AHA/ASA Guideline

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage

A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association

The American Academy of Neurology (AAN) affirms the value of this guideline as an educational tool for neurologists

Endorsed by the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS)

Endorsed by the Neurocritical Care Society (NCS)



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On behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, and Council on Clinical Cardiology



Slides Prepared by Members of the Stroke Professional Education Committee

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Applying classification of recommendations and levels of evidence

SIZE OF TREATMENT EFFECT

	CLASS I Benefit >>> Risk Procedure/Treatment	CLASS IIa Benefit >> Risk Additional studies with focused objectives needed	CLASS IIb Benefit ≥ Risk Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED	CLASS III No E or CLASS III H Proce Test	arm dure/ Treatmen
	SHOULD be performed/ administered	IT IS REASONABLE to per- form procedure/administer treatment		COR III: Not No benefit Helpfu COR III: Excess Harm w/o Be or Har	s Cost Harmful enefit to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	 Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	 Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	 Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	 Recommendation procedure or transmission of the second seco	eatment is tive and may dence from
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	 Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	 Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	 Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	 Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies 	
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	 Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	 Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	 Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	 Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care 	
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated	COR III: Harm potentially harmful causes harm
Comparative effectiveness phrases ¹	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		should not be performed/ administered/ other is not useful/ beneficial/ effective	associated w excess morbi ity/mortality should not be performed/ administered/ other

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ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

Outline

- I. Introduction
- II. Emergency Diagnosis and Assessment
- **III.** Medical Treatment for ICH
- IV. Inpatient Management and Secondary Prevention of Brain Injury
- V. Procedures/Surgery
- VI. Outcome Predictions and Withdrawal of Technological Support
- VII. Prevention of Recurrent ICH
- VIII. Rehabilitation and Recovery
- IX. Conclusion



I. Introduction

- Spontaneous, non-traumatic intracerebral hemorrhage (ICH) remains a significant cause of morbidity and mortality throughout the world.
- The last decade has seen a dramatic increase in the studies of ICH intervention.
- Excellent medical care likely has a potent, direct impact on ICH morbidity and mortality.



I. Introduction

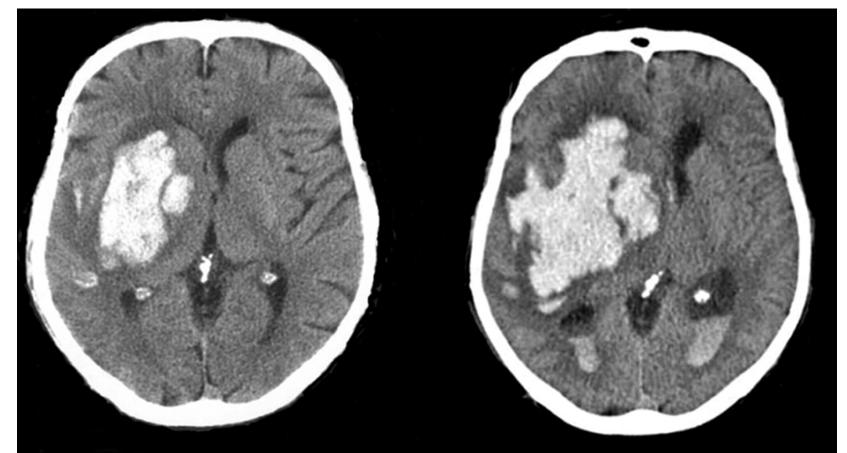
- This is an update to the last ICH Guidelines published in 2010, incorporating the results of new studies published in the interim.
- In addition, the current guidelines serve to remind clinicians of the importance of their care in determining ICH outcome as well as to provide an evidence-based framework for that care.
- Please refer to the 2010 guidelines for additional relevant references not contained in the current guideline.



- ICH is a medical emergency.
- Over 20% of patients will experience a decrease in the Glasgow Coma Score (GCS) of ≥ 2 points between the prehospital EMS assessment and the initial evaluation in the emergency department.
- Another 15-23% of patients demonstrate continued deterioration within the first hours after hospital arrival.
- The risk for early neurologic deterioration and the high rate of poor long term outcomes underscore the need for aggressive early management.



Images of early hematoma growth in a 48 year-old chronically hypertensive woman



2.0 hours after onset 6.5 hours after onset

American Heart Stroke Association

Stephan A. Mayer Stroke. 2007;38:763-767

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Prehospital Management

- Similar to that for ischemic stroke (see <u>2013 AHAASA Guidelines for the Early</u> <u>Management of Patients with Acute Ischemic Stroke</u>, Jauch EC, Saver JL et al.)
- <u>Primary objective</u> is to provide airway management if needed, cardiovascular support, and to transport to the closest facility prepared to care for patients with acute stroke.
- Secondary objectives
 - Obtain focused history of timing of symptoms onset
 - Obtain medical history, medication and drug use
 - Contact information for family
- EMS providers should provide **advance notice** to the ED of impending arrival
 - Allows for critical pathways to be initiated and consulting services alerted
 - Has been demonstrated to significantly shorten time to computed tomography (CT) scanning in the ED



Emergency Department Management

- Every ED should be prepared to treat patients with ICH or have a plan for rapid transfer to a tertiary care center.
- Crucial resources to manage ICH patients include:
 - Neurology, Neuroradiology, Neurosurgery, and critical care facilities with adequately trained RNs and physicians
- Consultation via telemedicine can be a valuable tool for hospitals without on-site presence of consultants.



Emergency Department Management

- Integral components of the History for a patient with ICH
 - Time of symptom onset (or time of last normal)
 - Initial symptoms and progression of symptoms
 - Medical history
 - Vascular risk factors: prior stroke/ICH, hypertension, diabetes and smoking
 - Dementia
 - Alcohol or illicit drug use
 - Seizures
 - Liver disease
 - Cancer and hematologic disorders
 - Medications: anticoagulants, antiplatelets, antihypertensives, stimulants, and sympathomimetics



Integral Components of the History

Time of symptom onset (or time last seen normal	
Initial symptoms and progression of symptoms	
Vascular risk factors	
Medication	Anticoagulants, antiplatelet agents, antihypertensive medications, stimulants (including diet pills), sympathomimetics
Recent trauma or surgery	Carotid endarterectomy or carotid stenting, as ICH may be related to hyperperfusion after such procedures
Dementia	Associated with amyloid angiopathy
Alcohol or illicit drug use	Cocaine and other sympathomimetic drugs are associated with ICH, stimulants
Seizures	
Liver disease	May be associated with coagulopathy
Cancer and hematologic disorders	May be associated with coagulopathy

Integral Components of the Physical Exam and Lab tests

Vital Signs	
A general physical examination focusing on the head, heart, lungs, abdomen, and extremities	
A focused neurologic examination	A structured examination such as the National Institutes of Health Stroke Scale can be completed in minutes and provides a quantification that allows easy communication of the severity of the event to other caregivers. GCS score is similarly well known and easily computed.
Serum and Urine Tests	
Complete blood count, electrolytes, blood urea nitrogen and creatinine, and glucose	Higher serum glucose is associated with worse outcome
Prothrombin time (with INR) and an activated partial thromboplastin time	Warfarin-related hemorrhages are associated with an increased hematoma volume, greater risk of expansion, and increased morbidity and mortality
Cardiac-specific troponin	Elevated troponin levels are associated with worse outcome
Toxicology screen to detect cocaine and other sympathomimetic drugs of abuse	Cocaine and other sympathomimetic drugs are associated with ICH
Urinalysis and urine culture and a pregnancy test in a woman of childbearing age	

Integral Components of the Work-up

Other Routine Tests	
Neuroimaging	CT or MRI: consider contrast enhanced or vascular imaging
ECG	To assess for active coronary ischemia or prior cardiac injury; ECG abnormalities can mark concomitant myocardial injury



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Emergency Department Management

- Integral components of the *Physical Examination* for a patient with ICH
 - General examination
 - Focused Neurologic examination
- A routine part of the evaluation should include a standardized severity score as such scales can help streamline assessment and communication between providers
 - NIH stroke scale (NIHSS)
 - Glasgow Outcome Scale (GSC)
 - Other severity scores, including the ICH score



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Neuroimaging

- Neuroimaging is mandatory to differentiate ICH from ischemia
- There are no specific clinical findings to diagnosis ICH in the absence of imaging.
- CT (considered the gold standard) and magnetic resonance imaging (MRI) are both reasonable for initial evaluation.



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Neuroimaging

- Hematoma expansion occurs early after ICH and increases risk of poor functional outcome and death.
 - 28-38% have hematoma expansion of > 1/3 of initial hematoma volume
 on follow-up CT
- Identifying patients at risk for hematoma expansion is an active area of research.
- CT angiography (CTA) and contrast-enhanced CT may identify patient at high risk of ICH expansion based on presence of contrast within the hematoma – called a "spot sign."

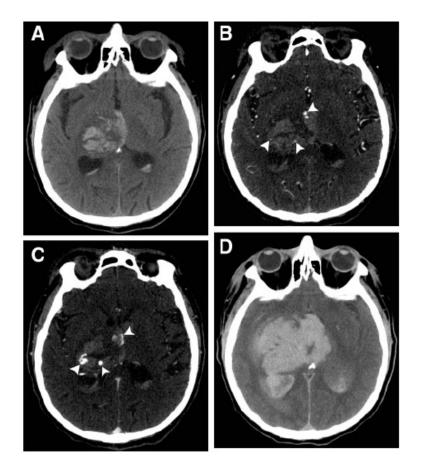


Identifying patients at risk for hematoma expansion – CTA and ICH: SPOT sign

• CT contrast extravasates into hematoma

- Spot sign, white arrows

- May predict hematoma expansion
 - Image from: Delgado Almandoz et al.Stroke, 40 (9): 2994. 2009





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Neuroimaging

- Early diagnosis of *underlying vascular abnormalities* can influence clinical management and guide prognosis
- Risk factors:
 - Age < 65,
 - Female
 - Nonsmokers,
 - Lobar ICH,
 - Intraventricular extension
 - No history of HTN or coagulopathy

CT scan showing left hemisphere intraparenchymal hematoma with intraventricular extravasation



Image courtesy the UTHSCSA



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Neuroimaging

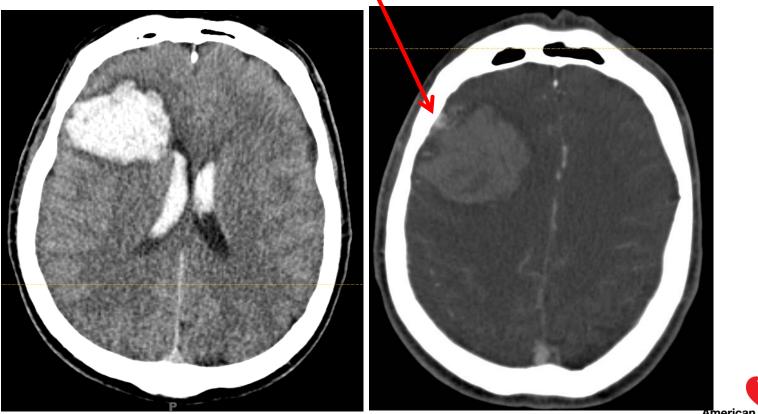
- MRI, MRA, MR venography (MRV) and CTA or CT venography (CTV) as well as catheter angiogram can identify specific causes of hemorrhage:
 - Arteriovenous malformation (AVM), tumors, moyamoya, and cerebral vein thrombosis
- Radiologic findings that are suspicious for underlying vascular abnormality:
 - Subarachnoid hemorrhage
 - Enlarged vessels or calcifications along margins of the ICH
 - Hyperattentuation within dural venous sinus or cortical vein
 - Presence of edema out of proportion to time of presumed ICH
 - Unusual hematoma shape
 - Presence of other abnormal structures in the brain (such as a mass)



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Neuroimaging

Arrow (on right image) shows small AVM associated with ICH (left image)



Images courtesy of C. Derdeyn, MD

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Emergency Department Management

- Following diagnosis, emergency physicians should:
 - Arrange for rapid admission to a stroke unit or neuroscience ICU (transfer if needed)
 - Initiate early management (blood pressure lowering, reversal of coagulopathy)



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Class I Recommendations	Class, Level of Evidence (LOE)
Rapid neuroimaging with CT or MRI is recommended to distinguish ischemic stroke from ICH. <i>(Unchanged from the previous guideline)</i>	Class I, LOE A
A baseline severity score should be performed as part of the initial evaluation of patients with intracerebral hemorrhage. (New recommendation)	Class I, LOE B



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Class II Recommendations	Class, Level of Evidence (LOE)
CT angiography and contrast-enhanced CT may be considered to help identify patients at risk for hematoma expansion. <i>(Unchanged from previous guideline)</i>	Class IIb, LOE B
CTA, CTV, contrast-enhanced CT, contrast-enhanced MRI, MRA, and MRV, and catheter angiography can be useful to evaluate for underlying structural lesions including vascular malformations and tumors when there is clinical and radiologic suspicion. <i>(Unchanged from previous guideline)</i>	Class IIa, LOE B



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Hemostasis and Coagulopathy, Antiplatelets and DVT prophylaxis

- Underlying hemostatic abnormalities can contribute to ICH.
- Patients on oral anticoagulation (OAC) constitute 12-20% of patients with ICH.
- This rate has increased with the aging population and increased use of anticoagulants in recent decades.
- Vitamin K antagonists (VKA) are the most frequently prescribed OAC but new agents (dabigatran, rivaroxaban, and apixaban) are being increasingly used.



Hemostasis and Coagulopathy, Antiplatelets and DVT prophylaxis

- For patients with a known coagulation factor deficiency or platelet disorder, replacement of the appropriate factor or platelets is indicated.
- For patients on an intravenous (IV) heparin infusion, protamine sulfate can be given IV at a dose of 1 mg per 100 U heparin (maximum dose 50 mg) with adjustment base on time elapsed since discontinuation of the heparin infusion.



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Vitamin K Antagonist-Related ICH

- Rapid correction of the international normalized ratio (INR) is recommended.
 - Specific target is unclear with various studies ranging from <1.3 to ≤ 1.5
- All treatment strategies should include IV vitamin K in a dose 5-10 mg given slowly IV
 - However, this is insufficient for reversal in the first hours
- Additional potential treatment strategies:
 - Fresh frozen plasma (FFP)
 - Prothrombin complex concentrates (PCCs)
 - The activated PCC FEIBA (factor VIII inhibitor bypassing activity)
 - Recombinant factor VIIa (rFVIIa)

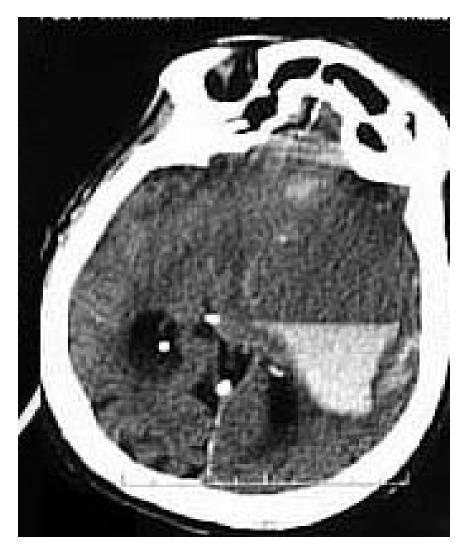


Vitamin K Antagonist-Related ICH

- FFP
 - Requires thawing and cross-matching, carries risk of allergic and infectious transfusion reactions, and often requires large volumes for INR correction
 - Study suggests that FFP may be insufficient for rapid correction of coagulopathy
- PCCs
 - Three-factor contains factors II, IX, and X (four-factor also contains factor VII)
 - Does not require cross-matching and is rapidly administered in small volumes
 - Studies have shown that PCCs provide a more rapid reversal of INR than FFP
 - May carry increased risk of thromboembolic events
- rFVIIa
 - Can rapidly normalized INR in VKA-associated ICH but does not replenish all of the vitamin K-dependent factors
 - May not restore thrombin generation as effectively as PCCs
 - Not currently recommended for use in warfarin-reversal



Anticoagulation and ICH



- CT scan of patient with OAC related ICH.
- Hematoma growth is common.
- Increases morbidity and mortality



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New Anticoagulant Medication-Related ICH

- There are no randomized trials of reversing agents for newer anticoagulants among patients with ICH
- Experience with reversal of these newer agents is limited
- Evaluation of aPTT/PT and consultation with hematologist is reasonable
- FEIBA or rFVIIa may be useful for dabigatran (direct thrombin agent)
- PCCs may be useful for rivaroxaban and apixaban (factor Xa inhibitors)
- Activated charcoal can be used if most recent dose was within previous couple of hours
- Hemodialysis is an option for dabigatran



Antiplatelet Medication-Related ICH

- Studies addressing the effect of prior antiplatelet agent use or platelet dysfunction on ICH growth and outcome have found conflicting results.
- Platelet function monitoring could be useful in assessing exposure to antiplatelet medications and guiding hemostatic interventions.
- Two randomized controlled trials are ongoing to evaluate the effectiveness of platelet transfusion in ICH patients taking antiplatelet agents.



Recombinant Factor VIIa in ICH Not Related to Anticoagulants

- rFVIIa has been tested in patients with non-OAC ICH
- A phase II randomized trial showed promising results of rFVIIa treatment compared to placebo in limiting hematoma growth but a subsequent phase III trial did not find clinical benefit.
- rFVIIa has been associated with increased frequency of thromboembolic events compared to placebo in both trials



Thromboprophylaxis in ICH Patients

- Patients with ICH have a high risk of thromboembolic disease.
- The CLOTS trials found overall that intermittent pneumatic compression begun as <u>early</u> as the day of admission reduced the occurrence of proximal DVT.
- These trials also found that graduated compression stockings did not reduce DVT, PE or death.



Thromboprophylaxis in ICH Patients

- ICH patients who develop DVT / PE may be considered for full systemic anticoagulation or placement of an inferior vena cava (IVC) filter
- Limited information is available to guide decision-making on IVC filter placement vs anticoagulation (as well as optimal regimen).
- Considerations:
 - Time from ICH to DVT/PE diagnosis
 - Hematoma size stability
 - Location of hematoma (lobar vs deep)
 - Potential to removed IVC filter at a later date



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III. Medical Treatment for ICH -Hemostasis

Class I Recommendations	Class, Level of Evidence (LOE)
Patients with a severe coagulation factor deficiency or severe thrombocytopenia should receive appropriate factor replacement therapy or platelets, respectively. <i>(Unchanged from previous guideline)</i>	Class I, LOE C
Patients with ICH whose INR is elevated due to VKA should have their VKA withheld, receive therapy to replace vitamin K dependent factors and correct the INR, and receive intravenous vitamin K <i>(Revised from previous guideline)</i>	Class I, LOE C
Patients with ICH should have intermittent pneumatic compression for prevention of venous thromboembolism beginning the day of hospital admission. <i>(Revised from previous guideline)</i>	Class I, LOE A



III. Medical Treatment for ICH -Hemostasis

Class II Recommendations	Class, Level of Evidence (LOE)
PCCs may have fewer complications and correct the INR more rapidly when compared with FFP and might be considered over FFP. <i>(Revised from the previous guideline)</i>	Class IIb, LOE B
For patients with ICH who are taking dabigatran, rivaroxaban, or apixaban treatment with FEIBA, other PCCs or rFVIIa might be considered on an individual basis. Activated charcoal might be used if the most recent dose was taken less than 2 hours previous. Hemodialysis might be considered for dabigatran. <i>(NEW recommendation)</i>	Class IIb, LOE C
The usefulness of platelet transfusion in ICH patients with a history of antiplatelet use is uncertain. <i>(Revised from the previous guideline)</i>	Class IIb, LOE C
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III. Medical Treatment for ICH -Hemostasis

Class II Recommendations (cont'd)	Class, Level of Evidence (LOE)
After documentation of cessation of bleeding, low-dose subcutaneous low-molecular-weight heparin or unfractionated heparin may be considered for prevention of venous thromboembolism in patients with lack of mobility after 1 to 4 days form onset. <i>(Unchanged from the previous guideline)</i>	Class IIb, LOE B
Protamine sulfate may be considered to reverse heparin in patients with acute ICH. (NEW recommendation)	Class IIb, LOE C
Systemic anticoagulation or IVC filter placement is probably indicated in ICH patients with symptomatic DVT or PE. The decision between these two options should take in to account several factors including time from onset, hematoma stability, cause of hemorrhage, and overall patient condition. <i>(NEW recommendation)</i>	Class IIa, LOE C



III. Medical Treatment for ICH -Hemostasis

Class III Recommendations	Class, Level of Evidence (LOE)
rFVIIa does not replace all clotting factors, and while the INR may be lowered, clotting may not be restored in vivo; therefore rFVIIa is not recommended for VKA reversal in ICH. <i>(Revised from the previous guideline)</i>	Class III, LOE C
Although rFVIIa can limit the extent of hematoma expansion in non-coagulopathic ICH patients, there is an increase in thromboembolic risk with rFVIIa and no clear clinical benefit in unselected patients. Thus rFVIIa is not recommended. <i>(Unchanged form previous guideline)</i>	Class III, LOE A
Graduated compression stockings are not beneficial to reduce DVT or improve outcome. (<i>Revised from previous guideline</i>)	Class III, LOE A



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III. Medical Treatment for ICH

Blood Pressure (BP) and Outcome in ICH

- Elevated BP is very common in acute ICH.
- High systolic BP is associated with:
 - Greater hematoma expansion
 - Neurological deterioration
 - Death and dependency



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III. Medical Treatment for ICH

Safety of Early Intensive BP Lowering Treatment

- Both the Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) trial and the pilot phase of the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage (INTERACT1) trial found *rapid reduction of SBP to < 140 mm Hg to be safe* within the early hours (3-6) following ICH
- The main phase of the INTERACT2 trial has shown no increase in death or serious adverse events from early intensive BP lowering



III. Medical Treatment for ICH



Efficacy of Early Intensive BP Lowering Treatment

- INTERACT2 phase III trial in 2839 patients with SBP 150-220 mm Hg within 6 hours of ICH (mild-to-moderate sized)
 - Intensive therapy (goal SBP < 140) group had a lower rate of death or major disability than the standard treatment (goal SBP < 180) group with an odds ratio of 0.87 (95% CI 0.75-1.01), p value = 0.06
 - Intensive therapy group were more likely to have better functional recovery (p=0.04) and better quality of life (p=0.002) than the standard group
 - There was no significant effect of intensive BP lowering treatment on hematoma growth
- There is less data available pertaining to safety and effectiveness of treatment in patients with very high BP (sustained BP > 220 mm Hg), larger and more severe ICH, and those requiring surgical decompression.



III. Medical Treatment for ICH – BP

Class I Recommendations	Class, Level of Evidence (LOE)
For ICH patients presenting with systolic BP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of systolic BP to 140 mm Hg is safe. <i>(Revised from the previous guideline)</i>	Class I, LOE A

Class II Recommendations	Class, Level of Evidence (LOE)
For ICH patients presenting with systolic BP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of systolic BP to 140 mm Hg can be effective for improving functional outcome. <i>(Revised from the previous guideline)</i>	Class IIa, LOE B
For ICH patients presenting with systolic BP above 220 mm Hg, it may be reasonable to consider aggressive reduction of BP with continuous intravenous infusion and frequent BP monitoring. <i>(NEW recommendation)</i>	Class IIb, LOE C

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General Monitoring

• Care of ICH patients in a dedicated neuroscience intensive care unit (ICU) is associated with lower mortality rate.

 Frequent vital sign checks, neurologic assessments, and continuous cardiopulmonary monitoring (including cycled BP cuff), ECG telemetry, and pulse oximetry probe should be standard.



Nursing Care

- Specific nursing care/training required for ICH patients in ICUs and delineated by the Brain Attack Coalition:
 - Surveillance and monitoring of ICP, cerebral perfusion pressure and hemodynamic function
 - Detailed assessments of neurologic function (NIHSS, GCS and Glasgow outcome scale)
 - Titration and implementation protocols for management of ICP, BP, mechanical ventilation, fever, and serum glucose
 - Prevention of complications of immobility through positioning, airway maintenance, and mobilization (within physiologic tolerance)



Class I Recommendations	Class, Level of Evidence (LOE)
Initial monitoring and management of ICH patients should take place in an ICU or dedicated stroke unit with physician and nursing neuroscience acute care expertise. <i>(Revised from the previous guideline)</i>	Class I, LOE B



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Glucose Management

- High blood glucose predicts an increased risk of mortality and poor outcome, independent of diabetes.
- Studies of tight glucose control with insulin infusions have shown conflicting results with concerns over increased incidence of hypoglycemia.
- Optimal management of hyperglycemia in ICH and the target glucose remain to be clarified.



Class I Recommendations	Class, Level of Evidence (LOE)
Glucose should be monitored. Both hyperglycemia and hypoglycemia should be avoided. (<i>Revised from the previous guideline</i>)	Class I, LOE C



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Temperature Management

- Fever is common after ICH
 - Especially in patients with intraventricular hemorrhage (IVH)
 - May be associated with hematoma growth
- Duration of fever is related to outcome and appears to be an independent prognostic factor in patient surviving the first 72 hours.
- Studies of fever treatment are limited and maintenance of normothermia has not been clearly demonstrated as beneficial.



Class II Recommendations	Class, Level of Evidence (LOE)
Treatment of fever after ICH may be reasonable. (NEW recommendation)	Class IIb, LOE C



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Seizure and Anti-Seizure Drugs

- Clinical seizures can be seen early (within one week) after ICH
 - Frequency may be as high as 16%
 - Cortical involvement of ICH is the most important risk factor
 - No association between clinical seizures and neurologic outcome or mortality has been shown
- Epilepsy occurs in up to 10% of young patients (18-50 years old) with risk factors including:
 - Stroke severity
 - Cortical location of the hematoma
 - Delayed initial seizures



Seizure and Anti-Seizure Drugs

- Studies of continuous electroencephalography (EEG) report electrographic seizures in 28-31% in select cohorts
- Prophylactic anticonvulsant medication has not been shown to be beneficial (and may be associated with increased death and disability when phenytoin is used).
- Clinical seizures or EEG seizures in patients with a change in mental status should be treated.
- Continuous EEG monitoring should be considered in patients with depressed mental status disproportionate to the degree of brain injury



Class I Recommendations	Class, Level of Evidence (LOE)
Clinical seizures should be treated with anti-seizure drugs. (Unchanged from previous guideline)	Class I, LOE A
Patients with a change in mental status who are found to have electrographic seizures on EEG should be treated with anti-seizure drugs. <i>(Unchanged from previous guideline)</i>	Class I, LOE C
Class II Recommendations	Class, Level of Evidence (LOE)
Continuous EEG monitoring is probably indicated in ICH patients with depressed mental status that is out of proportion to the degree of brain injury. (Revised from previous guideline)	Class IIa, LOE C
Class III Recommendations	Class, Level of Evidence (LOE)
Prophylactic anti-seizure medication is not recommended. (Unchanged from previous guideline)	Class III, LOE B

Management of Medical Complications

- Frequency of medical complications is high
 - One study noted at least one adverse event in 88% of placebotreated
- Most common complications:
 - Pneumonia
 - Aspiration
 - Respiratory failure/distress
 - Pulmonary embolism
 - Sepsis
- Approximately 50% of deaths after stroke are attributed to medical complications



Management of Medical Complications

- Dysphagia and aspiration are major risk factors for pneumonia
- Independent risk factors for dysphagia and percutaneous endoscopic gastrostomy (PEG) include:
 - Glasgow coma scale
 - Occlusive hydrocephalus
 - Mechanical ventilation
 - Sepsis
- Use of a formal screening protocol for dysphagia (e.g. water swallow test) has been associated with a decreased risk of pneumonia

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Management of Medical Complications

- Concurrent stroke and myocardial infarction (MI) are not uncommon
 - Austrian Stroke Registry noted 0.3% of patients suffered an MI over a median duration of 3 days
 - Other studies have shown that an elevated troponin level (>0.4 ng/mL) was found in 15-20% within 24 hours of admission and associated with increased in-hospital mortality
- History of prior MI and severity of deficits on admission are associated with occurrence of MI.
- Patients with an MI have higher in-hospital mortality and greater complications



Management of Medical Complications

- Neurogenic pulmonary edema (an increase in interstitial and alveolar fluid in setting of acute CNS injury) can occur in ICH
 - Presents abruptly and progresses quickly after the ICH
 - Intubation with mechanical ventilator support is often required
- ICH patient may also be at risk for acute respiratory distress syndrome (ARDS) from multiple causes
- Acute kidney injury, hyponatremia, gastrointestinal bleeding, impaired nutritional status, urinary tract infections, and post-stroke depression should also be screened and managed



Class I Recommendations	Class, Level of Evidence (LOE)
A formal screening procedure for dysphagia should be performed in all patients prior to the initiation of oral intake to reduce the risk of pneumonia. (NEW recommendation)	Class I, LOE B

Class II Recommendations	Class, Level of Evidence (LOE)
Systematic screening for myocardial ischemia or infarction with electrocardiogram and cardiac enzyme testing after ICH is reasonable. (NEW recommendation)	Class IIa, LOE C



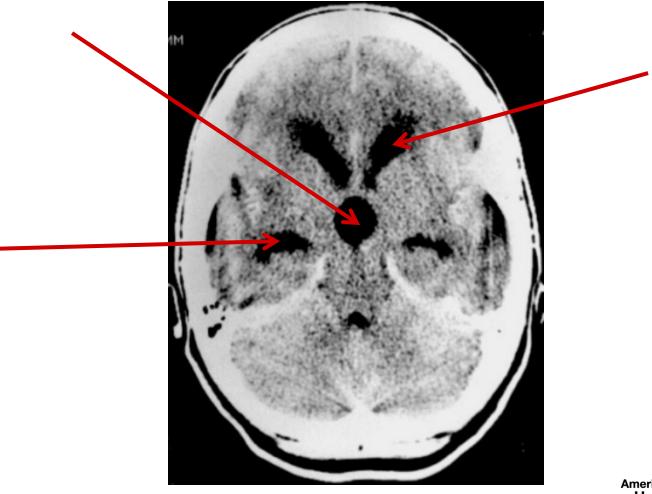
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ICP Monitoring and Treatment

- Limited data exist regarding the frequency of elevated ICP and its management in patients with ICH
 - Most indications for treatment and monitoring of ICP in ICH are generalized from those for traumatic brain injury (TBI)
- Intracranial hypertension is defined as ICP > 20 mm Hg
- There is evidence for differential pressure gradients in at least some cases so that ICP may be elevated in and around the hematoma but not distant from it
- Usual causes of elevated ICP are hydrocephalus from intraventricular hemorrhage (IVH) or mass effect from the hematoma (or surrounding edema)



Hydrocephalus





ICP Monitoring and Treatment

- Increased ICP also may be more common in younger patients and those with supratentorial ICH
- ICP is measured using devices inserted into the brain parenchyma or cerebral ventricles
 - Ventricular catheter (VC) allows for drainage of CSF, thereby reducing ICP
 - Parenchymal ICP device is inserted into brain parenchyma, does not allow for drainage of CSF
- There are risks (infection and and ICH) associated with these devices
- There is an absence of published studies showing that management of elevated ICP impacts ICH outcome



ICP Monitoring and Treatment

- Before insertion of a monitoring device, patient's coagulation status should be checked
- Decision to use a VC or a parenchymal catheter device should be based on whether there is a need to drain CSF to treat hydrocephalus or elevated ICP
- ICP monitoring & subsequent treatment might be considered in ICH with:
 - GCS score ≤ 8 (presumed related to hematoma mass effect)
 - Clinical evidence of transtentorial herniation
 - Significant IVH or hydrocephalus
- Goal is maintenance of ICP < 20 mm HG and cerebral perfusion pressure (CPP) of 50-70 mm Hg



ICP Monitoring and Treatment

- Methods of treating elevated ICP include:
 - Elevation of head to bed to 30°
 - Use of mild sedation
 - Avoiding collar-endotracheal tube ties that might constrict cervical veins
 - Mannitol or hypertonic saline may be used for **acute** elevations
 - CSF drainage (in patients with outflow obstruction)
 - Hematoma evacuation or decompressive craniectomy (see Surgical Treatment of ICH section)
 - Salvage therapies might include barbituate coma or mild hypothermia
- Corticosteriods should not be used as they are not effective in ICH and increase complications



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V. Procedures/Surgery – ICP

Class II Recommendations	Class, Level of Evidence (LOE)
Patients with a GCS score ≤ 8 , those with clinical evidence of transtentorial herniation, or those with significant IVH or hydrocephalus might be considered for ICP monitoring and treatment. A cerebral perfusion pressure of 50 to 70 mm Hg may be reasonable to maintain depending on the status of cerebral autoregulation. <i>(Unchanged from previous guideline)</i>	Class IIb, LOE C
Ventricular drainage as treatment for hydrocephalus is reasonable, especially in patients with a decreased level of consciousness. <i>(Revised from previous guideline)</i>	Class IIa, LOE B
Class III Recommendations	Class, Level of Evidence (LOE)
Corticosteroids should not be administered for treatment of elevated ICP in ICH. (NEW recommendation)	Class III, LOE B



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Intraventricular Hemorrhage

- Intraventricular hemorrhage (IVH)
 - Occurs in about 45% of patients with spontaneous ICH
 - Is an independent factor associated with poor outcome
 - Is associated with an increased risk of death
- Types of IVH:
 - Primary (confined to ventricles)
 - Secondary (originating as an extension of ICH)
- Most IVH is secondary and related to hypertensive hemorrhages in the basal ganglia and/or thalamus



Image courtesy of C. Derdeyn, MD

Intraventricular Hemorrhage

- Ventricular catheter (VC) alone may be ineffective treatment due to difficulty maintaining catheter patency and slow removal of blood
- Meta-analysis of studies using VC alone vs VC plus intraventricular administration of fibrinolytic agent found a significant decrease in mortality in VC plus fibrinolytic group
- CLEAR-IVH trial
 - − Included 100 patients with IVH due to spontaneous ICH ≤ 30 mm³
 - Evaluated VC versus VC plus rt-PA
 - VC plus rt-PA group had significantly lower ICP and fewer VC obstructions requiring replacement, non-significantly shorter duration of VC use
 - No significant difference in adverse events between 2 groups
 - Phase III (CLEAR III) trial is in progress



Intraventricular Hemorrhage

- Additional reported procedures for managing IVH include:
 - Endoscopic surgical evacuation
 - Ventriculostomy
 - Early ventriculoperitoneal shunting
 - Endoscopic third ventriculostomy
 - Lumbar drainage
- Studies of endoscopic surgical evacuation have not shown differences in long-term morbidity and mortality but report lower rates of permanent CSF diversion after endoscopy compared to VC



V. Procedures/Surgery – IVH

Class II Recommendations	Class, Level of Evidence (LOE)
Although intraventricular administration of rt-PA in IVH appears to have a fairly low complication rate, efficacy and safety of this treatment is uncertain. <i>(Revised from previous guideline)</i>	Class IIb, LOE B
The efficacy of endoscopic treatment in IVH is uncertain. (NEW recommendation)	Class IIb, LOE B



Surgical Treatment of ICH (Clot Removal)

- Role of surgery for most patients with spontaneous ICH remains controversial.
- Randomized trials comparing surgery (hematoma evacuation) to conservative management have not demonstrated a clear benefit.



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Craniotomy for Supratentorial Hemorrhage

- STITCH trial
 - Early surgery vs conservative management for supratentorial ICH when clinical equipoise is present
 - "early surgery" = within 24 hours of randomization
 - There was no overall statistically significant difference in mortality or functional outcome between the two groups
- STITH II trial
 - Early surgery vs conservative management for conscious patients with superficial lobar hemorrhage (10-100 mm³ within 1 cm of cortical surface), without IVH, and admitted within 48 hours of onset
 - 41% in early surgery vs 38% in conservative group with favorable outcome
 - 21% of conservative management ultimately underwent surgery
 - No advantage to early surgery for patients in good prognosis group
 - Non-significant survival advantage in the surgical group



Craniotomy for Supratentorial Hemorrhage

- Early hematoma evacuation has not been shown beneficial in the two largest randomized trials.
- Unclear whether surgery may benefit specific groups with supratentorial ICH.



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Craniotomy for Posterior Fossa Hemorrhage

- Deterioration can occur quickly in cerebellar hemorrhage
 - Obstructive hydrocephalus
 - Mass effect on brainstem
- Nonrandomized studies suggest that patients with cerebellar hemorrhage that is:
 - > 3 cm in diameter
 - Associated with brainstem compression
 - Associated with hydrocephalus
 - have better outcomes with surgical decompression
- Attempting to control ICP via means other than hematoma evacuation is not recommended and may be harmful



V. Procedures/Surgery

Craniectomy for ICH

- Potential of decompressive craniectomy (DC) to improve outcomes has not been well studied.
- STITCH trial suggests improved outcomes with DC in patients with:
 - Coma (GCS < 8)</p>
 - Significant midline shift
 - Large hematomas
 - ICP that did not normalize with medical management
- Systematic review suggests that DC with hematoma evacuation might be safe and improve outcomes.



V. Procedures/Surgery

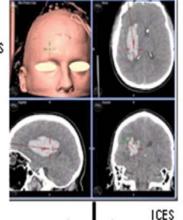
Minimally Invasive Surgical Evacuation of ICH

- Recent randomized studies suggest better outcomes with less invasive approaches compared to standard craniotomies
- MISTIE II trial
 - Minimally invasive surgery plus rt-PA for intracerebral hemorrhage evacuation vs medical management (small study)
 - Significant reduction in perihematomal edema in evacuation group
 - Trend towards improved outcomes in evacuation group
- MISTIE III trial in currently in progress



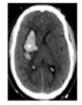
Example of minimally invasive surgical approach

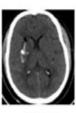
Common in MISTIE and ICES Preop stability and stereotactic approach



MISTIE Long axis trajectory One suction point, brief, no irrigation Catheter remains in hematoma Rt-R41 mg q8 hrs up to 72 hrs total

Long axis trajectory Two suction/irrigation points: 2/3 depth and 1/3 depth 30-60 minutes duration Endoscopic guided hemostasis





Postop

72 hrs

Post endoscopic

Paul M. Vespa et al. Stroke. 2013;44:S79-S82

The minimally invasive surgical approach for minimally invasive surgery thrombolysis plus recombinant tissue-type plasminogen activator for intracerebral hemorrhage evacuation (MISTIE) and intraoperative computed tomography (CT)–guided endoscopic surgery (ICES



V. Procedures/Surgery

Timing of Surgery

- Timing of surgery for ICH remains controversial
- Some trials suggest improved outcomes with early surgery (pooled analysis indicated within 8 hours of hemorrhage)
- Ultra-early (within 4 hours) craniotomy was found to increase the risk of rebleeding in a small study.



V. Procedures/Surgery – Surgical Treatment

	Class, Level of Evidence (LOE)
Patients with cerebellar hemorrhage who are deteriorating neurologically or who have brainstem compression and/or hydrocephalus from a ventricular obstruction should undergo surgical removal of the hemorrhage as soon as possible. <i>(Unchanged from previous guideline)</i>	Class I, LOE B

Class II Recommendations	Class, Level of Evidence (LOE)
For most patients with supratentorial ICH, the usefulness of surgery is not well established (<i>Revised from previous guideline</i>) Specific exceptions and potential subgroup considerations are outlined below:	Class IIb, LOE A
A policy of early hematoma evacuation is not clearly beneficial compared to hematoma evacuation when patients deteriorate (NEW recommendation)	Class IIb, LOE A
Supratentorial hematoma evacuation in deteriorating patients might be considered as a life-saving measure. (NEW recommendation)	Class IIb, LOE C



V. Procedures/Surgery – Surgical Treatment

Class II Recommendations, cont'd	Class, Level of Evidence (LOE)
Decompressive craniectomy with or without hematoma evacuation might reduce mortality for patients with supratentorial ICH who are in coma, have large hematomas with midline shit, or have elevated ICP refractory to medical management. (NEW recommendation)	Class IIb, LOE C
The effectiveness of minimally invasive clot evacuation utilizing stereotactic or endoscopic aspiration with or without thrombolytic usage is uncertain. <i>(Revised from previous guideline)</i>	Class IIb, LOE B
Class III Recommendations	Class, Level of Evidence (LOE)
Initial treatment of these patients (see Class I recommendation above) with ventricular drain rather than surgical evacuation is not recommended. <i>(Unchanged from previous guideline)</i>	Class III, LOE C



VI. Outcome Prediction and Withdrawal of Technological Support

- Models have been developed to predict mortality and function outcome based on:
 - GCS or NIHSS
 - Age
 - Hematoma volume and location
 - Presence and amount of IVH
- These models do not take into account impact of do not attempt resuscitation (DNAR) orders or withdrawal of technological support (and are thus overly pessimistic in outcome prediction)
- Most patient deaths from ICH occur during the initial acute hospitalization, usually in the setting of withdrawal of support for presumed poor prognosis



VI. Outcome Prediction and Withdrawal of Technological Support

- Palliative care is an important aspect of care for severe ICH
 - Please see new AHA Palliative Care in Stroke Guidelines (Holloway 2014)
- Withdrawal of medical support and DNAR orders within the first day of hospitalization have been identified as independent predictors of outcome.
- DNAR orders may be proxy for overall lack of aggressive care when administered early after ICH
- Limiting care early after ICH may result in self-fulfilling prophecies of poor outcome



VI. Outcome Prediction and Withdrawal of Technological Support

Class II Recommendations	Class, Level of Evidence (LOE)
Aggressive care early after ICH onset and postponement of new DNAR orders until at least the second full day of hospitalization is probably recommended. (<i>Revised from previous guideline</i>) Patients with pre-existing DNAR orders are not included in this recommendation.	Class IIa, LOE B

Class III Recommendations	Class, Level of Evidence (LOE)
Current prognostic models for individual patients early after ICH are biased by failure to account for the influence of withdrawal of support and early DNAR orders. DNAR status should not limit appropriate medical and surgical interventions unless otherwise explicitly indicated. <i>(Revised from previous guideline)</i>	Class III, LOE C



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- Patients with ICH are at high risk of a recurrent event and of other major vascular disease.
 - Highest in the first year following the initial event
 - Cumulative risk of recurrence is 1% to 5% per year
- Risk factors for recurrence:
 - Hypertension (for both deep and lobar hemorrhages)
 - Older age
 - Higher prevalence of cerebral amyloid angiopathy (CAA)
 - Increased use of antithrombotic medication
 - Location of the initial hemorrhage (deep vs lobar)
 - Carriers of APOE ε2 or ε4 alleles
 - A prior ICH before the current ICH
 - Greater number of microbleeds on gradient-echo MRI
 - History of ischemic stroke, particularly a small vessel "lacunar"



Blood Pressure Management

- Modifiable risk factor for recurrent ICH
- PROGRESS trial (treatment with perindopril and indapamide)
 - Baseline BP reduced by an average of 12/5 mm Hg
 - Lowered risks of first and recurrent ICH
 - Lowest risk of recurrence in patients with lowest follow-up BP levels (median 112/72 mm Hg)
- Secondary Prevention of Small Subcortical Strokes (SPS3) study
 - Lowering target SBP to < 130 mm Hg significantly reduced risk of ICH
 - Greatest benefit seen in prevention of ICH in patients with established small vessel stroke disease



Blood Pressure Management

- Optimal timing for initiating BP lowering after ICH is unknown
 - INTERACT2 showed reduction to SBP < 140 within a few hours was safe
- Frequent alcohol use (> 2 drinks per day) and illicit drugs have been linked to elevated BP and ICH and should be avoided
- Tobacco use is associated with increased ICH risk and should be discontinued.



Management of Antithrombotics

- Use of anticoagulants in an aging population is associated with increased risk of ICH and its recurrence
- Additional risks for recurrent ICH in warfarin use:
 - CAA is an important cause of lobar hemorrhage in the elderly
 - Presence of microbleeds might increase risk of ICH recurrence
- Limited prospective data on risk of ICH recurrence and mortality following re-initiation of warfarin
- Balancing act between recurrent ICH and thromboembolism
- It has been suggested (using quality-adjusted life year expectancy)
 - Anticoagulation should be avoided after lobar ICH
 - Anticoagulation can be considered in patients with deep hemorrhage if the risk of thromboembolism is particularly high



Management of Antithrombotics

- Optimal timing for resumption of anticoagulation after ICH, if necessary, is uncertain (and no RCTs have been performed)
- Survival model based on observational study found that total risk of ischemic plus hemorrhagic stroke was minimized when anticoagulation was re-initiated after approximately 10 weeks
 - Delay of at least one month post-ICH was recommended
- Timing often depends on indication for anticoagulation
 - For prosthetic heart valves, early resumption may be necessary
 - For atrial fibrillation, antiplatelet monotherapy or percutaneous left atrial appendage closure may be safer than warfarin in some patients



Management of Antithrombotics

- Antiplatelet agents appear to be generally safe for use following ICH, including ICH due to CAA
- Meta-analyses suggest aspirin is associated with modest increase in ICH but absolute ICH risk appears to be small relative to absolute numbers of MI and ischemic strokes prevented.
- Usefulness of dabigatran, rivaroxaban, or apixaban as alternatives to warfarin in atrial fibrillation patients following ICH remains to be determined



<u>Statins</u>

- There are conflicting reports regarding use of statins in ICH
- Stroke Prevention with Aggressive Reduction in Cholesterol Levels (SPARCL) study
 - Benefit of high dose atorvastatin was offset by increased risk of ICH
 - Later ICH recurrence associated with:
 - Statin treatment
 - Increasing age
 - ♦ ICH as the qualifying stroke for enrollment
- Meta-analysis of 31 RCTs found no significant association between statin use and ICH
- Continued statin use after ICH has been associated with early neurologic improvement and improved 6 month mortality in small study
- There is no data on effect of statin discontinuation after ICH



Class I Recommendations	Class, Level of Evidence (LOE)
BP should be controlled in all ICH patients. (Revised from previous guideline)	Class I, LOE A
Measures to control BP should begin immediately after ICH onset (NEW recommendation)	Class I, LOE A
Class II Recommendations	Class, Level of Evidence (LOE)
When stratifying a patient's risk for recurrent ICH may affect management decision, it is reasonable to consider the following risk factors for ICH recurrence: 1) lobar location of the initial ICH; 2) older age; 3) presence and number of microbleeds on gradient echo MRI; 4) ongoing anticoagulation; and 5) presence of APOE ϵ 2 and ϵ 4 alleles. <i>(Revised from previous guideline)</i>	Class IIa, LOE B
A long term goal of target BP < 130/80 is reasonable (NEW recommendation)	Class IIa, LOE B



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Class II Recommendations, cont'd	Class, Level of Evidence (LOE)
Life style modifications including avoidance of alcohol use greater than 2 drinks per day, tobacco, and illicit drugs, and treatment of obstructive sleep apnea are probably beneficial. <i>(Revised from previous guideline)</i>	Class IIa, LOE B
Avoidance of long-term anticoagulation with warfarin as a treatment for non-valvular atrial fibrillation is probably recommended following warfarin-associated spontaneous lobar ICH because of the relatively high risk of recurrence. <i>(Unchanged from previous guideline)</i>	Class IIa, LOE B
Anticoagulation following non-lobar ICH and antiplatelet monotherapy following any ICH might be considered, particularly when there are strong indications for these agents. <i>(Unchanged from previous guideline)</i>	Class IIa, LOE B
The optimal timing to resume oral anticoagulation following anticoagulant-related ICH is uncertain. Avoiding oral anticoagulation for at least 4 weeks, in patients without mechanical heart valves, might decrease the risk of ICH recurrence. <i>(NEW recommendation)</i>	Class IIb, LOE B



Class II Recommendations, cont'd	Class, Level of Evidence (LOE)
If indicated, aspirin monotherapy can probably be restarted in the days following ICH, though the optimal timing is uncertain. <i>(NEW recommendation)</i>	Class IIa, LOE B
The usefulness of dabigatran, rivaroxaban, or apixaban in patients with atrial fibrillation and past ICH to decrease the risk of recurrence is uncertain. <i>(NEW recommendation)</i>	Class IIb, LOE C
There is insufficient data to recommend restrictions on the use of statins in ICH patients. <i>(Unchanged from previous guideline)</i>	Class IIb, LOE C



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Recovery

- There is variation among ICH patients in regards to speed and degree of recovery
- Generally, recovery is more rapid in first few weeks but may continue for many months
- Factors that influence recovery include:
 - Cognition, mood, motivation, and social support
 - Age
 - ICH volume and location
 - Level of consciousness at admission
 - Pre-ICH cognitive impairment



Rehabilitation

- There is a need to tailor services to ensure optimal recovery for patients
- Early supported hospital discharge and home-based rehabilitation programs have been shown to be costeffective
- Home-based therapy in stable patients has been shown to produce comparable outcomes to conventional outpatient rehabilitation



Rehabilitation

- In-hospital rehabilitation programs result in better improvement and outcomes than standard in-patient care
- Success of rehabilitation depends on care-giver training and support
- Education on secondary stroke prevention and means to achieve rehabilitation goals is a key



Class I Recommendations	Class, Level of Evidence (LOE)
Given the potentially serious nature and complex pattern of evolving disability, and increasing evidence for efficacy, it is recommended that all patients with ICH have access to multidisciplinary rehabilitation. <i>(Revised from previous guideline)</i>	Class I, LOE A

Class II Recommendations	Class, Level of Evidence (LOE)
Where possible, rehabilitation can be beneficial when begun as early as possible and continued in the community as part of a well-coordinated ('seamless') program of accelerated hospital discharge and home-based re-settlement to promote ongoing recovery. <i>(Unchanged from previous guideline)</i>	Class IIa, LOE B



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IX. Conclusion

Future Considerations

- Ongoing and future studies will seek to solidify the evidence for efficacy of lowering BP and refine the BP ranges and targets
- Similarly, ongoing and future studies will address whether the spot sign or other neuroimaging findings identify individuals more likely to benefit from BP lowering
- Studies will continue to seek subgroups of patients who might benefit from early surgery as well as if minimally invasive surgery can provide greater net benefit



IX. Conclusion

Future Considerations

- Neuroprotection of surrounding brain tissue from the toxic effects of the hematoma remains an area to be explored
- An important part of gains seen in ICH outcome is improved hospital care and this should remain a key part of future ICH research
- Improved ICH prevention and recovery have the greatest potential for reducing overall disease burden
- There is tremendous opportunity for improving outcomes by studying treatments or therapies for enhancing post-ICH recovery



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