management

theoretical rationale & risks

- **Rationale**: Blood pressure reduction could theoretically reduce hematoma expansion. This would be expected to be most effective within the period that the hematoma is expanding (typically the first six hours, but potentially longer in coagulopathic patients).
- **Risks**
  - Neurological: Reduced blood pressure could impair perfusion of penumbra surrounding the hematoma. This could cause necrosis, leading to worsening edema and intracranial pressure (leading to a cascade of secondary brain insults).
  - Renal failure may result from excessive blood pressure reduction.

targets?

### Effect of blood pressure target on hematoma expansion

<table>
<thead>
<tr>
<th>Study</th>
<th>Endpoint</th>
<th>SBP &lt;140 mm group</th>
<th>SBP &lt;180 mm group</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERACT-2*</td>
<td>Baseline hematoma volume</td>
<td>15.7 +/- 15.7 ml</td>
<td>15.1 +/- 14.9 ml</td>
</tr>
<tr>
<td></td>
<td>Follow-up hematoma volume</td>
<td>18.2 +/- 19.1 ml</td>
<td>20.6 +/- 24.9 ml</td>
</tr>
<tr>
<td></td>
<td>Hematoma growth (Mean &amp; 95% CI)</td>
<td>3.1 ml (2.1-4.1 ml)</td>
<td>4.9 ml (3.1-6.6 ml)</td>
</tr>
<tr>
<td></td>
<td>Substantial hematoma growth</td>
<td>128/493 (26.1%)</td>
<td>125/473 (26.4%)</td>
</tr>
<tr>
<td>ATACH-2</td>
<td>Hematoma expansion</td>
<td>85/450 (18.9%)</td>
<td>104/436 (24.4%)</td>
</tr>
</tbody>
</table>

The entire goal of blood pressure reduction in intracerebral hemorrhage is to reduce hematoma size. Neither INTERACT-2 nor ATACH-2 demonstrated a statistically significant reduction in hematoma size or the fraction of patients experiencing hematoma expansion. This argues strongly against the mechanistic rationale for more aggressive blood pressure control.

*Pre-specified subgroups of 164 patients with repeat imaging data.

[https://emcrit.org/ibcc/ich/attachment/interactdata/]

- [INTERACT-2 Trial in 2013](https://pubmed.ncbi.nlm.nih.gov/23713578/)
  - RCT comparing a target of SBP <140 mm versus SBP <180 mm for a seven-day period among >2,800 patients within <6 hours of symptom onset.
• The primary endpoint of death or disability after 90 days showed no benefit. Likewise, there was no difference in the incidence of hematoma expansion (table above).
• There was a tiny improvement in a secondary endpoint (quality of life) in the more aggressively treated group. However, given that there was no difference in hematoma expansion, this isolated secondary endpoint is of dubious significance.
• The most commonly used antihypertensive agent was urapidil (an alpha-blocker), which may limit generalizability.
• This study has been traditionally used to justify the systolic Bp target of <140 mm.

**ATACH-2 trial in 2016** ([27276234](https://pubmed.ncbi.nlm.nih.gov/27276234/))

• This was a follow-up study to INTERACT-2, which likewise compared SBP targets of 110-140 mm versus 140-180 mm.
• This study utilized intravenous nicardipine, which may more closely resemble typical practice patterns.
• There was no benefit to more intensive blood pressure reduction (either in terms of functional endpoints or in terms of hematoma expansion).
• More aggressive reductions in Bp increased the risk of renal adverse events (from 4% to 9%, \(p=0.002\)).

**Guidelines?**

• American Heart Association / American Stroke Association (AHA/ASA) suggest reduction in a systolic blood pressure below 140 mm. However, these guidelines were written in 2015, prior to the ATACH-2 trial. ([26022637](https://pubmed.ncbi.nlm.nih.gov/26022637/))
• American Heart Association / American College of Cardiology guidelines from 2017 recommend against acutely lowering the systolic blood pressure below 140 mm (figure below 📊).([29133354](https://pubmed.ncbi.nlm.nih.gov/29133354/))

**Bottom line?**

• Despite repeated and well-powered trials, there is no evidence that more intensive blood pressure control can improve hematoma size. If lower blood pressure isn't reducing hematoma size, then it may be only harming patients due to malperfusion of compressed penumbra tissue.
• Targeting a systolic blood pressure <180 mm is consistent with available evidence and the most recent guidelines (shown below). ([29133354](https://pubmed.ncbi.nlm.nih.gov/29133354/))
  • If you shoot for a systolic Bp <180 mm, then you'll often end up with a systolic Bp around ~140-160 mm, which is good.
  • If you shoot for a systolic Bp <140 mm, then you'll often end up with a systolic Bp around ~100-120 mm, which is probably too low.
• **Before initiating antihypertensives, always make sure that pain and anxiety have been adequately treated.** Especially among intubated patients, hypertension can be a manifestation of pain. Proper analgesia and sedation may go a long way towards reduction of the blood pressure.

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**Clinical Practice Guideline**

**2017 ACC/AHA/ABC/ACP/M/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults**

[https://emcrit.org/ibcc/attachment/ahaguidelines/](https://emcrit.org/ibcc/attachment/ahaguidelines/) preferred agents

• Nicardipine or clevidipine infusion is the most common and effective approach to severely elevated blood pressure.
• Small labetalol boluses may be used PRN if the blood pressure is slightly above target (e.g., 10-20 mg IV every 15 minutes).

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**neurosurgical interventions**

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surgical hematoma evacuation for supratentorial hemorrhage

- **STITCH-I Trial** ([15680453](https://pubmed.ncbi.nlm.nih.gov/15680453/))
  - RCT involving 1,033 patients randomized to medical management vs. early surgical hematoma evacuation.
  - Outcomes were nearly identical between two groups. However, there was a non-significant trend toward benefit from surgery in patients with hematoma extending to within 1 cm of the cortical surface. Likewise, there were trends toward benefit from early surgery among patients with lobar hemorrhage and Glasgow Coma Scale score of 9-12.
  - Patients with ICH >1 cm from cortical surface or GCS<9 tended to do worse with surgery.

- **STITCH-II Trial** ([23726393](https://pubmed.ncbi.nlm.nih.gov/23726393/))
  - RCT involving 601 patients predicted to obtain maximal benefit from surgery based on the results of the STITCH-1 trial (patients were conscious, had superficial hemorrhage <1 cm from the cortical surface, had a hemorrhage volume of 10-100 ml, and had no intraventricular hemorrhage).
  - Patients were randomized to early surgery vs. early conservative approach.
  - Outcomes were nearly identical between the two groups.

- **Bottom line:**
  - Available evidence suggests no benefit for early hematoma evacuation. Some patients in the medical arm of these studies did cross over into the surgical arm due to progressive deterioration, so surgery might still be beneficial in selected cases with progressive deterioration over time.
  - Surgery or interventional radiology may be indicated in hemorrhage secondary to specific lesions (e.g., arteriovenous malformation or tumor).
  - Emerging evidence suggests that minimally invasive surgery could be more promising (with several ongoing trials).

surgical hematoma evacuation for cerebellar hemorrhage

- The cerebellum is somewhat unique due to its enclosed location. Swelling in the cerebellum threatens to cause catastrophic damage to the adjacent brainstem, which implies a greater benefit for hematoma evacuation in this location.
- No RCTs exist, because these patients were excluded from the STITCH trials.
- Observational data suggests benefit in the following situations:
  - Hematoma >3 cm diameter
  - Mass effect causing brainstem compression
  - Hydrocephalus due to ventricular obstruction

external ventricular drain (EVD)

- Ventricular drainage may be considered for hydrocephalus (e.g., due to ventricular extension of the hemorrhage).
- An ideal candidate might be a patient who was initially doing well, then subsequently developed hydrocephalus with neurologic deterioration.
- Unfortunately, overall evidence suggests that ventricular drainage increases survival without increasing the likelihood of a good neurologic outcome. This implies that patients whose lives are saved by drain placement generally have poor neurologic outcome. ([10751114](https://pubmed.ncbi.nlm.nih.gov/10751114/), [22732889](https://pubmed.ncbi.nlm.nih.gov/22732889/))

![Figure 4.](https://emcrit.org/ibcc/ich/attachment/evdreyes/)

other supportive measures

seizure prophylaxis / management

https://emcrit.org/ibcc/ICH/
Seizure prophylaxis isn't generally recommended

- Seizures are common, with an incidence of ~20% in all patients.
- Prior evidence has not revealed benefit with prophylactic phenytoin, which may relate to phenytoin's numerous side-effects.
- Whether seizure prophylaxis with more modern agents (e.g., levetiracetam) could be beneficial remains unknown.

Low threshold to evaluate for seizure with continuous EEG

- EEG should be considered in patients with impaired consciousness that is out of proportion to what would be expected based on the CT scan.
- Evaluation is also indicated based on any history or clinical signs of seizure.
- Anti-epileptic therapy is indicated for a patient with witnessed seizure or electroencephalographic seizure.

Fever control

- Any fever should be treated aggressively (e.g., with scheduled acetaminophen).
- If fever is refractory to antipyretics, an external cooling device may be used to achieve normothermia (similar to treatment of a post-arrest patient).

Sodium management

- Avoid hyponatremia or rapid decreases in sodium.
- Routine use of hypertonic saline isn't supported by evidence.
- Boluses of hypertonic saline or hypertonic bicarbonate may be used to manage elevated intracranial pressure, ideally as a bridge to more definitive therapy (e.g., an external ventricular drain).

DVT prophylaxis

- Intermittent pneumatic compression should be used initially for DVT prophylaxis.
- Heparin for DVT prophylaxis is generally safe >48 hours after initial bleed, if there has been no hematoma expansion on repeat CT scan. (1865215)

Prognostication

Overall prognosis

- Mortality is high, with only half of patients alive after one year and only ~30% alive after five years.
- Only ~20% of patients overall remain alive and independently functioning after one year.

Predictors of poor outcome

- Hematoma volume >60 ml
- Glasgow Coma Scale <8
- Deep or infratentorial location
- Intraventricular extension
- Increasing age

ICH score

- May be calculated using MDCalc here. One weakness of the ICH score is that it is designed to predict survival, rather than independent survival or quality of life.

FUNC score

- May be calculated using MDCalc here. Estimates the likelihood of functional independence at 90 days, potentially a more meaningful endpoint.
- Tables below provide more granular detail about how the score is obtained and interpreted. (18556582)
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Differential diagnosis

- Primary intraventricular hemorrhage
  - Aneurysm or arteriovenous malformation
  - Trauma
  - Anticoagulation
  - Choroid plexus tumor or ependymal lesion
- Secondary intraventricular hemorrhage
  - Intraparenchymal hemorrhage with extension into the ventricles

Role for external ventricular drain (EVD)

- Drainage is indicated for acute obstructive hydrocephalus.

Summary
For most patients, the best treatment seems to be high-quality supportive care. Aggressive interventions (e.g., causing dramatic drops in blood pressure and "prophylactic" hypertonic saline) may cause more harm than good.

Cerebellar hematomas may threaten brainstem compression as well as hydrocephalus, so these patients potentially benefit the most from urgent surgical evacuation and/or ventricular drainage.

Steroid doesn’t help ICH. Don’t use steroid in these patients unless there is some other indication.
Going further:

- Radiopaedia (https://radiopaedia.org/articles/intracerebral-haemorrhage) (Craig Hacking and Jeremy Jones)
- INTERACT-2 trial
  - EMMerd – The case of the differing perspectives (https://emcrit.org/emnerd/46147/)
- ATACH-2 trial
  - TheBottomLine review (https://www.thebottomline.org.uk/summaries/icm/atach-2/) by Adrian Wong
  - Don't bring my blood pressure down (intensively) (http://thesgem.com/2017/03/sgem172-dont-bring-my-blood-pressure-down-intensively-the-atach-2-trial/) ~ SGEM with Ken Milne

References


https://emcrit.org/ibcc/ICH/
The Internet Book of Critical Care is an online textbook written by Josh Farkas (@PulmCrit), an associate professor of Pulmonary and Critical Care Medicine at the University of Vermont.