

## NEUROSCIENCES AND NEUROANAESTHESIA

# Neurocritical care for intracranial haemorrhage: a systematic review of recent studies

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## Abstract

Intracerebral haemorrhage (ICH) is associated with significant early mortality (up to 50% at 30 days) and long-term morbidity (with permanent neurological deficits in 75–80% of patients) and represents a serious health issue worldwide. The past decade has seen a dramatic increase in clinical research on ICH diagnosis and treatment that has led to revision of the guidelines for the diagnosis and management of ICH from the American Heart Association and American Stroke Association in 2013. This systematic review reports recent clinical evidence (original studies published between September 2013 and July 2015) related to neurocritical care and intensive care unit management of patients with ICH. All but one publication included in this review report original studies related to management of patients with intracerebral or subarachnoid haemorrhage. These include insights on risk stratification and neurocritical care or intensive care unit treatment, management of haemodynamic variables and mechanical ventilation (goal-directed fluid therapy, advanced haemodynamic monitoring, and avoidance of hyperoxia and hyperventilation), and pharmacological neuroprotection.

**Key words:** intracranial haemorrhage; neurocritical care; stroke

## Editor's key points

- Intracerebral haemorrhage (ICH) is a common and devastating type of stroke and is a leading cause of disability among adults.
- Outcomes after spontaneous ICH remain poor, with mortality up to 50% at 30 days and permanent disability in 75–80% of survivors.
- Recent clinical evidence provides insights into risk stratification and neurocritical care management to optimize outcome.

Intracerebral haemorrhage (ICH) is one of the most common and most devastating types of stroke and is a leading cause of

disability among adults.<sup>1–2</sup> Occurrence of ICH is the result of a number of pathophysiological processes that lead to bleeding within the cranial vault as a result of blood vessel rupture and result in a localized haematoma in the brain parenchyma and associated compression of brain tissue.<sup>3–4</sup> Outcomes after spontaneous ICH remain bleak, with mortality up to 50% at 30 days and complications of permanent neurological deficits and disability present in 75–80% of survivors.<sup>5–8</sup> Although ICH has traditionally lagged behind acute ischaemic stroke (AIS) and subarachnoid haemorrhage (SAH) in terms of evidence from clinical trials to guide management, the past decade has seen a dramatic increase in the clinical research on ICH diagnosis and treatment.<sup>9</sup> The American Heart Association/American Society of Anesthesiologists guidelines for management of patients with ICH, published in July 2015, includes a formal literature search updated to August

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**Table 1** Class I recommendations from AHA/ASA guidelines for optimal clinical management of patients with ICH relevant for neurocritical care. BP, blood pressure; DVT, deep vein thrombosis; ICH, intracerebral haemorrhage; ICU, intensive care unit; INR, international normalized ratio; SAP, systolic arterial pressure; VKA, vitamin K antagonist

Class I Recommendation	
General monitoring	Monitoring and clinical management should take place in an ICU or dedicated stroke unit run by physician neuroscience acute care expertise
Arterial blood pressure management	For ICH patients presenting with SAP between 150 and 220 mm Hg and without contraindication to acute BP treatment, acute lowering of SAP to 140 mm Hg is safe and can be effective for improving functional outcome
Haemostasis and coagulopathy, antiplatelet agents, and DVT prophylaxis	(i) Coagulation factors or platelet replacement, or both when needed (ii) If INR is elevated because of VKA, withhold VKA therapy, replace vitamin K-dependent factors, and give vitamin K i.v. to correct INR (iii) Intermittent pneumatic leg compression beginning on hospital admission to prevent venous thromboembolism
Glucose management	Glucose should be monitored. Both hyperglycaemia and hypoglycaemia should be avoided
Seizures and antiseizure drugs	Clinical seizures should be treated with antiseizure drugs. Patients with a change in mental status who are found to have electrographic seizures should be treated with antiseizure drugs
Management of medical complications	A formal screening procedure for dysphagia should be performed in all patients before initiation of oral intake to reduce the risk of pneumonia
Prevention of recurrent ICH	BP should be controlled in all ICH patients. Measures to control BP should begin immediately after ICH

2013. Class 1 recommendations for neurocritical care (NCC) and intensive care unit (ICU) management are listed (Table 1).<sup>10</sup>

The purpose of this systematic review is to report recent clinical evidence, including original studies published between September 2013 and July 2015, related to NCC and ICU management of patients with ICH (spontaneous and post-traumatic) and SAH.

## Methods

A systematic literature search of PubMed, Medline, Current Controlled Trials, and EMBASE was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement recommendations.<sup>11</sup> Clinical literature (prospective randomized clinical trials, observational studies, and case series that have enrolled more than five patients) were searched using the PubMed database. The following search terms were used: 'brain injury' AND 'intracranial haemorrhage' (spontaneous and post-traumatic). The following filters were used: clinical studies; published between September 2013 and July 2015; full-length articles (no abstracts); and English language. After hand searching and revision of the full text, duplicates were eliminated.<sup>12</sup> Details of the studies were recorded using a dedicated data-extraction form. Titles, abstracts, or both, of studies retrieved using the search strategy and those from additional sources were screened independently, and the full text of potentially eligible studies was retrieved and assessed independently for eligibility. Disagreement over eligibility was resolved through open discussion.

## Results

A total of 51 articles were retrieved using the listed keywords. After screening for eligibility, 37 articles were excluded and 14 articles were selected (Fig. 1) and categorized into the following four subcategories: risk stratification and NCC or ICU treatment,<sup>13–16</sup> haemodynamic management,<sup>17–22</sup> mechanical ventilation,<sup>23 24</sup> and pharmacological neuroprotection<sup>25 26</sup> (Table 2).

## Risk stratification and neurocritical care or intensive care unit treatment

Recent literature provides insights on risk stratification of ICH in patients receiving non-vitamin K-antagonist anticoagulants [new oral anticoagulants (NOACs)] and in patients presenting with seizures, co-morbidity and complications associated with ICU treatment, and on limited benefit of ICU treatment in low-risk patients presenting with post-traumatic ICH.<sup>13–16</sup>

Clinical characteristics and the relationship with arterial blood pressure of ICH associated with chronic use of NOACs is reported in a retrospective cohort study in six patients (five receiving rivaroxaban and one apixaban).<sup>13</sup> In these patients, the mean time to onset was 146 (SD 112) days after starting NOACs, and mean systolic arterial pressure (SAP; recorded 1 month before ICH) was 138 (16) mm Hg. Although none of the therapies traditionally used to counteract coagulation abnormalities (infusion of fresh frozen plasma, activated prothrombin complex concentrate, recombinant activated factor VIIa, or haemodialysis) was used, ICH was not associated with haematoma expansion within the 24 h after onset of symptoms. The authors highlight how ICH occurred relatively soon after the start of NOAC therapy, and haematoma volume was small. These findings suggest that even stricter arterial pressure lowering and control within an acceptable range may be advisable to prevent ICH during NOAC therapy.

The relevance of seizures at presentation and relationship with in-hospital mortality was evaluated in a retrospective cohort study that recruited 247 patients presenting with seizures to the emergency department and admitted to the ICU for treatment.<sup>14</sup> In this subgroup of patients, ICH was detected as a possible underlying cause of the seizures in 36 of 247 patients (14.5%). Overall, in-hospital death occurred in 7.7%. The authors concluded that rates of death and discharge to hospice were relatively low in this patient population.

Associated complications (cardiac and ventilatory), intensity of treatment (with mechanical ventilation), and the relationship

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