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Overview

Spontaneous intracerebral hemorrhage

LJILJANA BESLAĆ-BUMBAŠIREVIĆ
VIŠNJA PAĐEN
DEJANA R. JOVANOVIĆ
MAJA STEFANOVIĆ-BUDIMKIĆ

Department of Emergency Neurology,
Neurology Clinic,
Clinical Center of Serbia,
School of Medicine,
University of Belgrade,
Belgrade, Serbia

Correspondence:
Ljiljana Beslać-Bumbaširević
Clinical Centre of Serbia
Neurology Clinic
Dr Subotića 6, PO Box 12
11129 Belgrade 102, Serbia
Email: bumbasirevic@sezampro.rs

List of abbreviations

CAA	cerebral amyloid angiopathy
CT	computerized tomography
CTA	CT angiography
HE	hematoma expansion
ICH	intracerebral hemorrhage
ICP	intracranial pressure
ICU	intensive care unit
MRA	magnetic-resonance angiography
MRI	magnetic resonance imaging
RCT	randomized control trial

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Abstract

Intracerebral hemorrhage (ICH) represents cerebral parenchymal bleeding that may also extend into ventricular, and rarely, subarachnoid space. As a stroke subtype, it is associated with poor neurological outcome as well as high mortality. The worldwide incidence of ICH ranges from 10 to 20 cases per 100,000 population and increases with age. Different risk factors can cause ICH: hypertension (the main and the most common risk factor), cerebral amyloid angiopathy, previous use of anticoagulant therapy, excessive use of alcohol, and also other risk factors such as serum cholesterol levels and some genetic factors. Its clinical presentation usually consist of a decreased level of consciousness with headache and vomiting (in patients with a large hematoma), and depending on localization some specific neurological signs could be present: contralateral sensory-motor deficits of varying severity, aphasia, neglect, gaze deviation, hemianopsia, abnormalities of gaze, cranial-nerve abnormalities, as well as ataxia, nystagmus, and dysmetria.

Emergency diagnosis and management in neurological intensive care, or stroke units, with hypertension treatment, administration of haemostatic agents and general therapeutic measures for critically ill neurological patients may positively influence the outcome. Nevertheless, a larger number of randomized controlled studies are needed to answer several important questions, including how to treat hypertension, which haemostatic agent to use, as well as determining place and time of surgical treatment.

Nontraumatic intracerebral hemorrhage (ICH) represents cerebral parenchymal bleeding that may also extend into ventricular, and rarely, subarachnoid space. ICH, as a stroke subtype, is associated with poor neurological outcome as well as high mortality (about 40% per month) *(1, 2)*.

ICH represents around 10–15% of all strokes in Europe, USA and Australia, while in Asia it accounts for about 20–30%. It has been reported that every year 2 million people worldwide have ICH. *(2)*. Despite the fact that reduction in overall age adjusted stroke incidence has been registered, findings of meta-analysis have shown that the incidence of ICH between 1980 and 2008 had not declined *(3)*.

ICH can be classified as either primary or secondary, depending on the underlying cause of bleeding *(1, 4)*. (*Table 1*) Primary ICH is more common (78–88% of cases) and has its origin from chronic hypertension or amyloid angiopathy *(1)*.

Secondary ICH is less common, and it is associated with vascular abnormalities (e.g. arteriovenous malformations and aneurysms), impaired coagulation or tumors. Even though hypertensive ICH is the most

TABLE 1

Causes of intracerebral hemorrhage *(1, 4)*.

Causes	Properties
Primary intracerebral hemorrhage	
• Hypertensive vasculopathy	Hemorrhage in the striatum, thalamus, cerebellum and brainstem due to rupture of small arterioles
• Amyloid angiopathy	Caused by amyloid deposition (A-beta) in vascular media and adventitia. Associated with frequent recurrent lobar ICH
Secondary intracerebral hemorrhage	
• Vascular malformations	Rupture of abnormal small vessels
• Arteriovenous malformation – Arteriovenous dural fistula – Cavernous angioma – Venous angioma	The high risk of recurrent ICH can be reduced by surgical resection, endovascular embolisation and stereotactic radiosurgery
• Intracranial aneurysm	Rupture of saccular dilatation from a medium sized artery
• Cerebral venous sinus thrombosis	Results of hemorrhagic venous infarction
• Brain tumors	Results of necrosis and bleeding within tumor
• Coagulopathy	Related to anticoagulant use or thrombolytic use; Thrombocytopenia; Decreased synthesis of clotting factors (e.g. hemophilia, liver disease); Increased consumption of clotting factors (e.g. disseminated intravascular coagulation)
• Hemorrhagic transformation of ischemic stroke	Due to the ischemic damage of blood-brain barrier
• Sympaticomimetic drug or alcohol use	Underlying vascular abnormalities may be present
• Trauma	

frequent type of ICH, vascular abnormalities should always be considered in these circumstances because of high risk of recurrent hemorrhage and also regarding the choice of the right therapy.(5,6) Also, it should always be kept in mind that nowadays ICH as a consequence of the use of anticoagulant therapy is becoming increasingly frequent, and it occurs in almost 20% of cases in the USA *(7)*.

EPIDEMIOLOGY

Incidence

The worldwide incidence of ICH ranges from 10 to 20 cases per 100,000 population and increases with age. ICH is more common in men than women, particularly those older than 55 years, and in certain populations (the incidence in the Japanese population is 55 per 100,000 and it is similar as the one among blacks). Differences in the prevalence correlate with hypertension and the level of education (it is considered that lower levels are probably related to the lack of awareness regarding access to health care and primary prevention). Also, it is considered that high prevalence of hypertension and alcohol use in the Japanese population may influence the incidence *(1, 8)*.

Risk factors

Hypertension is the main and the most common risk factor in the development of ICH, particularly in the basal ganglia, thalamus, pons and deep cerebellar white matter. Hypertensive ICH in these localizations are particularly common in patients with chronic hypertension, and they are not in compliance with blood pressure management. In chronic uncontrolled hypertension the pathophysiologic mechanism is the development of Charcot Bouchard aneurysms within the distal microarteriolar vascular bed in three arterial territories: lenticulostriates, thalamoperforators and paramedian branches of the basilar artery *(9)*.

Most bleeding in ICH related to hypertension occur at or near the bifurcation of small penetrating arteries that originate from basilar arterie or the anterior, middle or posterior cerebral arteries. Multiple sites of rupture can be found in small artery branches of 50–700 μm in diameter, and some ruptures are associated with layers of platelet and fibrin aggregates *(10, 11)*. These lesions include breakage of elastic lamina, atrophy and fragmentation of smooth muscle, dissections and granular or vesicular cellular degeneration. In elderly patients lipid deposition as a result of severe atherosclerosis can be found. In small proportion of patients fibrinoid necrosis of the subendothelium with subsequent focal dilatations (microaneurysms) which can lead to rupture in small proportion of patients is being described *(10)*.

In case of elderly patients, especially those with lobar hemorrhage and without previous history of hypertension, amyloid angiopathy is most likely to be the cause of ICH. Cerebral amyloid angiopathy (CAA) is characterized by the deposition of amyloid-â peptide and degenerative changes (microaneurysm formation, concentric splitting, chronic inflammatory infiltrates, and fibrinoid

necrosis) in the capillaries, arterioles, and small and medium sized arteries of the cerebral cortex, leptomeninges, and cerebellum *(10)*. CAA can cause ICH especially in elderly people, and is commonly associated with variations in the gene encoding apolipoprotein E, as well as with familial syndrome in young patients, typically associated with mutations in the gene encoding amyloid precursor protein *(12)*. The risk of both sporadic and familial ICH is increased in case of white-matter abnormalities (e.g., leukoariosis), which suggest a shared vascular pathogenesis *(13)*.

In recent reports the incidence of primary ICH associated with pre-stroke hypertension seems to have declined, whereas there seems to have been an increase associated with antithrombotic use and presumed CAA in those aged over 75 years *(14)*. In patients who take oral anticoagulants ICH typically occurs in cases of either chronic hypertension or CAA, which might represent exacerbation of an existing risk of clinical and subclinical disease *(13)*. While the overall incidence of ICH in the general population is approximately 10 to 20 per 100,000 person-years, in patients on warfarin it is 2 to 3 per 100 per year, and appears to be increasing *(15, 16)*. In addition, once ICH occurs, the risk of death is up to twice as high in those on warfarin *(17)*.

Asymptomatic cerebral microbleeds are often associated with ICH. They represent perivascular deposits of hemosiderin which are remains from previous hemorrhages and can be seen on MRI as small MRI signal voids. It has been reported that they occur in about 5% of healthy population, especially in elderly people, with estimated 2 million of these asymptomatic hemorrhages per year in the USA. However, their long term effects are still undetermined. They represent a marker of existing vascular pathological processes and also a risk factor for other cerebrovascular diseases (e.g. the risk of warfarin associated ICH is >80-fold if microbleeds are present) *(18–20)*. They occur in 70% of patients with spontaneous ICH and in 40% with ischemic cerebrovascular diseases. They are often associated with CAA and small vessel diseases (leucoaraiosis and lacunes) – which are also associated with ICH as well. It is considered that lobar microbleeds are caused by CAA, while deep infratentorial microbleeds are caused by hypertension and atherosclerosis *(18, 19)*. The results from Rotterdam Scan Study have showed that cerebral microbleeds on MRI more frequently occur in elderly patients who use antiplatelet therapy, than in those who don't. Also, it is considered that the presence of microbleeds may increase the risk of ICH, especially if antiplatelet and/or anticoagulant therapy is being used *(20)*. However, no clear evidence has been found of this association and therefore the presence of microbleeds is not considered as a contraindication for thrombolytic therapy in patients with acute stroke *(19)*.

Another well defined risk factor for ICH is the excessive use of alcohol. Its mechanisms of actions are believed to be the impairment of normal coagulation mechanisms which directly affect the integrity of cerebral microvasculature.

Other risk factors for ICH include serum cholesterol levels of less than 160 mg per deciliter (4.1 mmol per liter), particularly among patients with hypertension, and genetic factors such as mutations in genes encoding the *a*subunit of factor XIII (which is involved in the formation of cross-linked fibrin) *(1)*.

CLINICAL FEATURES

A decreased level of consciousness is usually presented in patients with a large hematoma and it represents the result of increased intracranial pressure and the direct compression or distortion of the thalamic and brain-stem reticular activating system *(1, 2)*.

In case of a supratentorial ICH that involves the putamen, caudate, and thalamus contralateral sensory-motor deficits of varying severity are present, and they are a result of the involvement of the internal capsule. Abnormalities indicating higher level cortical dysfunction, including aphasia, neglect, gaze deviation, and hemianopsia, may occur as a result of the disruption of connecting fibers in the subcortical white matter and functional suppression of overlying cortex, known as diaschisis *(1)*.

In case of infratentorial ICH signs of brain-stem dysfunction are presented: abnormalities of gaze, cranial-nerve abnormalities, and contralateral motor deficits. Ataxia, nystagmus, and dysmetria are prominent when ICH involves the cerebellum.

Common nonspecific symptoms include headache and vomiting due to increased intracranial pressure (ICP) and meningismus resulting from blood in the ventricles.

In one fourth of patients with intracerebral hemorrhage who are initially alert, a deterioration in the level of consciousness occurs within the first 24 hours after onset of the hemorrhage *(21)*. The presence of a large hematoma and ventricular blood increases the risk of subsequent deterioration and death. The most common cause of the neurological worsening within the first three hours after the onset of hemorrhage is expansion of the hematoma. Worsening cerebral edema is also implicated in neurologic deterioration that occurs within 24 to 48 hours after the onset of hemorrhage *(2, 21)*.

Late deterioration is associated with progression of edema during the second and third weeks after the onset *(1, 2)*.

DIAGNOSIS

Patients with suspected stroke presenting to the emergency department should quickly be imaged with CT or MRI after initial stabilization in order to distinguish ischemic stroke from ICH. MRI with gradient echo can detect hyperacute ICH and is more accurate for the detection of microhaemorrhages, but it is much more time consuming and requires more patient cooperation, therefore most hospitals use CT scanning as the initial imaging modality for patients with suspected ICH *(22, 23)*.

In order to determine the etiology of ICH the initial imaging can be important. Hemorrhages in the deep nuclei of the brain including the putamen and thalamus, along with the pons and cerebellum, are more likely to be hypertensive in etiology while lobar hemorrhages near the surface of the brain may have an alternative etiology such as underlying vascular malformation or amyloid angiopathy. Imaging studies in patients with ICH can also identify hydrocephalus or other signs of ICP that may necessitate emergent therapy.

CT angiography (CTA) and magnetic-resonance angiography (MRA) can identify secondary causes of ICH but in some cases cerebral angiography is needed to diagnose aneurysms, arteriovenous malformations, dural venous thromboses, or vasculitis *(24)*.

Important factor for identification of continued bleeding is contrast extravasation seen on CTA. The CTA spot sign refers to one or more foci of contrast enhancement within an acute primary parenchymal hematoma visible on the source images of CTA. Data from several single--centre studies show that the CTA spot sign is a marker of increased risk of hemorrhage growth *(25-28)*. The CTA spot sign occurs in about a third of patients scanned within 3 h, and on the basis of data from the single-centre studies, the predictive value for substantial hematoma expansion within 3 h is high. The CTA spot positive sign was associated with a more severe clinical presentation, and it is highly predictive of hematoma expansion and for both intraparenchymal and intraventricular hemorrhage growth. The CTA spot sign is associated with a poor prognosis, high rates of early clinical deterioration, and mortality, often occurring within days after onset *(29)*. Anticoagulation therapy might simply result in a greater phenotypic expression of the spot sign, such as multiple spot signs, and result in greater hematoma expansion by prevention of clotting *(27-29)*. The study has concluded that CTA can identify a subpopulation of patients with ICH with the spot sign who are at high risk of substantial intracerebral and intraventricular hematoma expansion, early neurological deterioration, and early mortality *(28, 29)*. Randomized trials of haemostatic treatment, such as rFVIIa, should be done in ICH patients with a positive spot sign on CTA.

The other evaluation of patients with ICH focuses on identifying ICH risk factors in an attempt to discern the etiology of the hemorrhage. The physical examination looks for signs that may indicate head trauma such as lacerations or fractures. Blood pressure elevation after ICH is common and may provide a clue that hypertension or drug abuse is responsible. Laboratory investigations should focus on excluding systemic coagulopathy and urinary toxicology screen is important in order to rule-out drug-related ICH from cocaine or amphetamine abuse. Also, it should be kept in mind that some herbal substances can have either sympathomimetic properties (such as ephedrine) or interfere with normal coagulation, increasing the risk of ICH.

MANAGEMENT

Patients with ICH should be managed initially in an intensive care unit (ICU) which allows close, frequent monitoring of the neurologic and medical condition of the patient. A Cochrane meta-analysis of 31 RCTs showed that organized inpatient care in stroke units benefits patients with stroke (ischemic or due to ICH) by reducing the odds of death or dependency by 18% *(30)*. Large observational studies corroborate these findings in patients with ICH *(31, 32)*. One small, non-randomized, observational analysis, which was adjusted for some of the known influences on ICH prognosis, found survival after ICH to be better when managed in neuro-ICU compared to general ICU *(33)*.

The first line of action consists of airway support, blood-pressure control, ICP treatment, and anticoagulation reversal. Observational studies have shown that about 30% of patients with supratentorial hemorrhage and almost all patients with brainstem or cerebellar hemorrhage have either decreased consciousness or bulbar muscle dysfunction that require intubation *(1)*. In case of rapid deterioration, clinical evidence of transtentorial herniation, mass-effect or obstructive hydrocephalus on neuroimaging the neurosurgical consultation is necessary for possible intraventricular catheter placement or surgical evacuation and concomitant use of hyperventilation and intravenous mannitol *(1, 10, 34)*. The risk of neurological deterioration and cardiovascular instability is greatest in the first 24 h after symptom onset, therefore frequent assessment of patients' neurological status and hemodynamic variables in dedicated ICU is needed. 10% of ICU patients with ICH need tracheotomies, and early use might reduce the risk of aspiration and long-term mechanical ventilation *(10)*.

Early Hematoma Expansion (HE)

The frequent complication of ICH is the increase of hematoma which can be observed in 70% of cases and is defined as any increase in parenchymal volume or intraventricular invasion. Brott and coworkers found that the majority of relevant growth (defined as an increase of 33% of the hematoma volume on admission CT) occurs in 26% of cases within 4 hours after symptom onset, whereas an additional 12% of patients developed growth within the next 21 hours *(35)*. This suggests that growth occurs early in the course of ICH and early CT scan repetition is warranted to detect it.

Several studies have investigated various potential predictors of HE, and have identified several parameters (hematoma volume, intraventricular invasion, early neurological deterioration, treatment with recombinant coagulation factor VIIa, nonintensified blood pressure treatment), radiological characteristics (shorter time between onset and first CT, hematoma density heterogeneity on admission CT, occurrence of a »spot sign« in CT angiography), and laboratory characteristics (reduced platelet activity, elevated interleukin-6, elevated cellular fibro-

nectin) *(36)*. Contradictive results were found for elevated D-dimers and prior use of platelets *(36)*.

CT (PREDICT) study was to validate previous single centre observations in a prospective multicentre study with blinded evaluation of hematoma volume and CTA spot sign interpretation. This prospective multicentre study confirmed the association between the CTA spot sign and HE *(37)*. The primary analysis included 228 patients. Their median baseline ICH volume was 19.9 mL (range 1.5–80.9) in the CTA spot-sign positive group and 10.0 mL (0.1–102.7) in the CTA spot-sign negative group. For the primary study outcome, median ICH volume expansion was 8.6 mL (–9.3 to 121.7) in the CTA spot-sign positive group versus 0.4 mL (–11.7 to 98.3) in the CTA spot-sign negative group ($p<0.001$).

Therapeutic options to restrict HE can be divided into nonsurgical and surgical approaches, whereas the 2 might complement each other.

Nonsurgical approach

Nonsurgical approach includes therapeutic measures for restriction of HE (lowering blood pressure, and haemostatic treatment.) and conventional treatment of intracranial hypertension, hyperglycemia and high core body temperature, seizures and deep vein thrombosis prophylaxis

Blood Pressure Treatment

Since hypertension is a common cause of ICH, management of high blood pressure remains the central treatment early after a hemorrhage. Most experts agree that lowering the blood pressure of patients with ICH decreases the chances of continued bleeding and expansion of hemorrhage. Intravenous, short-acting blood pressure-lowering agents are usually initially used in the ICU, followed by a transition to oral long-acting blood pressure medications prior to discharge from the hospital. If blood pressure is reduced too aggressively, there is at least the theoretical risk of secondary ischemia due to decreased blood flow to areas of injured brain *(1, 10, 38)*.

The largest randomized trial addressing the effect of lowering blood pressure in ICH has recently been published, INTERACT (INTEnsive blood pressure Reduction in Acute Cerebral hemorrhage Trial), and it has compared intensive (target SBP 140 mm Hg) with guideline-based (target SBP 180 mm Hg) blood pressure reduction within the first 6 hours in 404 patients with acute ICH *(39)*. It has reported a trend toward reduction of HE, but no difference in outcome. Another prospective trial investigating this issue is the ATACH (Antihypertensive Treatment of Acute Cerebral Hemorrhage) trial: 60 patients with lobar, supratentorial ICH and a presenting SBP 170 mm Hg were treated with intravenous nicardipine within 6 hours from onset to achieve the blood pressure target tiers: (1) 170 to 200 mmHg; (2) 140 to 170 mmHg and (3) 110 to 140 mm Hg *(40)*. The authors report on HE, as judged by CT detection of 33% change in ICH volume at 24 hours which was observed in 33% (Tier 1), 15% (Tier 2), and 22% (Tier 3). The authors state that, together with INTERACT, their results form the basis for a larger RCT to compare intensive (target SBP 140 mm Hg) with standard (target SBP 180 mm Hg) treatment by intravenous nicardipine within 3 hours.

INTERACT has also analyzed the associations between measures of absolute and relative hematoma growth and 90-day poor outcomes of death and dependency (modified Rankin Scale score 3–5) in patients with ICH. The study has shown that a total of 10.7 mL (1 SD) increase in hematoma volume over 24 hours was strongly associated with poor outcome (adjusted OR 1.72, 95% CI 1.19–2.49; $p=0.004$). A 1 mL increase in hematoma growth was associated with a 5% (95% CI 2%–9%) higher risk of death or dependency. The study has concluded that medical treatments, such as rapid intensive blood pressure lowering, could achieve 2–4 mL absolute attenuation of hematoma growth which could contribute to modest but still clinically worthwhile (10%–20% better chance) outcome from ICH *(39)*.

Suggested Recommended Guidelines for Treating Elevated Blood Pressure in Spontaneous ICH

1. If SBP is ›200 mm Hg or MAP is ›150 mm Hg, then consider aggressive reduction of blood pressure with continuous intravenous infusion, with frequent blood pressure monitoring every 5 minutes.

2. If SBP is ›180 mm Hg or MAP is ›130 mm Hg and there is evidence of or suspicion of elevated ICP, then consider monitoring ICP and reducing blood pressure using intermittent or continuous intravenous medications to keep cerebral perfusion pressure 60 to 80 mm Hg.

3. If SBP is ›180 mm Hg or MAP is ›130 mm Hg and there is not evidence of or suspicion of elevated ICP, then consider a modest reduction of blood pressure (e.g., MAP of 110 mm Hg or target blood pressure of 160/90 mm Hg) using intermittent or continuous intravenous medications to control blood pressure, and clinically reexamine the patient every 15 minutes.

Haemostatic treatment

Various haemostatic therapies have been considered for use in ICH treatment, however most of them have not been tested in larger clinical trials so far. (24,41–43) In particular, rFVIIa seemed to be a promising candidate. In the Phase 2b trial that included 399 patients, it demonstrated treatment to significantly restrict HE, improve functional outcome, and reduce mortality despite the fact that significantly more arterial thromboembolic events occurred in the group with the highest dose of 160 g/kg. (6) The Phase III trial FAST (Factor seven for Acute hemorrhagic Stroke Trial) included 816 patients who did either receive 20 or 80 g/kg of rFVIIa or placebo(41) This trial confirmed the HE-restrictive properties of rFVIIa. However, this had no clinical effect either on functional outcome or on mortality.

TABLE 2

Factors arguing pro and contra restarting oral anticoagulation after ICH *(44)*.

	PRO	CONTRA
Cause of ICH		
• Hypertensive vasculopathy (hypertension adequately controlled)	+	
• Cerebral amyloid angiopathy		+
Microbleeds on gradient-echo magnetic resonance imaging		+
Indication for oral anticoagulation		
• Secondary prevention	+	
• Primary prevention		+
• Atrial fibrillation, high $CHADS_2$ score	+	
• Atrial fibrillation, low $CHADS_2$ score		+
• Mechanical heart valve	+	
• Anticipated difficulty in controlling the PT -INR		+
• Hypercoagulable state	+	

The use of oral anticoagulants such as warfarin, although probably rather a contributing than a causative factor, does not only lead to a higher incidence of ICH, but also to HE in 27% to 54% of the cases and well beyond the 24-hour time window that we define as early expansion *(13, 42, 43)*. This might at least partially explain a substantial increase in mortality of up to 70% *(43)*. Those with ICH secondary to treatment with warfarin should be reversed using vitamin K or fresh frozen plasma in order to replete clotting factors that have been inhibited by this medication. It has been recognized recently that coagulation abnormalities in the setting of warfarin can be reversed much more rapidly, and with smaller volumes of fluid, using compounds containing high levels of purified or recombinant clotting factors such as prothrombin complex concentrate *(2, 36)*. Future trials will be needed to weight the benefit of this more rapid strategy against the high cost of these medicines.

In ICH patients with coagulopathy the rapid reversal of these blood clotting abnormalities should be conducted in order to prevent continued HE. Patients with low platelet counts should receive a platelet transfusion.

There are no uniform criteria when oral anticoagulation should be restarted after ICH. There are multiple factors arguing pro or contra restarting anticoagulants after ICH *(44)*, (Table 2).

Mass-effects resulting from hematomas, edematous tissue surrounding hematomas, and obstructive hydrocephalus with subsequent herniation are a major cause of death in the first few days after ICH. Monitoring of ICP might identify the risk of neurological deterioration in patients with impaired consciousness. Two randomized trials showed no benefit on neurological improvement, mortality, and functional outcomes from regular use of intra venous mannitol boluses *(45, 46)*. Therefore, only short-term use of mannitol in patients with ICH and acute neuro logical deterioration or transtentorial herniation should be considered.

Hyperglycemia and high core body temperature in patients with ICH have each been associated with worse outcomes and should be treated. Glucose should be monitored and normoglycemia is recommended. Optimal management of hyperglycemia in ICH and the target glucose remains to be clarified. Hypoglycemia should be avoided *(38)*. Fever control can be accomplished with medications such as acetaminophen or through use of external or internal cooling devices *(38)*.

Seizures occur in 4-8% of patients with ICH and are more common with lobar (superficial) ICH location. Once seizures occur in these patients they should be treated aggressively with anti-epileptic medications (1, 10, 38). Patients with a change in mental status who are found to have electrographic seizures on EEG should be treated with antiepileptic drugs. Patients with seizures and ICH should be discharged from the hospital with anti-epileptic drugs for at least 3-6 months in order to prevent further seizures *(38)*. A more controversial issue is whether all ICH patients should be treated with anti-epileptic medications in order to prevent the initial occurrence of seizures. Currently, the decision to administer prophylactic anti-seizure medications varies widely by institution and individual physician, since there is little evidence to support this strategy and the relatively low frequency of seizures following most ICHs.

Deep vein thrombosis prophylaxis with low dose subcutaneous low-molecular-weight heparin or unfractionated heparin may be considered after 1 to 4 days from onset *(38)*.

TABLE 3

Management algorithm for patients with intracerebral hemorrhage.

Events	Emergency department	24 h	Days 1–7	Days 8–14	Post discharge
Neurological, respiratory, and haemodynamic monitoring	Intensive-care-unit monitoring		Reduce intensity of monitoring if clinically indicated		Regular outpatient monitoring of blood-pressure
Impaired consciousness (initial Glasgow coma scale score <8)	Early intubation and mechanical ventilation; consider monitoring of intracranial pressure			Consider tracheostomy if extubation not possible	
Airway compromise	Early intubation and mechanical ventilation; consider monitoring of intracranial pressure			Consider tracheostomy if extubation not possible	
High blood pressure (systolic blood pressure =180 mm Hg)	Intravenous antihypertensive medication titrated to effect		Oral antihypertensive drugs may be started	Oral antihypertensive drugs	Regular outpatient monitoring of blood-pressure
Emergent CT scan (or MRI)	Lobar haemorrhages	Consider surgical assessment in selected patients; cerebral angiography and MRI to exclude other vascular abnormalities			
	Cerebellar haemorrhage	Consider surgical evacuation; cerebral angiography in normotensive patients age =45 years			
	Basal ganglionic, thalamic, or pontine haemorrhage	Consider surgical evacuation; cerebral angiography in normotensive patients age =45 years			
	Intraventricular haemorrhage/hydro cephalus	Consider external ventricular drainage; cerebral angiography in patients with isolated intraventricular haemorrhage			
High international normalised ratio	Rapid reversal with fresh frozen plasma, prothrombin concentrate, factor VII, and vitamin K	Monitor INR for recurrent elevation			Restart anticoagulation in patients at high risk for embolism and low risk for recurrent intracerebral haemorrhage
High serum glucose (serum glucose =11.1 mmol/L)	Consider Intravenous insulin infusion		Oral hypoglycaemic drugs or subcutaneous insulin if required		
Hyperpyrexia	Oral paracetamol	Consider surface cooling or intravascular cooling; treat underlying aetiology			
Neurological deterioration	Emergency assessment, repeat CT scan, monitor intracranial pressure (if related to intracranial hypertension), and electroencephalography (for unexplained deterioration); neurosurgical assessment for patients with lobar or cerebellar haematomas				
Clinically significant intracranial mass-effect or transtentorial herniation	Consider short-term hyperventilation, hyperosmotic treatment, and neurosurgical assessment				
Clinical or electroencephalographic seizures	Consider short-term anticonvulsive treatment				Long-term anticonvulsant treatment in selected patients

Surgical Approach

Neurosurgical intervention can have the following aims: removal of the source of hemorrhage, staunching of the bleeding, and elimination of the effects of blood degradation products. The mere removal of blood by open craniotomy or stereotactic aspiration, that is, reduction of mass, cannot be regarded as a measure to restrict HE. Morgenstern and coworkers performed 2 small trials to answer the question of intervention timing. The first study revealed better outcome for those patients operated within 12 hours after onset *(47)*. However, the follow-up study with a time window of 4 hours showed a higher mortality due to an increased rebreeding rate *(48)*. Release of tamponating tissue pressure at this early stage of the disease may have caused rebleeding. Some authors therefore consider a combination of haemostatic with early surgery a promising alternative.

A Cochrane meta-analysis of ten RCTs involving 2,059 participants found a reduction in death or dependence from the neurosurgical evacuation of spontaneous supratentorial ICH *(49)*. However, most of the RCTs included in this meta-analysis were of modest quality, their methods differed, and the largest RCT (Surgical Trial in Intracerebral Hemorrhage STICH) found no difference between early surgery or initial conservative management *(50)*. A sub-group with lobar ICH within 1 cm of the cortical surface appeared to benefit from surgery *(38, 50)*. Timely decompression in cerebellar hematomas can lower morbidity and mortality related to compression of the brainstem *(10)*.

Table 3 shows management algorithm for patients with ICH according to the time after ICH onset *(10)*.

OUTCOME

In the study of Broderick et al. patients who initially had a score of less than 9 on the Glasgow Coma Scale and a hematoma volume of more than 60 ml had a mortality rate of 90 percent at one month, whereas patients with a score of 9 or greater and a hematoma volume of less than 30 ml had a mortality rate of 17 percent *(51)*.

The mortality rate six months after spontaneous intracerebral hemorrhage ranges from 23 to 58 per cent *(1, 10)*. A low score on the Glasgow Coma Scale, a large volume of the hematoma, and the presence of ventricular blood on the initial CT scan are factors that have been consistently identified as predictive of a high mortality rate *(1)*.

CONCLUSION

ICH is a small vessel disease with high mortality and morbidity. Emergency diagnosis and management in neurological intensive care, or stroke units, with hypertension treatment, administration of haemostatic agents and general therapeutic measures for critically ill neurological patients may positively influence the outcome. Nevertheless, a larger number of randomized controlled studies are needed to answer several important questions, including how to treat hypertension, which haemostatic agent to use as well as, determining place and time of surgical treatment.

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