AHA Scientific Statement

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage

A Statement for Healthcare Professionals From a Special Writing Group of the Stroke Council, American Heart Association

Joseph P. Broderick, MD; Harold P. Adams, Jr, MD; William Barsan, MD; William Feinberg, MD†; Edward Feldmann, MD; James Grotta, MD; Carlos Kase, MD; Derek Krieger, MD; Marc Mayberg, MD; Barbara Tilley, PhD; Joseph M. Zabramski, MD; Mario Zuccarello, MD

Intracerebral hemorrhage (ICH) is more than twice as common as subarachnoid hemorrhage (SAH) and is much more likely to result in death or major disability than cerebral infarction or SAH.[1] Although >315 randomized clinical therapeutic trials for acute ischemic stroke and 78 trials for SAH were complete or ongoing (oral communication, Cochrane Collaboration, May 16, 1995) as of 1995, only the results of 4 small randomized surgical trials (353 total patients)[2–5] and 4 small medical trials (513 total patients)[6–9] of ICH had been published. In these small randomized studies, neither surgical nor medical treatment has been shown conclusively to benefit patients with ICH.

Advancing age and hypertension are the most important risk factors for ICH.[10–15] ICH occurs slightly more frequently among men than women and is significantly more common among young and middle-aged blacks than whites of similar ages.[10,16] Reported incidence rates of ICH among Asian populations are also higher than those reported for whites in the United States and Europe. Pathophysiological change in small arteries and arterioles due to sustained hypertension is generally regarded as the most important cause of ICH.[11,12,14,17,18] Cerebral amyloid angiopathy is increasingly recognized as a cause of lobar ICH in the elderly.[19–23] Other causes of ICH include vascular malformations, ruptured aneurysms, coagulation disorders, use of anticoagulants and thrombolytic agents, hemorrhage into a cerebral infarct, bleeding into brain tumors, and drug abuse.[10]

Of the estimated 37 000 Americans who experienced an ICH in 1997, 35% to 52% were dead at 1 month; half of the deaths occurred within the first 2 days.[1,17,24] Only 10% of patients were living independently at 1 month; 20% were independent at 6 months.[10,24]

Although guidelines for medical treatment and surgical removal of ICH are available, management of ICH by neurologists and neurosurgeons varies greatly throughout the world.[25,26] Despite a lack of proven benefit for surgery to remove an ICH, it is estimated that 7000 such operations are performed annually in the United States.[10]

To address this understudied but common and devastating stroke subtype, the American Heart Association Stroke Council formed a task force to develop practice guidelines for the management of ICH and to suggest areas for future research. Task force members used the rules of evidence for specific treatments used by other panels (Table 1). These rules give greater credence to the results of well-designed clinical trials than anecdotal case reports or case series. The limited number of randomized controlled studies of treatment of ICH severely limit strong, positive recommendations for any intervention. Thus, these guidelines should be viewed as a basis for the development of future clinical trials, which are desperately needed.

Emergent Diagnosis of ICH and Its Causes

The classic presentation of ICH is sudden onset of a focal neurological deficit that progresses over minutes to hours with accompanying headache, nausea, vomiting, decreased consciousness, and elevated blood pressure. In the Harvard Stroke Registry and the Michael Reese Stroke Registry, 51% to 63% of patients with ICH had a smooth progression of neurological symptoms whereas 34% to 38% of patients had maximal symptoms at onset. By comparison, only 5% to 20% of the various ischemic stroke subtypes and 14% to 18% of patients with SAH had gradual progression of symptoms.[28] The early progression of neurological deficit in many patients with an ICH is frequently due to ongoing bleeding and enlargement of the hematoma during the first few hours.[29]

Patients with ICH uncommonly present with symptoms on awakening from sleep (15%).[28] An early decrease in level of consciousness is seen in ≈50% of patients with ICH, an uncommon early finding in patients with ischemic stroke.[28] Headache occurs in ≈40% of patients with ICH, compared with 17% of patients with ischemic stroke.[30] Vomiting is an important diagnostic sign, particularly if the hematoma lies within the cerebral hemisphere. In the Harvard Stroke Registry,[28] 49% of persons with a supratentorial ICH vomited

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†Deceased.

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TABLE 1. Levels of Evidence and Strength of Recommendation for Treatment of Patients With Acute Ischemic Stroke*

Level of evidence	
Level I	Data from randomized trials with low false-positive (α) and low false-negative (β) errors
Level II	Data from randomized trials with high false-positive (α) or high false-negative (β) errors
Level III	Data from nonrandomized concurrent cohort studies
Level IV	Data from nonrandomized cohort studies using historical controls
Level V	Data from anecdotal case series
Strength of recommendation	
Grade A	Supported by Level I evidence
Grade B	Supported by Level II evidence
Grade C	Supported by Levels III through V evidence

*Adapted from Cook et al.[27]

compared with 2% of patients with ischemia in the carotid territory and 45% of patients with SAH. Vomiting is common in patients with a stroke of any type in the posterior fossa. Elevation in blood pressure, often to very high levels, occurs in as many as 90% of patients with ICH. Seizures occur in only ≈6% to 7% of patients with ICH but are more common with lobar than deep hemorrhages.

A careful history from prehospital care providers or the family can identify head trauma as a possible cause, although this diagnosis may be difficult if onset of hemorrhage occurred while a patient was alone and if the patient was found unconscious. A good general medical history should be obtained to elicit other factors that may predispose to ICH, such as hypertension, use of anticoagulants or thrombolytics, use of illicit drugs, heavy use of alcohol, or hematologic disorders.

Despite the differences in clinical presentation between hemorrhagic and ischemic strokes, no collection of clinical features has sufficient predictive value to forego brain imaging.[15,31] Computed tomography (CT) is the key part of the initial diagnostic evaluation. First, it clearly differentiates hemorrhagic from ischemic stroke. In addition, CT demonstrates the size and location of the hemorrhage and may reveal structural abnormalities such as aneurysms, arteriovenous malformations, and brain tumors that caused the ICH as well as structural complications such as herniation, intraventricular hemorrhage, or hydrocephalus. Administration of contrast by the radiologist can often highlight suspected vascular abnormalities.

Clinicians try to determine the likely cause of a hemorrhage by its location in the brain as seen on the CT scan, the presence of structural abnormalities as seen in brain imaging, associated medical conditions such as hypertension, and the patient's age. Hemorrhages that originate in the putamen, global pallidum, thalamus, internal capsule, deep periventricular white matter, pons, and cerebellum, particularly in a patient with known hypertension, are often attributed to hypertensive small-vessel disease. In contrast, lobar hemorrhages in the very elderly are often thought to be due to amyloid angiopathy. These assumptions may be incorrect. For example, the majority of patients with lobar hemorrhage, including the elderly, have a history of hypertension.[32] Subtle vascular malformations may also be the cause of deep or lobar hemorrhages.

Halpin and colleagues[33] conducted a study to examine the role of angiography in ICH patients whose mean age was 49 years (range 10 to 70). CT findings that prompted the impression of a structural lesion were the presence of subarachnoid or intraventricular hemorrhage, abnormal intracranial calcification, prominent vascular structures, or the site of hemorrhage (eg, perisylvian hemorrhage). Of the 44 patients with these CT findings, 38 underwent angiography. Angiographic findings were positive in 32 of the 38 cases (84%) with identification of arteriovenous malformations in 23 patients and aneurysms in 9. Angiography was not performed for clinical reasons in 6 patients, and no abnormality was seen in the remaining 6. On the basis of CT findings, 58 patients were not thought to have an underlying structural lesion, but 42 underwent delayed angiography. Angiographic findings were positive in 10 patients in this group (24%), revealing unsuspected arteriovenous malformation in 8 (19%) and aneurysms in 2 (5%). A prospective study of angiography in patients with ICH by Zhu and colleagues[34] indicated that cerebral angiography has a low yield in identifying an underlying vascular abnormality in patients >45 years old who have a history of hypertension and a thalamic, putaminal, or posterior fossa ICH.

Timing of cerebral angiography depends on the patient's clinical state and the neurosurgeon's judgment about the urgency of surgery, if needed. For example, a young patient with a large lobar hematoma and acute herniation is not a candidate for preoperative angiography. By contrast, a stable older patient with a smaller temporal lobe hematoma, mild focal deficits, and CT findings suggestive of an arteriovenous malformation should undergo angiography before removal of the hemorrhage.

Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) have emerged as other useful tools for detecting structural abnormalities such as malformations and aneurysms.[35] Although MRI may miss small aneurysms and vascular malformations, it is superior to CT and angiography in detecting cavernous malformations. MRI can also provide detailed information about the time course of brain hemorrhage.

Other useful diagnostic tools include a complete blood count, prothrombin time, activated partial thromboplastin time, electrolytes, electrocardiography, and chest x-ray. The white blood cell count can detect underlying infection such as hemorrhages associated with endocarditis. Hemoglobin analysis may also provide clues to diagnosis and is an indicator of blood loss. Prothrombin time and activated partial thromboplastin time may offer clues to coagulation problems, either iatrogenic or acquired. Electrolytes can reveal evidence of primary renal failure as an associated cause of ICH or disturbances in sodium that may accompany brain hemorrhage. Electrocardiography can reveal underlying dysrhythmia or myocardial ischemia associated with brain hemor-

rhage. Chest x-ray may reveal underlying aspiration or another pulmonic process that may complicate treatment.

Diagnosis of ICH: Summary and Recommendations

1. ICH is a medical emergency of the highest degree with frequent early neurological deterioration or death. Vomiting, early change in level of consciousness, and high elevation of blood pressure in a patient with acute stroke suggest ICH.
2. CT of the head is the imaging procedure of choice in the initial evaluation of suspected ICH (level of evidence I, grade A recommendation).
3. Angiography should be considered for all patients without a clear cause of hemorrhage who are surgical candidates, particularly young, normotensive patients who are clinically stable (level of evidence V, grade C recommendation).
4. Angiography is not required for older hypertensive patients who have a hemorrhage in the basal ganglia, thalamus, cerebellum, or brain stem and in whom CT findings do not suggest a structural lesion. Most older patients with deep hemorrhages die or have severe morbidity related to the hemorrhage and are not candidates for angiography (level of evidence V, grade C recommendation).
5. Timing of cerebral angiography depends on the patient's clinical state and the neurosurgeon's judgment concerning the urgency of surgery, if needed.
6. MRI and MRA are helpful and may obviate the need for contrast cerebral angiography in selected patients. They should also be considered to look for cavernous malformations in normotensive patients with lobar hemorrhages and normal angiographic results who are surgical candidates (level of evidence V, grade C recommendation).

Treatment of Acute ICH

The lack of a proven medical or surgical treatment for ICH leads to great variation among physicians concerning both surgical and medical treatment.[26,31] Although guidelines based on scant data from randomized trials are uncertain at best and may be wrong at worst, they can provide a reasonable treatment approach at present while outlining questions for future study. Well-designed and well-executed randomized treatment studies of ICH are urgently needed.

Initial Management in the Emergency Department

Initial management should first be directed toward the basics of airway, breathing, and circulation, and detection of focal neurological deficits. In addition, particular attention should be given to detecting signs of external trauma. A complete examination should also include looking for complications such as pressure sores, compartment syndromes, and rhabdomyolysis in patients with a prolonged depressed level of consciousness (patients "found down").

Airway and Oxygenation

Although intubation is not required for all patients, airway protection and adequate ventilation are critical. Patients who exhibit a decreasing level of consciousness or signs of brain stem dysfunction are candidates for aggressive airway management. Intubation should be guided by imminent respiratory insufficiency rather than an arbitrary cutoff such as a specific Glasgow Coma Scale (GCS) score. Intubation is indicated for insufficient ventilation as indicated by hypoxia (pO_2 <60 mm Hg or PCO_2 >50 mm Hg) or obvious risk of aspiration with or without impairment of arterial oxygenation. Orotracheal intubation should be performed carefully, following institutional protocols such as maximal preoxygenation and administration of drugs to avoid reflex arrhythmias and/or blood pressure derangement, eg, atropine, thiopental, midazolam, propofol, and succinylcholine. Precautions should always be taken to prevent aspiration of gastric contents. All patients with endotracheal tubes receive nasogastric or orogastric tubes to prevent aspiration and are monitored for cuff pressure every 6 hours. Endotracheal tubes with soft cuffs can generally be maintained for ≤2 weeks. In the presence of prolonged coma or pulmonary complications, elective tracheostomy should be performed after ≈2 weeks. Oxygen should be administered to all patients presenting with a possible ICH.

Medical Management: Randomized Trials

Four small randomized trials of medical therapy for ICH have been conducted:[6–9] steroid versus placebo treatment (2),[8,9] hemodilution versus best medical therapy (1),[6] and glycerol versus placebo (1).[7] None of the 4 studies showed any significant benefit for the 3 therapies. In the study by Poungvarin et al,[8] patients who were treated with steroids were more likely to develop infectious complications than those treated with placebo. Thus, the medical guidelines below are based on the reported experience of treatment of ICH in clinical series as well as general guidelines for treatment of any acutely ill patient in a neuro–intensive care unit.

Blood Pressure Management

The optimal level of a patient's blood pressure should be based on individual factors such as chronic hypertension, elevated intracranial pressure (ICP), age, presumed cause of hemorrhage, and interval since onset. In general, recommendations for treatment of elevated blood pressure in patients with ICH are more aggressive than those for patients with ischemic stroke.[36] The theoretical rationale for lowering blood pressure is to decrease the risk of ongoing bleeding from ruptured small arteries and arterioles. A prospective observational study of growth in the volume of ICH did not demonstrate a relation between baseline blood pressure and subsequent growth of ICH, but frequent early use of hypertensive agents in this study may have obscured any relationship.[29] Conversely, overaggressive treatment of blood pressure may decrease cerebral perfusion pressure and theoretically worsen brain injury, particularly in the setting of increased intracranial pressure.

To balance these 2 theoretical rationales, the writing group recommends that blood pressure levels be maintained below a mean arterial pressure of 130 mm Hg in persons with a history of hypertension[37] (level of evidence V, grade C recommendation). In patients with elevated ICP who have an

TABLE 2. Blood Pressure Management in ICH

Elevated blood pressure (some suggested medications)	
Labetalol	5–100 mg/h by intermittent bolus doses of 10–40 mg or continuous drip (2–8 mg/min)
Esmolol	500 μg/kg as a load; maintenance use, 50–200 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Nitroprusside	0.5–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Hydralazine	10–20 mg Q 4–6 h
Enalapril	0.625–1.2 mg Q 6 h as needed
The following algorithm adapted from guidelines for antihypertensive therapy[95] in patients with acute stroke may be used in the first few hours of ICH (level of evidence V, grade C recommendation):	
1. If *systolic* BP is >230 mm Hg or *diastolic* BP >140 mm Hg on 2 readings 5 minutes apart, institute nitroprusside.	
2. If *systolic* BP is 180 to 230 mm Hg, *diastolic* BP 105 to 140 mm Hg, or mean arterial BP ≥130 mm Hg on 2 readings 20 minutes apart, institute intravenous labetalol, esmolol, enalapril, or other smaller doses of easily titratable intravenous medications such as diltiazem, lisinopril, or verapamil.	
3. If *systolic* BP is <180 mm Hg and *diastolic* BP <105 mm Hg, defer antihypertensive therapy. Choice of medication depends on other medical contraindications (eg, avoid labetalol in patients with asthma).	
4. If ICP monitoring is available, cerebral perfusion pressure should be kept at >70 mm Hg.	
Low blood pressure	
Volume replenishment is the first line of approach. Isotonic saline or colloids can be used and monitored with central venous pressure or pulmonary artery wedge pressure. If hypotension persists after correction of volume deficit, continuous infusions of pressors should be considered, particularly for low systolic blood pressure such as <90 mm Hg.	
Phenylephrine	2–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Dopamine	2–20 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Norepinephrine	Titrate from 0.05–0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$

See text for algorithm for antihypertensive therapy in patients with acute stroke.

ICP monitor, cerebral perfusion pressure (MAP–ICP) should be kept >70 mm Hg (level of evidence V, grade C recommendation). Mean arterial blood pressure >110 mm Hg should be avoided in the immediate postoperative period. If systolic arterial blood pressure falls below 90 mm Hg, pressors should be given. Antihypertensive agents and pressors recommended for treatment of blood pressure in ICH are presented in Table 2.

Nitroprusside, the most commonly used agent for severe elevations of blood pressure, is a vasodilatory agent that theoretically can increase cerebral blood flow and thereby intracranial pressure. This possible disadvantage has yet to be demonstrated in a clinical study.

Management of Increased ICP

ICP is considered a major contributor to mortality after ICH; thus, its control is essential. ICP may be managed through osmotherapy, controlled hyperventilation, and barbiturate coma.

Elevated ICP is defined as intracranial pressure ≥20 mm Hg for >5 minutes. A therapeutic goal for all treatment of elevated ICP is ICP <20 mm Hg and cerebral perfusion pressure (CPP) >70 mm Hg.[37] Optimal head position can be adjusted according to ICP values. Patients with suspected elevated ICP and deteriorating level of consciousness are candidates for invasive ICP monitoring. The GCS level that requires ICP monitoring should be based on rate of decline and other clinical factors such as CT evidence of mass effect and hydrocephalus. In general, ICP monitors should be placed in (but not limited to) patients with a GCS score of <9 and all patients whose condition is thought to be deteriorating due to elevated ICP (level of evidence V, grade C recommendation). The type of device depends on availability, experience, and situation. Intraventricular ICP monitors and intraparenchymal fiberoptic ICP devices are 2 commonly used methods of monitoring ICP.

In addition to the mass effect of the hematoma, secondary hydrocephalus may contribute to elevated ICP. Ventricular drains should be used in patients with or at risk for hydrocephalus. Drainage can be initiated and terminated according to clinical performance and ICP values. Because of infectious complications, external drainage devices must be checked regularly, and duration of placement ideally should not exceed 7 days (level of evidence V, grade C recommendation). Use of anti-infectious prophylaxis is recommended (level of evidence V, grade C recommendation).

Although universally accepted standardized therapy protocols for elevated ICP have not been established, the stepwise escalation of initial procedures to control ICP outlined in Table 3 can be followed. The beneficial effect of *sustained* hyperventilation on ICP is unresolved. In theory, reduction of ICP by hyperventilation ceases when the pH of cerebrospinal fluid (CSF) reaches equilibrium. In practice, this may not occur for many hours. Some authors believe that prolonged hyperventilation has a beneficial effect on brain water volume. As with osmotherapy, adverse rebound effects can occur if normal ventilation is resumed too quickly. When hyperventilation is deemed no longer necessary, gradual normalization of serum P_{CO_2} should occur over a 24- to 48-hour period. In general, if hyperventilation is instituted for elevated ICP, P_{CO_2} should be maintained between 30 and 35 mm Hg until ICP is controlled. In addition, most patients will require sedation with agents such as *propofol, benzodiazepines,* or *morphine* and treatment with intermittent muscular paralysis.

If elevated ICP cannot be controlled with the treatment alternatives in Table 3, induced barbiturate coma may be instituted. However, high-dose barbiturate therapy should be viewed as an option and not part of a standardized algorithm in the treatment of elevated ICP in patients with ICH. Short-acting barbiturates such as *thiopental* are known to effectively reduce elevated ICP. The effect is presumably mediated through reduction of cerebral blood flow and volume. In addition to reducing the volume of the normal brain, barbiturates reduce brain swelling, perhaps as a result of mild systemic hypotension, and may act as free radical scavengers. The complications of high-dose barbiturate administration (safe limit: ≈10 mg/kg per day) include hypotension, which is most pronounced at the time of bolus administration, and possible predisposition to infection. Systemic hypotension mainly results from decreased venous

TABLE 3. Management of ICP

Osmotherapy
The first medical line of defense is osmotherapy. However, it should not be used prophylactically. Mannitol 20% (0.25–0.5 g/kg every 4 h) is reserved for patients with type B ICP waves, progressively increasing ICP values, or clinical deterioration associated with mass effect (level of evidence V, grade C recommendation). Due to its rebound phenomenon, mannitol is recommended for only ≤5 d. To maintain an osmotic gradient, furosemide (10 mg Q 2–8 h) may be administered simultaneously with osmotherapy. Serum osmolality should be measured twice daily in patients receiving osmotherapy and targeted to ≤310 mOsm/L.
No steroids
Corticosteroids in ICH are generally avoided because multiple potential side effects must be considered and clinical studies have not shown benefit (level of evidence II, grade B recommendation).
Hyperventilation
Hypocarbia causes cerebral vasoconstriction. Reduction of cerebral blood flow is almost immediate, although peak ICP reduction may take up to 30 minutes after pCo_2 is changed. Reduction of pCo_2 to 35–30 mm Hg, best achieved by raising ventilation rate at constant tidal volume (12–14 mL/kg), lowers ICP 25% to 30% in most patients (levels of evidence III through V, grade C recommendation). Failure of elevated ICP to respond to hyperventilation indicates a poor prognosis.
Muscle relaxants
Neuromuscular paralysis in combination with adequate sedation can reduce elevated ICP by preventing increases in intrathoracic and venous pressure associated with coughing, straining, suctioning, or "bucking" the ventilator (levels of evidence III through V, grade C recommendation). Nondepolarizing agents, such as vecuronium or pancuronium, with only minor histamine liberation and ganglion-blocking effects, are preferred in this situation (levels of evidence III through V, grade C recommendation). Patients with critically elevated ICP should be pretreated with a bolus of a muscle relaxant before airway suctioning. Alternatively, lidocaine may be used for this purpose.

tone, baroreflex tone, and sympathetic activity. Cardiovascular side effects may be aggravated by concomitant dehydration promoted by osmotherapy and diminished cardiac filling pressures. Maximal reduction in cerebral metabolism is accompanied by electrocerebral silence (continuous EEG recording). Since some tolerance develops with continued administration of barbiturate, use of multiple small boluses may be considered (0.3 to 0.6 mg/kg).

Fluid Management

The goal of fluid management is euvolemia. Optimal central venous pressure (CVP) or pulmonary wedge pressure may vary from patient to patient. If hypovolemia is thought to contribute to hypotension, CVP should be maintained between 5 and 12 mm Hg or pulmonary wedge pressure at ≈10 to 14 mm Hg. Fluid balance is calculated by measuring daily urine production and adding for insensible water loss (urine output plus 500 mL for insensible loss plus 300 mL per degree in febrile patients). Electrolytes (sodium, potassium, calcium, and magnesium) should be checked and substituted according to normal values. Acidosis and alkalosis should be corrected according to blood gas analysis.

Prevention of Seizures

Seizure activity can result in neuronal injury and destabilization of an already critically ill patient and must be treated aggressively. Additionally, nonconvulsive seizures may contribute to coma in ≤10% of neuro–critical care patients. In patients with ICH, prophylactic antiepileptic therapy (preferably phenytoin with doses titrated according to drug levels [14 to 23 μg/mL]) may be considered for 1 month and then tapered and discontinued if no seizure activity occurs during treatment, although data supporting this therapy are lacking (level of evidence V, grade C recommendation).

Management of Body Temperature

Body temperature should be maintained at normal levels. *Acetaminophen 650 mg* or cooling blankets should be used to treat hyperthermia >38.5° C. In febrile patients or those at risk for infection, appropriate cultures and smears (tracheal, blood, and urine) should be obtained and antibiotics given. If ventricular catheters are used, CSF analysis should be performed to detect signs of meningitis; if present, appropriate antibiotic therapy should follow.

Other Medical Management Issues

Many patients who are delirious or stuporous are agitated. Hyperactivity is distressing to patients, caregivers, and family and may lead to self-injury. If psychological support is insufficient, prudent use of minor and major tranquilizers is recommended. Short-acting benzodiazepines or propofol are preferred. Other drugs such as analgesics and neuroleptics can be added if necessary. Doses and regimen should be titrated to clinical needs.

Pulmonary embolism is a common threat during the recovery period, particularly for bedridden patients with hemiplegia. Pneumatic devices decrease the risk of pulmonary embolism during hospitalization.

Depending on the patient's clinical state, physical therapy, speech therapy, and occupational therapy should be initiated as soon as possible.

Surgical Treatment of ICH

The ideal goals of surgical treatment of ICH should be to remove as much blood clot as possible as quickly as possible with the least amount of brain trauma from the surgery itself. If possible, surgery should also remove the underlying cause of ICH, such as an arteriovenous malformation, and prevent complications of ICH such as hydrocephalus and mass effect of the blood clot.

Craniotomy has been the standard approach for removal of ICH. Its major advantage is adequate exposure to remove the clot. More complete clot removal may decrease elevated ICP and local pressure effects of the blood clot on the surrounding brain. The major disadvantage of a more extensive surgical

TABLE 4. Randomized Surgical Trials of Supratentorial Hemorrhage (as of January 1998)

Trial	Treatment Groups	No. of Patients per Treatment Group	Dead or Disabled at 6 mo, %	Distinguishing Features of Study
McKissock[4]	Craniotomy	89	88	Pre-CT
	Best medical treatment	91	89	
Juvela et al[5]	Craniotomy	26	96	Mean time to treatment:
	Best medical treatment	26	81	14.5 h; earliest at 6 h
Batjer et al[2]	Craniotomy	8	75	Randomized only putaminal hemorrhages ≥3 cm in diameter
	ICPM	4	100	
	Best medical treatment	9	78	
Auer et al[3]	Endoscopic removal	50	74*	Positive benefits limited to patients with lobar hemorrhages
	Best medical treatment	50	90*	

ICPM indicates intracranial pressure monitor.
*Significant difference at $P<.05$ level; percentages estimated from Figure 2 in Reference 3.

approach is that it may lead to further brain damage, particularly in patients with deep-seated hemorrhages. In addition, the effectiveness of clot removal by craniotomy is far from ideal (Reference 31 and M. Zuccarello, et al, unpublished data, December 1998).

Technical advances in removal of ICH include improved localization of the hemorrhage by stereotactic devices or intraoperative ultrasound and better surgical techniques.[31,38,39]

Randomized studies, if properly performed, provide the best data on which to base clinical decisions. Unfortunately, as of January 1998, only 4 small randomized studies of surgical removal of ICH have been reported.[2–5] Most of the published reports, many of which are in the Japanese literature, are nonrandomized case series of surgically and medically treated patients. Technical innovations to remove blood clot are evolving but have not been tested in a randomized trial.

Randomized Studies: Surgical Removal of ICH

McKissock[4] reported the first randomized study of surgical removal of ICH for 180 patients during the pre-CT era (Table 4). Cases were included if clinical history, physical signs, and angiography supported the diagnosis of ICH. Hemorrhages thought to be located in the posterior fossa were excluded. Of 303 potentially eligible cases, 123 were excluded because of early death, rapid recovery, structural cause of the hemorrhage such as an aneurysm, or refusal of the primary physician. Of the 180 randomized cases, 9 patients did not have a hemorrhage or had a posterior fossa hematoma. Almost no patients underwent surgery before 24 hours after onset; most underwent surgery within 3 days. The proportion of surgically treated patients who were dead or totally disabled (71 of 89 cases [80%]) 6 months after discharge was higher than the proportion of patients treated medically (60 of 91 cases [66%]) (level of evidence II). McKissock's study was done when surgical and anesthesiological techniques, as well as monitoring of patients in intensive care units, differed substantially from those used today.

Juvela and colleagues[5] reported a randomized study of surgery versus best medical therapy for 52 patients with spontaneous supratentorial ICH. Hemorrhage was removed by craniotomy within a mean time of 14.5 hours after onset (range 6 to 48 hours). Surgically treated patients were significantly more likely than medically treated patients to have a worse GCS score on admission, a larger deep hemorrhage, and an intraventricular hemorrhage. A difference between the proportion of operated patients who were dead or dependent at 6 months (25 of 26 [96%]) and the proportion of patients treated medically (21 of 26 [81%]) was not detected ($P>$NS).

Batjer and colleagues[2] conducted a randomized trial of 3 strategies: best medical management, best medical management plus ICP monitoring, and surgical evacuation. Only patients with a deficit secondary to a putaminal hematoma ≥3 cm in diameter were eligible. All patients were randomized within 24 hours of onset. None of the 21 patients in the study were capable of returning to prestroke activity at 6 months, and only 4 were living independently at home. The proportion of surgical patients who were dead or in a vegetative state at 6 months (4 of 8 [50%]) was not significantly different from the proportion of patients in the group who had medical care and ICP monitoring (4 of 4 [100%]) or medical treatment without ICP monitoring (7 of 9 [78%]). The study was stopped prematurely because of poor recruitment and poor outcome in all 3 patient groups (level of evidence II).

Auer and colleagues[3] conducted a randomized trial of endoscopic aspiration of hemorrhage compared with best medical treatment. Patients were between 30 and 80 years old, had a hemorrhage >10 cm^3 in volume, received treatment and angiography within 48 hours of onset, had no identifiable vascular cause of hemorrhage, and were suitable for surgery from a general medical and anesthesiological point of view. Of 723 patients with intracerebral hematomas, 100 patients met the criteria for study entry. In the 50 patients randomized to surgery, the hemorrhage was evacuated through a burr hole by a neuroendoscope. After the endoscope was introduced, the hematoma was continuously rinsed with artificial CSF at a pressure of 10 to 15 mm Hg. The

mixture of blood clots and blood-stained CSF was removed by suction at regular intervals. Oozing vessels in the wall of the hematoma were coagulated with a laser built into the system, and the entire procedure was under direct visual control. More than 90% of the clot was evacuated in 15% of patients, between 70% and 90% in 29% of patients, and between 50% and 70% in 56% of patients. At 6 months, the mortality rate of the surgical group (42%) was significantly lower than that of the medical group (70%, $P<0.01$) (level of evidence II). A good outcome with minimal or no deficit was also seen more frequently in the surgically treated group (level of evidence II). In patients with large hematomas (>50 cm^3), quality of life was not affected by surgery, whereas the mortality rate was significantly lower. By contrast, endoscopic evacuation of smaller hematomas led to significantly better quality of life compared with those treated medically, but survival was similar for the 2 groups. Surgical benefit was mainly limited to patients with lobar hematomas and patients <60 years old.

Two other small randomized pilot studies that focus on early surgery for ICH have been reported recently. Morgenstern and colleagues[40] reported a single-center, randomized trial (STICH Trial) of standard craniotomy versus best medical therapy in patients with ICH; the goal was to perform surgery ≤12 hours after symptom onset. Patients had to have a supratentorial ICH with a volume ≥10 cm^3 and a GCS score of 5 to 15. Of the 34 patients in the randomized trial, 17 were randomized to removal of the ICH by standard craniotomy. The median time to surgery for the 17 patients was 8.3 hours (minimum 3.75 hours and maximum 26.1 hours). The 6-month mortality for the surgical group was 17.6% compared with 23.5% for the medical group (P=NS). The median 6-month Barthel index score for survivors in the surgical group was also similar to the median Barthel index score for the medical group. However, the groups were not balanced with regard to ICH location. Only 1 of the 17 patients (6%) in the surgical group had a lobar hemorrhage compared with 7 of 17 patients (41%) of the medical group ($P=0.04$).

M. Zuccarello and colleagues (unpublished data, December 1998) reported another single-center, randomized pilot trial of surgery versus best medical therapy whose goal was to treat patients within 24 hours of symptom onset and perform surgery within 3 hours of randomization. The 20 patients enrolled in this trial had to have an ICH with a volume >10 cm^3 on the baseline CT scan and a GCS score of 5 to 15. Patients randomized to the surgical group who had a large ICH that extended to the cortical surface had a standard craniotomy (n=6), whereas those who had a deep subcortical hemorrhage underwent stereotactic removal of the ICH with instillation of urokinase into the bed of the clot (n=4).

The median time from symptom onset to the operating room for the 10 patients in the trial who were randomized to surgery was 8.6 hours (25th to 75th percentile, 5.2 to 12.2 hours). The median reduction in volume of ICH from baseline (median 35 cm^3) to 24-hour CT (median 16 cm^3) was 44% (25th percentile to 75th percentile, 44% to 76%). Forty-four percent of the surgical group had a GCS score >3 at 3 months (prospective definition of good outcome—primary outcome measure of study) compared with 64% of the medical group (P=NS). The only 3-month outcome variable that favored surgery was the median National Institutes of Health Stroke Scale score (4 in the surgical group versus 14 in the medical group, $P=0.04$). Patients who underwent stereotactic removal of the ICH did well (3-month Barthel index scores of 100, 100, 90, and 85). However, as with the STICH trial, the 2 randomized groups were imbalanced. The medical group had more thalamic hemorrhages (n=3) than the surgical group (n=0), and the ICHs were smaller in patients who underwent stereotactic removal than in patients who underwent craniotomy.

These 2 pilot studies demonstrate the feasibility of very early surgical evacuation of ICH. The study by Zuccarello and colleagues suggests that stereotactic removal of ICH should be considered a part of future randomized studies. However, neither these 2 more recent small trials nor the 4 prior trials of surgery provide a clear rationale for surgical evacuation of ICH at present.

Nonrandomized Surgical Studies: Conventional Craniotomy

Numerous nonrandomized series comparing craniotomy and best medical treatment of ICH have been reported.[25,38,41–56] The most consistent finding of these series is variability in treatment.[25]

Nonrandomized treatment series of patients with cerebellar hemorrhage report good outcomes for surgically treated patients who have large (>3 cm) cerebellar hemorrhages or cerebellar hemorrhages with brain stem compression or hydrocephalus.[31,51–53] In these patients, medical management alone often results in bad outcomes. Smaller cerebellar hemorrhages without brain stem compression that are managed medically do reasonably well in the case series. For these reasons, neurosurgeons and neurologists advocate that large cerebellar hemorrhages with compression of the brain stem or obstruction of the fourth ventricle should be surgically removed as soon as possible. Surgical removal of large lobar hemorrhages in young patients who are clinically deteriorating has also been recommended based on anecdotal experience.[15,31] Standard craniotomy for surgical removal of primary brain stem or thalamic hemorrhages has been all but abandoned because of the extremely poor outcomes in almost all patients.[31]

A large, nonrandomized, multicenter study from Kanaya and Kuroda[38] in Japan evaluated conservative and surgical treatment of putaminal hemorrhages during the 1980s. Of the 7010 patients studied, 3635 received medical treatment alone and 3375 underwent surgery. The majority of patients who were alert or confused were treated medically and included 56% of all medically treated patients. However, 25% of all surgically treated patients were also in this category. Mortality in alert and confused patients was significantly lower in medically treated patients compared with surgically treated patients (level of evidence III). However, mortality in patients who were stuporous or worse was significantly lower in those who were surgically treated (level of evidence III).

Nonrandomized Studies: Newer Surgical Approaches

Kaneko and colleagues[41,57] reported the surgical removal of 100 putaminal hemorrhages within 7 hours of symptom onset

TABLE 5. Recommendations for Surgical Treatment of ICH

Nonsurgical candidates
1. Patients with small hemorrhages (<10 cm^3) or minimal neurological deficits (levels of evidence II through V, grade B recommendation).
2. Patients with a GCS score ≤4 (levels of evidence II through V, grade B recommendation). However, patients with a GCS score ≤4 who have a cerebellar hemorrhage with brain stem compression may still be candidates for lifesaving surgery in certain clinical situations.
Surgical candidates
1. Patients with cerebellar hemorrhage >3 cm who are neurologically deteriorating or who have brain stem compression and hydrocephalus from ventricular obstruction should have surgical removal of the hemorrhage as soon as possible (levels of evidence III through V, grade C recommendation).
2. ICH associated with a structural lesion such as an aneurysm, arteriovenous malformation, or cavernous angioma may be removed if the patient has a chance for a good outcome and the structural vascular lesion is surgically accessible (levels of evidence III through V, grade C recommendation).
3. Young patients with a moderate or large lobar hemorrhage who are clinically deteriorating (levels of evidence II through V, grade B recommendation).
Best therapy unclear
All other patients.

and 60 hemorrhages within 3 hours of onset. Patients had a baseline GCS score of 6 to 13 with obvious hemiplegia. Most of the patients "had a hematoma volume of more than 20 to 30 cc, with a midline shift of more than 5 mm." The surgical technique was craniotomy by a transsylvian or transtemporal approach, depending on the size and location of the hemorrhage. Patients with mild symptoms or GCS scores ≤5 were treated conservatively. At 6 months, 7 (7%) of the patients had died, 15 (15%) had full recovery, and 35 (35%) were living independently at home (level of evidence IV).

Simple aspiration of ICH through a burr hole is relatively noninvasive and associated with lower morbidity than craniotomy. However, early series reported poor localization of the hematoma and inadequate removal.[48]

In 1978, Backlund and von Holst[58] reported a new surgical method for aspiration of hematoma in which a CT-guided stereotactic technique and a specially developed cannula were used. Many kinds of CT-guided stereotactic equipment have developed subsequently. Innovations in devices to break up and remove the blood clot include modifications of an Archimedes screw inside a cannula,[58] a specially designed ultrasonic aspirator,[59] a specially designed endoscope,[3] a modified nucleotome,[39,59] a double track aspiration,[60] intraoperative CT monitoring,[61] and repeated instillation of thrombolytics into the bed of a partially aspirated hematoma. Intraoperative ultrasound has also been used to identify the hemorrhage and monitor its removal in real time.[38] These innovative stereotactic aspiration techniques have been used on hemorrhages in all brain locations.

Kanaya and Kuroda[38] reported that rebleeding after surgery was seen in 10% of patients who underwent craniotomy, 5% who underwent CT aspiration, and 6% who had ultrasound-guided aspiration. On average, CT-guided aspiration removed 71% of the original hematoma whereas ultrasound-guided aspiration removed 81%. The percentage of hemorrhage removed did not significantly vary with the timing of the operation.

Other investigators using various CT-guided aspiration techniques, including thrombolytic instillation, have reported aspiration rates ranging on average from 30% to 90% over the first several days.[3,38,39,42,48,56,58–79] The rebleeding rate in aspiration studies without thrombolytics ranged from 0% to 16% with a mean of 5% among 896 cases.[3,38,39,59,64–67] With instillation of thrombolytics, the rebleeding rate in aspiration studies ranged from 0% to 10% with a mean of 4% among 392 cases.[39,42,56,62,64,69–79]

The most commonly used thrombolytic protocol has been administration of 6000 U of urokinase once or twice daily via a catheter into the bed of the hematoma with subsequent drainage and aspiration. This procedure is often repeated over several days until the majority of the hematoma has been aspirated. Some investigators have reported that aspiration with thrombolytic agents is less successful in removing clotted blood in the first hours after hemorrhage onset compared with removal of hemorrhage that has been present for several days.[39] Instillation of thrombolytics has also been used successfully for hemorrhage within the ventricular system.[80,81]

Guidelines for Surgical Removal of ICH: Summary

The decision about whether and when to operate remains controversial. Table 5 lists the current recommendations of the writing group based on the available literature. Patients with small hemorrhages (<10 cm^3) or minimal neurological deficits should be treated medically because they generally do well with medical treatment alone (levels of evidence II through V, grade B recommendation). Patients with a GCS score ≤4 should also be treated medically because they uniformly die or have extremely poor functional outcome that cannot be improved by surgery (levels of evidence II through V, grade B recommendation). Patients with cerebellar hemorrhage >3 cm in diameter who are neurologically deteriorating or who have brain stem compression and hydrocephalus from ventricular obstruction should have surgical removal of the hemorrhage as soon as possible (levels of evidence III through V, grade C recommendation). Stereotactic aspiration may be associated with better outcomes than standard craniotomy for moderate-sized cerebellar hemorrhages, but this hypothesis has yet to be tested in a randomized study (no recommendation). Young patients with large lobar hemorrhages (≥50 cm^3) who deteriorate during observation often undergo surgical removal of the hemorrhage. However, the efficacy of this approach is supported only by the small endoscopic study of Auer and colleagues[3] (levels of evidence II through V, grade B recommendation). An ICH

associated with a structural lesion such as an aneurysm or a vascular malformation may be removed if the patient has a chance for a good outcome and the structural vascular lesion is surgically accessible (levels of evidence III through V, grade C recommendation). Ultra-early removal of ICH by localized, minimally invasive surgical procedures is promising but untested (no recommendation).

Prevention of ICH

Because of the high morbidity and mortality associated with ICH and the lack of a proven therapy, prevention of ICH is critical. Until recently, most epidemiological studies and randomized trials did not categorize strokes by subtypes. Thus, much of the available data concerning the effectiveness of various treatments or lifestyle changes in reducing the risk of stroke do not indicate whether this effect includes ICH.

Blood Pressure Control

Treatment of mild to moderate hypertension significantly decreases the risk of stroke in both the middle-aged and elderly by 36% to 48%.[82–85] Unfortunately, few data concerning the effect on incidence of ICH have been reported for these intervention trials. Only the Systolic Hypertension in the Elderly Program Study (SHEP)[86] reported that treatment of isolated systolic hypertension in the elderly decreased the risk of ICH by 50%. Despite the lack of conclusive evidence, these intervention studies and the high prevalence of hypertension in persons with ICH indicate that treatment of hypertension is probably the most effective means of preventing ICH.

Other Risk Factors

A recent report from the Framingham Study[87] indicates that increased daily consumption of fruits and vegetables may decrease risk of stroke, including hemorrhagic stroke. Smoking cessation, although important in prevention of many diseases, including ischemic stroke and SAH, has not been shown to lower risk of ICH in an interventional or observational cohort study. Because heavy use of alcohol is a potential risk factor for ICH, control of alcohol intake is a reasonable but unproven recommendation.[88–90] A decline in the use of cocaine and other sympathomimetic agents should result in a decrease in ICH rates. Finally, 2 other means of preventing ICH are close monitoring of the anticoagulation level in patients treated with warfarin[91–93] and careful selection of patients. The ICH rate in patients who are receiving anticoagulation increases with an INR >3.[93] Careful selection of patients for thrombolysis for myocardial infarction and acute ischemic stroke can also decrease the risk of ICH.[94]

Prevention of ICH: Summary and Recommendations

1. Treatment of hypertension is strongly recommended as the most effective means to decrease morbidity and mortality due to ICH (levels of evidence I through II, grade A recommendation).
2. Careful control of the anticoagulation level in patients prescribed warfarin decreases risk of subsequent ICH (level of evidence I, grade A recommendation).
3. Careful selection of patients for thrombolytic treatment for acute myocardial infarction and acute ischemic stroke should result in a decline in ICH rates (level of evidence I, grade A recommendation).
4. Increased consumption of fruits and vegetables and avoidance of heavy alcohol and use of sympathomimetic drugs may decrease risk of ICH (levels of evidence III through V, grade C recommendation).

In the Future

The efficacy of any medical or surgical treatment has yet to be proved in a large randomized trial. We hypothesize that ultra-early treatment will be critical for patients with ICH, as it is for patients with ischemic stroke who are candidates for thrombolytic therapy.[94] Animal studies are needed to define the therapeutic window for surgical and medical treatment of ICH. Innovative surgical techniques to remove the hemorrhage quickly with minimal associated brain injury or rebleeding must be pursued. We hope that future large, multicenter, randomized studies will demonstrate that very early clot evacuation coupled with aggressive medical treatment of ICH may improve the dismal outcome of most patients with ICH after present therapies.

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KEY WORDS: AHA Scientific Statements ■ intracerebral hemorrhage ■ stroke, hemorrhagic ■ intracranial pressure ■ surgery