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Diagnosis and Management of Acute Intracerebral Hemorrhage

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SYNOPSIS

Intracerebral hemorrhage (ICH) is the deadliest type of stroke and up to half of patients die in-hospital. Blood pressure management, coagulopathy reversal and intracranial pressure control are the mainstays of acute ICH treatment. Prevention of hematoma expansion and minimally invasive hematoma evacuation are promising therapeutic strategies under investigation. The aim of this paper is to provide an updated review on ICH diagnosis and management in the emergency department (ED).

Keywords

Intracerebral hemorrhage; hemorrhagic stroke; neurocritical care; blood pressure; coagulopathy; hematoma expansion

INTRODUCTION AND EPIDEMIOLOGY

Intracerebral hemorrhage (ICH) refers to primary, spontaneous, non-traumatic bleeding occurring in the brain parenchyma. ICH accounts for 10 to 20 % of all cerebrovascular events in the US[1] and is the deadliest type of stroke, with 30-day mortality up to 40% and severe disability in the majority of survivors[2]. Older age, hypertension (HTN), cerebral amyloid angiopathy (CAA) and oral anticoagulant treatment (OAT) are the most important risk factors for ICH[1,3,4]. Other ICH risk factors are summarized in box 1.

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DISCLOSURES

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Box 1

Risk factors for ICH

- **Hypertension** is the most important modifiable risk factor for ICH[1]. Poor control of blood pressure values is also associated with increased risk of recurrent ICH[85].
- **Cerebral amyloid angiopathy** (CAA) accounts for up to 20 % of all spontaneous ICH cases [4]. CAA related bleedings typically arise from cortico-subcortical brain regions and frequently affects elderly patients [4].
- **Alcohol intake:** this relationship appears to be dose-dependent [1].
- **Smoking**: current smoking increases the risk of ICH [1,3].
- **Cholesterol levels and statin use:** in contrast to ischemic stroke, hypercholesterolemia has a protective effect against the risk of ICH [1]. The association between statins and ICH risk is still unclear [86].
- **Diabetes:** a meta-analysis including almost 70.000 subjects provided evidence in favor of diabetes as a risk factor for ICH[87].
- **Genetics:** the gene most strongly associated with ICH is the Apolipoprotein E (APOE) gene and its ε2 and ε4 alleles [1]
- **Ethnicity:** ICH incidence is higher in Asian populations [1,2].
- **Drug abuse:** illicit drug consumption, such as cocaine and metamphetamine, is an important risk factor for ICH, especially in young adults [88].

PATHOPHYSIOLOGY

ICH represents an acute manifestation of an underlying progressive small vessel disease. Primary brain damage in the acute phase of ICH is caused by mechanical mass effect of the hematoma, leading to increased intracranial pressure (ICP) and consequent reduced cerebral perfusion and possible herniation[5]. Intraventricular extension of the hemorrhage (IVH) occurs in up to 40 % of ICH cases and is another important determinant of clinical deterioration and independent predictor of mortality [6].

CLINICAL PRESENTATION AND DIAGNOSIS

The clinical presentation of ICH and ischemic stroke is similar, typically consisting of abrupt onset of a focal neurologic deficit. Decreased level of consciousness, vomiting, headache, seizures and very high blood pressure might suggest the presence of ICH. However, none of these symptoms/signs is specific enough to distinguish hemorrhagic from ischemic stroke and therefore the diagnosis of ICH must always rely on neuroimaging[7]. A significant proportion of patients with ICH manifest a loss of at least two points on the

Glasgow Coma Scale (GCS) during acute evaluation[7] and coma can be the presenting symptom of posterior fossa hemorrhages [5].

Clinical assessment

Vital sign measurement and general physical examination should be performed in all patients. The American Heart Association and American Stroke Association (AHA/ASA) recommend routine application of a neurological baseline severity score, and the National Institutes of Health Stroke Scale (NIHSS) score appears to be feasible and useful in ICH patients[7]. The GCS is a widely known, rapid and reproducible tool for consciousness evaluation. The ICH score is a reliable and validated scale for rapid assessment of ICH severity [8].

Blood tests

In ICH patients complete blood count, electrolytes and creatinine, glucose and coagulation studies should be obtained.

Neuroimaging

A) Noncontrast computerized tomography—Noncontrast computerized tomography (NCCT) is a fast technique with excellent sensitivity for identifying acute ICH, and given its wide availability is considered the gold standard for the diagnosis of ICH in the ED[7,9]. Beyond the diagnosis of ICH, NCCT can provide useful elements such as ICH location, intraventricular extension, hydrocephalus, presence and degree of edema, and midline shift or brainstem compression secondary to the mass effect from the hematoma. Furthermore, ICH volume is a strong predictor of ICH outcome[10] and can be rapidly estimated in the ED with the ABC/2 technique (figure 1).

B) CT angiography—CT Angiography (CTA) is a useful diagnostic tool in the acute setting of ICH[11]. It is the most widely available, non-invasive technique for the detection of vascular abnormalities as secondary causes of ICH. The presence of lobar ICH, significant IVH, young age and absence of traditional cerebrovascular risk factors should trigger the suspicion of ICH secondary to vascular malformation or other intracranial pathology[7,11]. Prompt detection of these lesions is crucial and has a significant impact on patient management. Although CTA is an excellent noninvasive screening tool, digital subtraction angiography remains the gold standard investigation for diagnosis, and frequently endovascular treatment, of cerebral vascular malformations[9].

Presence of contrast extravasation within the hematoma on CTA images, also termed spot sign, is an independent predictor of hematoma expansion and poor outcome in patients with supratentorial ICH [12,13] (Figure 2). Furthermore, CTA spot sign is associated with active bleeding during surgical evacuation, and may help guide which patients may benefit from surgery [14]. The main drawback of CTA is cost and the additional radiation exposure[11]. While some are concerned about the risk of contrast induced nephropathy (CIN), there is debate in the literature about whether this entity exists, and there is no evidence that CTA increases the risk of nephropathy in ICH patients[15–17].

C) Magnetic resonance imaging—Magnetic resonance imaging (MRI) sensitivity for the diagnosis of ICH is equivalent to NCCT. MRI can be a useful technique to detect underlying secondary causes of ICH such as neoplastic lesions or hemorrhagic transformation of ischemic stroke[9]. Finally, in patients with poor kidney function, contrast allergies or other contraindication to CTA, brain vessel imaging can be achieved without contrast through magnetic resonance angiography (MRA). Given the cost, duration of the exam and poor tolerability for some patients, MRI is rarely used in the ED workup of ICH[7].

Natural history and clinical evolution

Even though ICH was traditionally viewed as a monophasic disease, growing evidence suggests that ICH is a dynamic disease, characterized by early significant expansion in up to one third of patients[18]. Early imaging after symptom onset, large baseline hematoma volume, anticoagulant therapy and presence of CTA spot sign are consistently the most powerful predictors of significant hematoma growth[13]. Other factors associated with clinical deterioration include perihematomal edema, intraventricular extension of the ICH, hydrocephalus, seizures, fever and infections[19].

ACUTE MANAGEMENT

Prehospital Care

The main goal of prehospital management of ICH is to provide airway and cardiovascular support to unstable patients, along with careful reconstruction of symptom onset timing, medical history and current medications[7]. Moreover, early notification reduces the time to NCCT scan in the ED and allows therefore a faster diagnosis of ICH[7]. Mobile stroke units have been developed to reduce the time from symptom onset to intravenous (IV) thrombolysis administration in patients with ischemic stroke[20]. This approach seems feasible and potentially useful also for ICH patients, allowing the possibility of early blood pressure management, reversal of coagulopathy and delivery of patients to tertiary care centers with neurosurgical and neurocritical care facilities[21].

Airway protection

Patients with ICH are often unable to protect the airway because of reduced consciousness. Endotracheal intubation may be therefore necessary, but this decision should be balanced against the risk of losing the neurologic examination. Rapid sequence intubation is typically the preferred approach in the acute setting. Pretreatment with lidocaine may be preferred as it may blunt a rise in intracranial pressure (ICP) associated with intubation[22].

Blood pressure management

The majority of patients suffering ICH present with elevated BP levels in the acute phase. BP elevation is associated with higher risk of hematoma growth and poor outcome[5] and is therefore an appealing target for ICH treatment. The most robust data on BP management comes from the INTERACT2 study, a large clinical trial randomizing patients to one of two different BP control strategies (SBP<140mmHg vs. SBP<180mmHg for the first 24 hours). The study failed to meet its primary endpoint, and did not definitively demonstrate improved outcome with intensive BP treatment (Systolic BP target<140 mmHg)[23]. However, intensive

BP lowering appeared safe, and numerous secondary measures of outcome appeared to be superior with the intensive strategy. As a result, some argue that the weight of evidence is now in favor of maintaining SBP<140mmHg in the acute phase. However, this study had numerous limitations, including the disproportionate inclusion of those with small ICH, difficulty achieving target BP quickly, and a heterogeneous range of pharmacological agents were used[24,25]. The current AHA/ASA guidelines indicate that intensive BP treatment is safe and might be associated with better outcome in patients presenting with systolic BP between 150–220 mmHg. Elevated BP should be treated with short half-life agents such as labetalol or nicardipine to avoid overshoot hypotension. Hydralazine and nitroprusside should be avoided given their possible association with increased ICP[24].

Hemostatic treatment

A) Platelet function—The utility and safety of platelet transfusion in ICH patients taking antiplatelet medications remains unclarified and there is not enough evidence to support routine application of a reversal strategy to improve platelet function[7]. Platelet transfusion is indicated in patients with severe thrombocytopenia with suggested thresholds between 50.000 and 100.000 platelets per microliter[26,27].

B) Warfarin-associated coagulopathy—OAT is associated with higher baseline ICH volume, increased risk of hematoma expansion and poor outcome[28]. Coagulopathy correction is aimed at preventing continued bleeding. Warfarin discontinuation and IV administration of vitamin K are the first therapeutic steps. Vitamin K should be infused slowly (over 10 minutes), at the dose of 10 mg with close monitoring of vital signs given the rare but not negligible risk of anaphylaxis (1/10.000)[28]. Given its slow onset of action (6 to 24 h), emergent factor repletion is typically provided in addition. Fresh Frozen Plasma (FFP) and Prothrombin Complex Concentrates (PCCs) are commonly used. According to the AHA/ASA guidelines PCCs may be preferred over FFP because of more rapid action[7]. Two randomized controlled trials of PCC vs. FFP showed that PCCs restore coagulation factors and reverse the International Normalized Ratio (INR) more rapidly than FFP, with no clear difference in thromboembolic risk[29–31]. While these trials failed to demonstrate improved clinical outcome in ICH patients, some observational studies have suggested improved outcome from more rapid INR reversal [323334]. The optimal INR target is still debated and proposed target values range from 1.3 to 1.5 [3536]. While it is not clear whether INR values below 1.7 represent clinically relevant coagulation abnormalities, one observational study found that achievement of an INR value below 1.3 within 4h from admission was associated with reduced risk of hematoma expansion[37]. The European Stroke Organization guidelines do not provide a specific recommendation about the warfarin reversal strategy [38] while the Neurocritical Care Society recommends warfarin reversal with either PCCs or FFP with a target INR<1.5 [39]. Characteristics of FFP and PCCs and one reasonable reversal strategy for warfarin-associated ICH are shown in table 1 and box 2.

Box 2

Reversal strategy for Warfarin-associated ICH

1. Discontinue warfarin treatment

2. Obtain complete blood count and INR
3. Administer 10 mg of Vitamin K IV (Infuse over 10 minutes)
4. Administer 4-Factor PCC in weight and INR based dosing:
   - PCC 20 IU/kg if INR<2.0
   - PCC 30 IU/kg if INR 2.0–3.0
   - PCC 50 IU/kg if INR>3.0
5. If PCCs are not available or desired, administer FFP 10–20 mL/kg
6. Repeat INR after infusion

C) Heparin-associated coagulopathy—If ICH occurs during IV heparin or low molecular weight heparin treatment, protamine sulfate administration can be used for coagulopathy reversal, at the dose of 1 mg per 100 units of heparin[728]. The maximum dosage should be 50 mg and the infusion must be slow (maximum infusion speed: 5 mg/minute) with vital signs monitoring given the significant risk of hypotension[28].

D) Direct Oral Anticoagulants (DOACs)—Alternatives to warfarin are now available, and the most commonly used are the Factor Xa inhibitors Apixaban, Rivaroxaban, and Edoxaban, and the direct thrombin inhibitor Dabigatran[40]. These agents were traditionally termed NOACs but the International Society of Thrombosis and Hemostasis has recommended the term DOACs; we will use this terminology here [41]. Unlike warfarin, there is no specific commercially available laboratory test to assess level of DOAC function; however, some traditional and novel blood tests may assist the clinical provider in estimation of anticoagulant effect. These tests are listed in table 2. Compared to warfarin, DOACs have shorter half-lives and their blood concentration typically follows a peak-trough format[42]. Therefore, timing of last intake and renal function should always be considered considering whether the patient is still, at the time of presentation, coagulopathic[4344]. Current evidence for DOACs reversal is limited and comes from in-vitro and animal models or studies on healthy volunteers[45]. For dabigatran reversal, a specific antagonist is now available, which addresses coagulopathy but has not yet been shown to reduce expansion [46,47]. For reversal of other agents, it may be that no currently available product is effective for this purpose, although more specific reversal agents are under investigation (ClinicalTrials.gov Identifiers NCT02329327 - NCT02220725). Subjects taking DOACs are not deficient in Vitamin K dependent factors, so vitamin K administration is not likely to be of value. Some authorities use activated PCCs for this purpose, to provide excess coagulation factor activity [48,4950,51]. Activated charcoal can be considered if administered within 2 to 3 hours from the last drug intake[42,48,49].

E) Recombinant tissue plasminogen activator (rtPA) – associated coagulopathy—Symptomatic intracerebral hemorrhage (sICH) is the most dangerous complication of rtPA administration in ischemic stroke patients, occurring in about 6 % of patients and leading to increased morbidity and mortality [52]. Older age, stroke severity,

longer time from onset to treatment, pre-stroke antiplatelet therapy and significant elevation of BP are among the most important predictors of sICH [53]. Preventive strategies include strict control of BP (target 180/105 mmHg), and avoidance of any antithrombotic medication in the first 24 h following the infusion of rtPA [52]. However, once ICH occurs, it is unclear how best to treat this. Given the short half-life of rtPA, by the time sICH is diagnosed, the agent itself may no longer be present at meaningful levels. As a result, there is great heterogeneity in clinical practice [52,54]. One concern is that rtPA can induce a relative hypofibrinogenemia which is present long after rtPA, and if so, this can be treated. As a result, the AHA/ASA guidelines recommend immediate discontinuation of rtPA and administration of cryoprecipitate [55]. The optimal dosage of cryoprecipitate is unclear and some suggest empiric treatment with 10 U of cryoprecipitate, followed by further administration until normalization of fibrinogen level [56]. Other options can include the anti-fibrinolytic aminocaproic acid (Amicar ®) as a 5 g IV bolus over 15–30 minutes. While other therapeutic approaches including vitamin K, FFP, PCC, platelet transfusion, or rFVIIa have been used, there is no clear biological reason or evidence to support them [52]. Finally, decompressive craniotomy or surgical hematoma evacuation may be considered for large hemorrhages with severe mass effect and intracranial hypertension [52,55].

Intracranial pressure management

The more common causes of elevated intracranial pressure (ICP) in ICH patients are mass effect from the hematoma and surrounding edema and IVH with secondary hydrocephalus. The indications for ICP monitoring in ICH are mainly derived from traumatic brain injury studies. Current AHA/ASA guidelines suggest ICP monitoring in patients with coma, significant IVH with hydrocephalus and evidence of transtentorial herniation, with a cerebral perfusion pressure (CPP) target of 50 to 70 mmHg [7]. ICP can be measured with parenchymal or ventricular devices. The latter (an external ventricular drain, or EVD) might be preferred in hydrocephalus as it allows cerebrospinal fluid (CSF) drainage. Elevation of the head to 30 degrees, adequate sedation, and avoidance of hyponatremia are mainstays of therapy; hyperosmolar therapy with mannitol or hypertonic saline can be considered in patients at risk of transtentorial herniation[7].

Seizures and antiepileptic treatment

Up to 14% of patients with ICH experience seizures in the early course of the disease [57]. The main risk factors for development of early seizures are cortical location of the ICH and occurrence of medical complications[57,58]. However, it is not clear that prophylactic antiepileptic (AED) therapy provides benefit to patients, and some data suggests phenytoin may worsen outcome in this population [59]. Therefore, prophylactic administration of AED therapy is not recommended and only subjects with clinical or electroencephalographic (EEG) evidence of seizures should receive antiepileptic drugs[7]. Continuous EEG monitoring should be considered in patients with impaired mental status that is disproportionate to the degree of brain damage[7].

Blood glucose management

Hyperglycemia has been shown to be associated with poor outcome in ICH[60] and declining values of glucose appear to be associated with lower risk of hematoma expansion[61]. Some

data suggest that careful glucose control (with sliding scale insulin) may improve neurologic outcome[62]. However, it is not clear that continuous insulin infusion improves outcomes in this population[6364]. The AHA/ASA guidelines suggest to avoid both hyperglycemia and hypoglycemia although a specific blood glucose target level is not provided[7].

Temperature management

The presence of fever is a common finding in ICH patients, especially in those with extensive IVH and appears to be independently associated with poor outcome[62]. Treatment of fever appears therefore reasonable but the optimal temperature management is still unclear[7]. Therapeutic normothermia failed to improve outcome in one trial [65] although treatment of fever did improve outcome in another[62]. It appears reasonable to minimize fever, and the role of targeted temperature management in ICH is still under investigation in a randomized clinical trial[66].

Surgical treatment

A) IVH management—IVH occurs in nearly half of ICH patients, particularly in those with deep hematomas, and is an independent predictor of poor outcome[6]. EVD placement is recommended for patients with hydrocephalus, coma and significant IVH, in order to drain blood and CSF and avoid significant elevation of ICP[7]. Several other approaches have been proposed for IVH treatment [67]. A recent meta-analysis showed that EVD placement in conjunction with thrombolytic drugs is associated with reduced mortality and better outcomes[68]. However, intraventricular fibrinolysis for IVH treatment is still considered investigational[7] and further insights will be provided by the ongoing CLEAR III trial[69].

B) Surgical hematoma evacuation—Two large randomized controlled trials, the STICH I and STICH II trials, investigated the role of surgical hematoma evacuation, compared to conservative treatment in patients with supratentorial ICH[70,71]. Neither trial demonstrated a statistically significant benefit of surgery in comparison to best medical management. As a result, the role of surgical therapy remains controversial and surgical evacuation of supratentorial hematomas should be considered only as a life-saving measure in deteriorating patients[7]. The only case in which there is consensus in favor of surgical intervention is in cerebellar hematomas with clinical or imaging signs of hydrocephalus and/or brainstem compression [7]. In these cases, surgical decompression and hematoma evacuation should probably be performed as soon as possible.

C) Decompressive craniotomy with or without hematoma evacuation—Decompressive craniotomy appears a feasible and safe procedure and may be associated with better outcome in a subset of patients with supratentorial ICH[72,73]. This subset includes those with coma, large hematoma with significant midline shift, or elevated ICP not controlled by optimal medical therapy[7].

D) Minimally invasive surgery—While open surgical evacuation has failed to definitively demonstrate benefit, it may be that minimally invasive surgical techniques (MIS) can still offer benefit. The development of less invasive techniques might allow hematoma evacuation with less damage to viable brain tissue and reduce the rate of secondary

complications compared to traditional craniotomy[67,74]. Another potential advantage of MIS over conventional surgery is faster access to the hematoma, with reduction of surgical and anesthesia duration in patients with clinical deterioration and elevated ICP[75]. Several MIS techniques have been proposed, ranging from endoscopic treatment of IVH to parenchymal hematoma evacuation with or without combined administration of rtPA[74,75]. The clinical efficacy of all these MIS approaches is still uncertain and clinical trials are ongoing.

ADMISSION TO STROKE UNIT OR NEUROSCIENCE INTENSIVE CARE UNIT

Following diagnosis of ICH, patients should be admitted to a dedicated stroke or neuroscience intensive care unit. Management of ICH in a dedicated stroke unit is associated with reduced mortality and better functional outcome compared to treatment in a general neurology ward[76].

PROGNOSIS PREDICTION

Despite progress in primary prevention and acute treatment, ICH is still a disease with high morbidity and mortality. Outcome estimation, palliative care and withdrawal of support are therefore important aspects of care in ICH patients. The ICH score predicts one-month mortality risk while the FUNC score predicts three-month functional independence (Table 3, Table 4)[8,77]. However, none of these tools should be used as a singular indicator of outcome or guide the decision of medical support withdrawal[7]. Early limitation of care is an independent predictor of poor prognosis[78] and the AHA/ASA guidelines recommend full medical support for all ICH patients at least until the second day of admission, apart from those with preexisting specific directives[7].

FUTURE PERSPECTIVES

Acute treatment of ICH is an active area of research. Hematoma expansion is an appealing target and identification of patients with the higher likelihood to benefit from anti-expansion therapy will be an important challenge. Aggressive BP treatment, hemostatic therapy, neuroprotection, reduction of secondary injury and perihematomal edema development, and MIS are some of the therapeutic strategies under investigation. Some ongoing clinical trials in acute ICH management are listed in table 5.

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KEY POINTS

- ICH is a dynamic disease and up to one third of the patients experience early clinical deterioration due to hematoma expansion.
- Intensive blood pressure reduction is safe and might improve neurological outcome.
- Rapid correction of coagulopathy may minimize the risk of ongoing bleeding.
- Surgical evacuation of the hematoma should be considered for patients with clinical deterioration due to cerebellar ICH.
- ICH patients should be admitted to a neuroscience intensive care unit or stroke specialty unit.

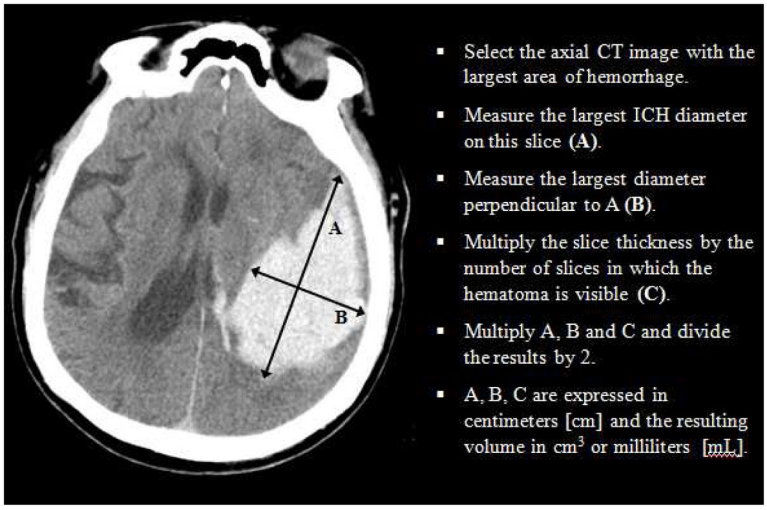

Figure 1.
ABC/2 method for ICH volume estimation

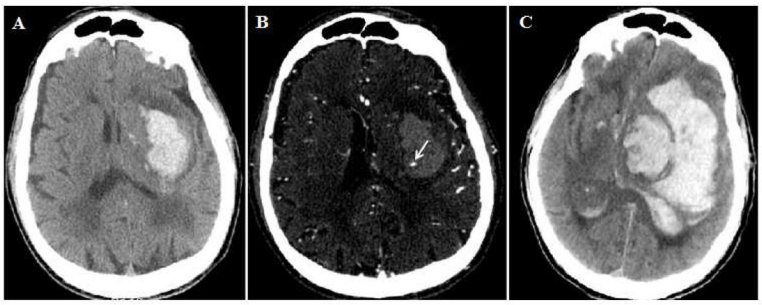

Figure 2. Spot sign and hematoma expansion

A) Left deep ICH on NCCT, with baseline volume of 45 mL; B) CTA showing presence of spot sign (arrow); C) Follow-up NCCT at 19 hours demonstrated significant hematoma growth to a volume of 192 mL with severe midline shift and massive intraventricular extension.

Table 1

Comparison between FFP and PCCs for warfarin reversal in ICH

FFP	PCCs
• Low cost and widely available	• More expensive than FFP
• Contains all coagulation factors	• 3 Factor PCCs *: contain Factors II, IX, X, with small amounts of Factor VII
• Large volume infusion is required	• 4 Factor PCCs *: contain Factors II, VII, IX, X and small amounts of protein C and S
• Prolonged time to infuse in routine clinical practice	• Can be rapidly infused (<20 minutes) with small volumes.
• Contents of Vitamin K-dependent factors in each unit of FFP can vary considerably	• Rare risk of allergic reaction
• Compatibility testing and thawing are necessary	• Rare risk of infectious agent transmission
• Rare risk of allergic reaction	
• Rare risks of infectious agent transmission	
• Rare risk of transfusion-related acute lung injury	

* **3 Factor PCCs:** Profilnine SD ® or Bebulin VH ®.

* **4 Factor PCCs:** KCentra ®, Beriplex ®, Octaplex ®, or Confidex ®.

Table 2

Effect of DOACs on blood tests Data from refs[79,8081]

	DABIGATRAN	RIVAROXABAN	APIXABAN	EDOXABAN
aPTT	• Abnormal only at moderate/high levels of drug. • Provides only qualitative indication	• Low sensitivity • ossible paradoxical response	• Low sensitivity • Possible paradoxical response	• Low sensitivity
PT/INR	• High inter-individual variability • Mild effect (INR ranging from 0.9 to 1.2)	• Provides qualitative indication only with specific reagents	• Unaffected	• Linear dose-dependent association but low sensitivity at lower therapeutic drug levels
Diluted Thrombin time (dTT)	• Already prolonged at low drug concentration. • Normal dTT can rule out anticoagulant activity • Needs calibration			
Ecarin clotting time (ECT)	• Sensitive indicator • Not widely available • Time consuming			
Anti Xa activity		• Sensitive indicator • Normal value rules out anticoagulant activity. • Not widely available • Needs calibration	• Sensitive indicator • Normal value rules out anticoagulant activity. • Not widely available • Needs calibration	• Sensitive indicator • Normal value rules out anticoagulant activity. • Not widely available • Needs calibration
Specific test system	Hemoclot ®: dabigatran calibrated dTT	Rivaroxaban calibrated anti Xa activity	Apixaban calibrated anti Xa activity	Edoxaban calibrated anti Xa activity

Table 3

ICH score for prediction of 30-day mortality

Component	ICH score
GCS	
3–4	2
5–12	1
13–15	0
ICH volume (mL)	
≥ 30	1
< 30	0
IVH presence	
Yes	1
No	0
Infratentorial ICH	
Yes	1
No	0
Age (years)	
≥ 80	1
<80	0
TOTAL SCORE	0 – 6

The mortality rate increases linearly with the ICH score. A total score of 3 is associated with a 30-day fatality rate around 70 %. A total score > 4 confers a 30-day mortality risk close to 100%.

Table 4

FUNC score for prediction of 90-day functional independence

Component	FUNC score
GCS	
≥ 9	2
3 – 8	0
ICH volume (mL)	
< 30	4
30 – 60	2
> 60	0
ICH location	
Lobar	2
Deep	1
Infratentorial	0
Age (years)	
< 70	2
70 – 79	1
≥ 80	0
Pre-ICH cognitive impairment	
No	1
Yes	0
TOTAL SCORE	0 – 11

The probability of reaching functional independence at 3 months increases steadily with the total score. Total scores > 7 are associated with a functional independence probability over 70%.

Table 5

Some ongoing clinical trials in acute ICH management

TRIAL	INTERVENTION
ATACH II [82]	Intensive BP treatment within 4.5 h from symptom onset with SBP target < 140 mmHg
SCORE-IT [83]	Investigate whether CTA spot sign or other imaging markers identify patients with high likelihood to benefit from BP lowering
INCH ClinicalTrials.gov NCT00928915	FFP vs PCCs for reversal of coumarin-related coagulopathy
TICH II Tich-2.org	Administration of intravenous tranexamic acid
STOP-AUST ClinicalTrials.gov NCT01702636	Administration of intravenous tranexamic acid to ICH patients with CTA spot sign
STOP-IT ClinicalTrials.gov NCT00810888	Administration of recombinant activated factor VII (rFVIIa) to ICH patients with CTA spot sign
SPOTLIGHT ClinicalTrials.gov NCT01359202	Administration of recombinant activated factor VII (rFVIIa) to ICH patients with CTA spot sign
iDEF ClinicalTrials.gov NCT02175225	Iron chelation with administration of intravenous Deferoxamine
SHRINC ClinicalTrials.gov NCT00827892	Enhancing hematoma reabsorption with administration of Pioglitazone
MISTIE III ClinicalTrials.gov NCT01827046	MIS plus rtPA for parenchymal hematoma evacuation
CLEAR III [69] ClinicalTrials.gov NCT00784134	EVD placement combined with intraventricular administration of rtPA for IVH treatment
MISTICH [84]	MIS for evacuation of supratentorial hematomas
SATIH ClinicalTrials.gov NCT00752024	Stereotactical hematoma aspiration combined with thrombolysis
SWITCH Clinical Trials.gov NCT02258919	Decompressive craniectomy plus best medical therapy