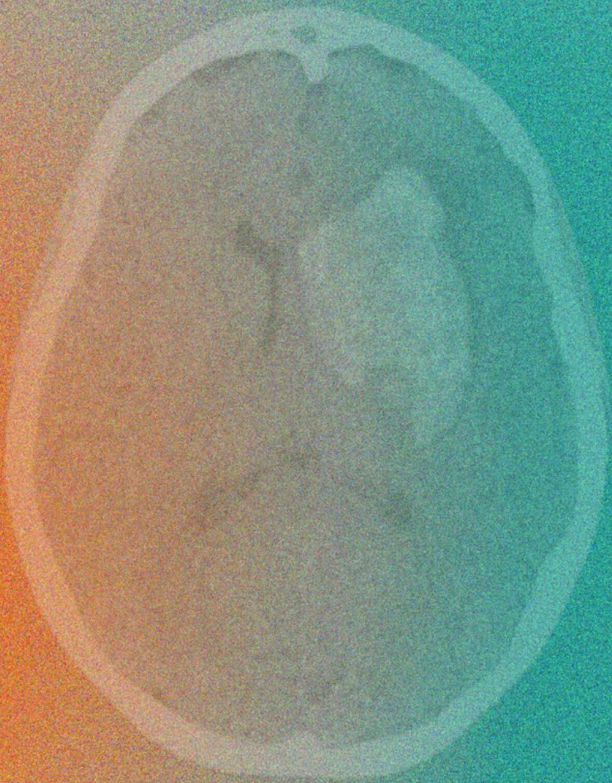
Academy of Medicine of Malaysia

MALAYSIA STROKE COUNCIL

Malaysian Society of Neurosciences
Persatuan Neurosains Malaysia

Clinical Practice Guidelines



First Edition

Management of Spontaneous Intracerebral Haemorrhage 2025

MOH/P/PAK/614.25(GU) - e

PUBLISHED BY :

Malaysian Society of Neurosciences
(Persatuan Neurosains Malaysia)
Neurology Laboratory, 6th Floor, South Tower
University of Malaya Medical Centre
50603 Kuala Lumpur
Malaysia

ISBN 978-629-96368-2-3

Available on the following websites:
http://www.acadmed.org.my
http://neuro.org.my
http://www.moh.gov.my

Also available as an app for Android and IOS platform: MyMaHTAS

STATEMENT OF INTENT

This guideline was developed to be a guide for best clinical practice, based on the best available evidence at the time of development. Specific attempts were made to use local data and publications to ensure local relevance. Adherence to this guideline does not necessarily lead to the best clinical outcome in individual patient care. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical presentation and management options available locally.

UPDATING THE CPG

This guideline was issued in 2025 and will be reviewed in a minimum period of four years (2029) or sooner if new evidence warrants earlier revision. When it is due for updating, the Chairperson of the CPG or National Advisor of the related specialty will be informed about it. A discussion will be done on the need for a revision including the scope of the revised CPG. A multidisciplinary team will be formed and the latest systematic review methodology used by MaHTAS will be employed. Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions, corrections will be published in the web version of this document, which will be the definitive version at all time.

Guideline Development Group

Chairperson
Associate Prof Dr Law Zhe Kang
Consultant Neurologist
Hospital Canselor Tuanku Muhriz
Universiti Kebangsaan Malaysia

Members (in alphabetical order)

Associate Prof Dr Abdul Hanif Khan Yusof Khan
Consultant Neurologist
Hospital Sultan Abdul Aziz Shah
Universiti Putra Malaysia

Dr Alisha Chin Yen Theng
Consultant Neurologist
Hospital Sultanah Aminah

Associate Prof Dr Aznida Firzah Abdul Aziz
Senior Family Medicine Consultant
Hospital Canselor Tuanku Muhriz
Universiti Kebangsaan Malaysia

Dr. Aznita Binti Ibrahim
Consultant physician
Hospital Sultan Abdul Halim Sungai Petani

Dr Chow Chee Toong
Consultant Emergency Physician
Hospital Seberang Jaya

Dr. Doris George Visuvasam
Clinical Pharmacist
Hospital Taiping

Dr. Emi Noorina Binti Mohd Nor
Consultant Emergency Physician
Hospital Tuanku Ja'afar Seremban

Associate Prof Dr Hilwati Hashim
Consultant Radiologist
Faculty of Medicine & Hospital Al-Sultan Abdullah
Universiti Teknologi MARA

Dr Iskasymar Bin Itam @ Ismail
Consultant Emergency Physician
Unit Kecemasan Strok RESQ
Hospital Sultan Abdul Aziz Shah
Universiti Putra Malaysia

Associate Prof Dato Dr Jegan Thanabalan
Consultant Neurosurgeon
Hospital Canselor Tuanku Muhriz
Universiti Kebangsaan Malaysia

Dr Mohd Azmarul bin A Aziz
Speech and Language Therapist
Hospital Pakar Universiti Sains Malaysia

Dr. Muhammad Ihfaz bin Ismail
Consultant Neurosurgeon
Hospital Pakar Universiti Sains Malaysia

Dr. Noor Ayuni Bazura Muhamad
Senior Principal Assistant Director
MaHTAS, MoH, Putrajaya

Prof Dr Nor'azim bin Mohd Yunos
Consultant Intensivist and Anaesthesiologist
Universiti Malaya Medical Centre

Dr. Norazlina Bt Abdul Aziz
Consultant Rehabilitation Physician
Hospital Rehabilitasi Cheras

Dr Nor Haslinda Ishak
Family Medicine Specialist
Klinik Kesihatan Ayer Molek Melaka

Dr Presaad Pillai Perianen
Consultant Neurologist
Hospital Queen Elizabeth

Dr Saiful Azli Mat Nayan
Consultant Neurosurgeon
Hospital Sungai Buloh

Dr Sheela Theivanthiran
Consultant Rehabilitation Physician
Hospital Rehabilitasi Cheras

Dr. Siti Nasrina Binti Yahaya
Consultant Emergency Physician
Hospital Putrajaya

Dr Lee Jen Ping
Consultant Rehabilitation Physician
Hospital Rehabilitasi Cheras

Dr Leong Yuh Yang
Consultant Interventional Neuroradiologist
Hospital Canselor Tuanku Muhriz
Universiti Kebangsaan Malaysia

Dr Lim Swee San
Consultant Neurosurgeon
Hospital Umum Sarawak

Professor Dr Mazlina bt Mazlan
Consultant Rehabilitation Physician
Universiti Malaya Medical Centre

Dr Mohamed Azlam Mohamed Micdhadhu
Consultant Neurologist
Hospital Seberang Jaya

Dr. Mohd Aminuddin Mohd Yusoff
Malaysian Health Technology Assessment Section (MaHTAS), MoH, Putrajaya

Associate Prof Dr Tan Kit Mun
Senior Consultant Geriatrician
Universiti Malaya Medical Centre

Dr Tay Chai Li
Family Medicine Specialist
Klinik Kesihatan Simpang

Dr Vilasini A/P Sinniah
Consultant Emergency Physician
Hospital Sultan Abdul Halim Sungai Petani

Associate Prof Dr Wan Asyraf Wan Zaidi
Consultant Neurologist
Hospital Canselor Tuanku Muhriz
Universiti Kebangsaan Malaysia

Associate Prof Dr Wan Mohd Nazaruddin Wan Hassan
Consultant Neuroanaesthesiologist and Critical Care specialist, School of Medical Sciences, Universiti Sains Malaysia

Dr Zainura Che Isa
Consultant Acute Internal Medicine Physician
Hospital Sultan Abdul Halim Sungai Petani

Secretariate

Dr Dayang Anis Mat Baki
Research assistant,
Hospital Canselor Tuanku Muhriz
Universiti Kebangsaan Malaysia

Dr Wang Hooi Xian
Medical officer
Hospital Kepala Batas

Information and search specialist

En Azlan Mohamad Hamzah
Librarian
Hospital Canselor Tuanku Muhriz UKM

External reviewers

Dr. Albert Wong Sii Hieng
Consultant Neurosurgeon
Hospital Umum Sarawak

Prof Dato' Jafri Malin bin Abdullah
Senior Consultant Neurosurgeon
Hospital Pakar Universiti Sains Malaysia

Dr Karen Sharmini Sandanasamy
Public Health Physician
Clinical Practice Guidelines Unit Head
Malaysian Health Technology Assessment Section (MaHTAS), MoH, Putrajaya

Dr Looi Irene
Senior Consultant Neurologist and Deputy Head of Neurology Service (Ministry of Health)
Hospital Seberang Jaya

Prof Dr Sabariah Faizah bt Jamaluddin
Senior Consultant Emergency Physician
Hospital Al-Sultan Abdullah UiTM

Associate Prof Dr Muhammad Hafiz Bin Hanafi
Consultant Rehabilitation Physician
Hospital Pakar Universiti Sains Malaysia

Dr. Norzaini Rose Binti Mohd Zain
Senior Consultant Neuroradiologist and Head of Specialty for Clinical Radiology Ministry of Health
National Cancer Institute, Putrajaya

Ms Tracy Chan Yan Peng
Physiotherapist and patient advocate

TABLE OF CONTENTS

RATIONALE, OBJECTIVES AND PROCESS OF GUIDELINE DEVELOPMENT

Stroke is a common medical emergency and a leading cause of mortality in Malaysia. In Malaysia, approximately 18% of all stroke are intracerebral haemorrhage (ICH).[1] Patients with ICH are often management by a multidisciplinary team consisting of internists, acute internal medicine physicians, emergency physicians, neurologists, neurosurgeons, neuroradiologists, intensivists, geriatricians, primary care physicians, rehab physicians, pharmacists, nurses, physiotherapists, occupational therapists, and speech therapists. Therefore, there is a need to have a standardised clinical practice guideline to inform evidence-based treatment across multiple specialties.

This is the first national clinical practice guideline of Malaysia recommending management of spontaneous intracerebral haemorrhage. This CPG has been prepared by a panel of committee members from the Malaysia Stroke Council (MSC), the Ministry of Health (MOH) and the Ministry of Higher Education (MOHE). The committee members were multidisciplinary and comprised of internists, acute internal medicine physicians, emergency physicians, neurologists, neurosurgeons, neuroradiologists, intensivists, geriatricians, primary care physicians, rehab physicians, pharmacists and speech therapists. The external reviewers included were also consultants from multidisciplinary branches of medicine.

Objectives
The objective of the CPG is to provide evidence-based recommendations on the management of spontaneous intracerebral haemorrhage in following aspects:
a) Diagnosis and prognostication
b) Acute medical management
c) Acute surgical management
d) Rehabilitation
e) Secondary prevention
The goal of this CPG is to improve the implementation of evidence-based management and avoidance of harmful or unbeneficial treatment, and with it, improvement in patients' outcome.

Target Users
This document is intended to guide healthcare professionals and relevant stakeholders involved in the management of ICH. This includes:
i healthcare professionals (doctors, pharmacists, allied health professionals)
ii professional organisations
iii policy makers
iv patients and NGOs

Target Population
Inclusion Criteria
- Spontaneous Intracerebral Haemorrhage, which includes intraparenchymal haemorrhage with or without intraventricular extension.

Exclusion Criteria
The following topics are covered by separate guidelines, and hence, have been excluded:
- Ischaemic stroke
- Other types of intracranial haemorrhage- subdural haemorrhage, extradural haemorrhage, subarachnoid haemorrhage
- Traumatic brain injury including traumatic intracerebral haemorrhage

Process
The current CPG is the initiative of the Malaysia Stroke Council (MSC) of the Malaysia Society of Neurosciences (MSN). The CPG is developed by a multidisciplinary Development Group (DG) consisting of healthcare providers from the Ministry of Health and Ministry of Higher Education using an evidence-based approach with guidance from Malaysian Health Technology Assessment Section (MaHTAS), Ministry of Health.

Twenty-nine clinical questions were formulated using the PICO (population, intervention, comparator, outcomes) format for the CPG (**Appendix 1-Clinical questions**). Evidence for each question were searched from scientific databases and grey literature using pre-determined search terms. We searched MEDLINE and Cochrane database for articles published in English or Malay language from year 2000 onwards till 12th September 2023 (see **Appendix 2-Example of search strategy**). The details of the search strategy can be obtained upon request from the CPG Secretariat. Literature searches were repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 30 September 2024 to be included. We included human studies only that involved adults > 18 years. We excluded case reports, case series, editorial, commentaries and studies published as abstracts only.

In addition, we also referred to other guidelines on spontaneous intracerebral haemorrhage including:
- American Heart Association/American Stroke Association Guideline for the Management of Patients With Spontaneous Intracerebral Haemorrhage (2022)
- European Stroke Organisation (ESO) and European Association of Neurosurgical Societies (EANS) guideline on stroke due to spontaneous intracerebral haemorrhage (2025)

These guidelines were evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II prior to them being used as references.

DG members met for a total of 28 times. All literature retrieved were appraised by at least two DG members using Critical Appraisal Skill Programme (CASP) checklist, presented in evidence tables and further discussed in each DG meetings. A consensus was made following the review of the evidence. Where evidence was ambiguous or of lower quality, the DG reached consensus through structured discussion and voting, with justification recorded in evidence tables. For conflicting studies, preference was given to higher-quality or locally applicable evidence. The strength of recommendations reflects both the certainty of evidence and contextual feasibility within Malaysian healthcare settings. The CPG were drafted by the Development Group. Local practicalities and principles of GRADE were taken into consideration in formulating the recommendations. Relevant algorithms were developed in the CPG. This is important as it can be used in the management of ICH by healthcare providers. The CPG drafts were reviewed by External Reviewers and Technical Advisory Committee.

The following summarises the process of CPG development and updates.
a. **Feedback on draft CPG and preparation of final CPG**
   Feedbacks from External Reviewers were be addressed by the Development Group.
b. **Evaluation of CPG by TAC CPG**
   The CPG draft was reviewed by the Technical Advisory Committee (TAC) using the AGREE II instrument.
c. **Presentation of guidelines to HTA & CPG Council**
   A presentation of the CPG was done to the HTA & CPG Council for approval.
d. **Implementation of guidelines**
   Implementation strategies will include a Quick reference and Training Module for healthcare providers and others as required.
e. **Audit**

An audit will be carried out on the implementation and impact of the guideline.

f. **Update**
The CPG will be updated in a minimum of 4 years or when new important evidence becomes available.

LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II-1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

FORMULATION OF RECOMMENDATION

In line with new development in CPG methodology, the CPG Unit of MaHTAS is in the process of adapting Grading Recommendations, Assessment, Development and Evaluation (GRADE) in its work process. The quality of each retrieved evidence and its effect size are carefully assessed/reviewed by the CPG Development Group. In formulating the recommendations, overall balances of the following aspects are considered in determining the strength of the recommendations: -

- overall quality of evidence
- balance of benefits versus harms
- values and preferences
- resource implications
- equity, feasibility and acceptability

The more criteria being fulfilled, the more certain is the evidence leading to strong recommendations using the word "**should**" being considered. Otherwise, weak recommendations use the word "**may**" in proposing an action to be made.

In the CPG, a yellow box highlights important message(s) in the management while a blue box contains evidence-based recommendation(s) for the particular condition.

KEY RECOMMENDATIONS

The following recommendations are highlighted by the CPG Development Group as the key recommendations that answer the main questions addressed in the CPG and should be prioritised for implementation.

Diagnosis

- Computed tomography scan or magnetic resonance imaging should be used to confirm diagnosis of intracerebral haemorrhage (ICH).
- ICH patients with the following features should undergo vascular imaging (CT angiography/MR angiography) and/or MRI to look for macrovascular causes of ICH:
  - Lobar or posterior fossa ICH
  - Age<45 years
  - Absence of cerebral small vessel disease
  - Non-hypertensive
  - Presence of subarachnoid haemorrhage

Medical management

- Care bundle, to be achieved within one hour of treatment initiation and consisting of the following, should be offered to patients with acute intracerebral haemorrhage (ICH):
  - Intensive blood pressure reduction to target systolic blood pressure of 130 - 140 mmHg
  - treating pyrexia to achieve a body temperature of ≤37.5°C
  - glycaemic control with a target of 6.1 - 7.8 mmol/L (non-diabetic) and 7.8 - 10.0 mmol/L (diabetic)
  - reversal of abnormal anticoagulation in those taking warfarin using prothrombin complex concentrates or fresh frozen plasma to reach an INR of <1.5.
- Patients with ICH should be admitted to an organised stroke unit staffed by a multidisciplinary team.
- Early Do Not Attempt Resuscitation (DNAR) decision should be avoided in the first 48 hours in patients with acute intracerebral haemorrhage who do not have pre-existing DNAR status.
- Prophylactic antiseizure medications should not be given in patients with spontaneous intracerebral haemorrhage without seizures.
- In patients with early clinical seizures, antiseizure medications should be considered.
- Venous thromboembolism (VTE) prophylaxis may be initiated in non-ambulatory patient with spontaneous intracerebral haemorrhage:
  - intermittent pneumatic compression on the day of diagnosis
  - heparin prophylaxis after 24 hours of admission
- Graduated compression/thromboembolic deterrent (TED) stockings alone should not be prescribed for VTE prophylaxis.
- Swallowing assessments should be performed for patients with intracerebral haemorrhage using standardised protocols

Neurosurgical management

- In view of potential benefit of specific neurosurgical intervention, patients with the following should be referred to the neurosurgical service for assessment and management:
  - Large and/or expanding supratentorial intracerebral haemorrhage (ICH) (>20 ml volume)
  - Any intraventricular extension
  - Posterior fossa ICH irrespective of volume
  - Deteriorating consciousness level and/or signs of raised intracranial pressure
  - Suspicion of a vascular malformation, independent of volume or location
- In patients with severe and large supratentorial deep intracerebral haemorrhage decompressive craniectomy may be considered.
- Haematoma evacuation for deep supratentorial intracerebral haemorrhage using open craniotomy may be considered for patients who are deteriorating as a life-saving measure.
- Minimally invasive surgery may be considered for patients with lobar intracerebral haemorrhage with a volume of 30 to 80mL within 24 hours of symptoms onset.
- In patients with cerebellar intracerebral haemorrhage with a volume of ≥15mL, haematoma evacuation with or without external ventricular drain should be considered.
- In patients with intracerebral haemorrhage complicated with intraventricular haemorrhage and hydrocephalus, external ventricular drain should be offered. In addition, intraventricular fibrinolysis with alteplase or neuroendoscopy may be considered

Intensive care

- Intracranial pressure (ICP) monitoring in patients with acute intracerebral haemorrhage should not be routinely performed.
- Early tracheostomy in intracerebral haemorrhage should not be routinely performed.
- Hyperosmolar therapy should not be routinely administered for cerebral oedema in patients with spontaneous intracerebral haemorrhage.

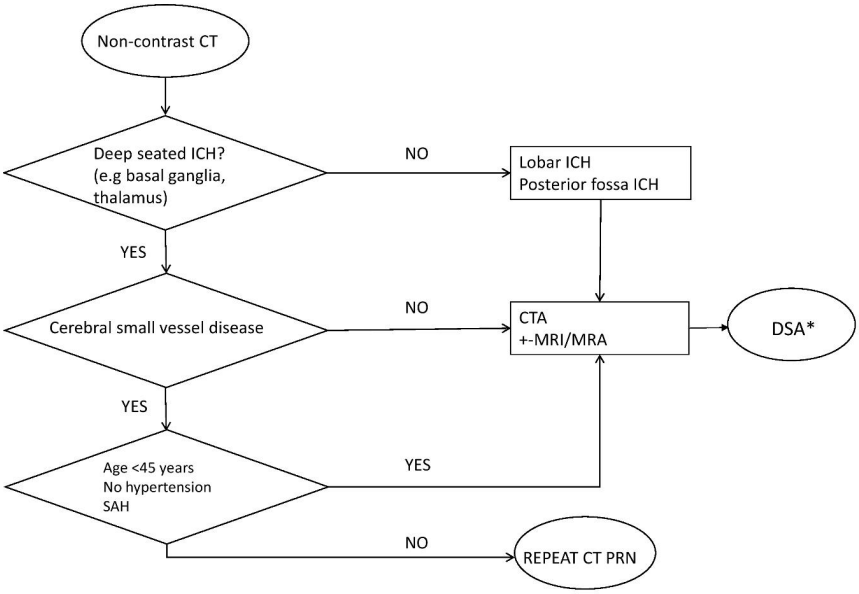
Rehabilitation

- Early initiation of rehabilitation should be offered within 24 - 72 hours of admission for patients with intracerebral haemorrhage (ICH).
  - Very early intensive rehabilitation (<24 hours) should be avoided.
- Neuropharmacological augmentation may be offered to post-ICH patients during rehabilitation phase.
- Oral muscle relaxants such as dantrolene, benzodiazepines, gabapentin, and baclofen may be considered to treat spasticity
- Botulinum toxin injection should be considered to treat muscle spasticity after ICH
  - The optimal timing for treatment is 4 to 12 weeks after stroke
- Transcutaneous Electrical Nerve Stimulation (TENS) should be considered as a adjunctive therapy for muscle spasticity

Secondary prevention

- Long term blood pressure control with a target of <130/80 mmHg should be initiated.
  - A combination of angiotensin converting enzyme inhibitor and thiazide diuretic may be considered as antihypertensive agents of choice.
- In patients with intracerebral haemorrhage (ICH) and concomitant non-valvular atrial fibrillation, resumption of an oral anti-coagulant (OAC) may be considered.
  - Non-vitamin K antagonist OAC is preferred to warfarin.
  - Timing of resumption after ICH should be individualised based on patient's bleeding and thrombotic risks, preferably not earlier than two weeks.
- In patients with ICH and mechanical heart valve requiring anti-coagulant, the earliest timing for resumption of anti-coagulant should be at least six days after ICH, with vigilant monitoring for both bleeding and thromboembolic complication upon resumption of the therapy.
- Statin may be used to reduce cardiovascular risk in patients with intracerebral haemorrhage.

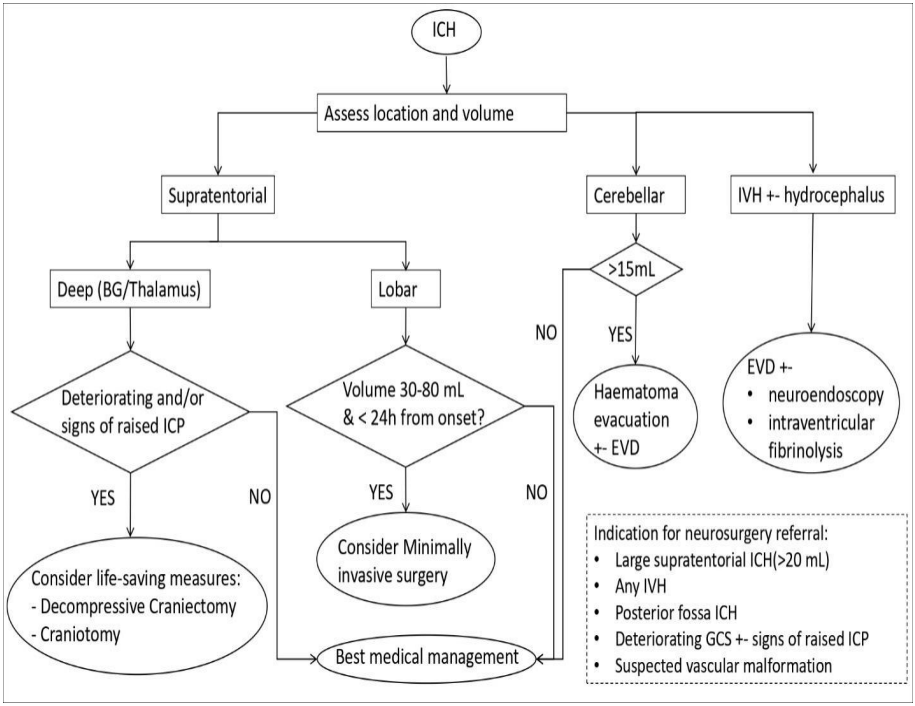
ALGORITHM 1: NEUROIMAGING FOR ICH



CT=computed tomography; CTA= computed tomography angiography; DSA= digital subtraction angiography; ICH=Intracerebral haemorrhage; MRI/MRA=magnetic resonance imaging/magnetic resonance angiography; PRN= pro re nata (when needed); SAH= subarachnoid haemorrhage

*Patients diagnosed with or suspected to have vascular lesions (e.g arteriovenous malformation, intracranial aneurysm, dural arterio-venous fistula etc) on CTA/MRA may undergo DSA for confirmation and intervention.

ALGORITHM 2: NEUROSURGERY FOR ICH



BG= basal ganglia; EVD=external ventricular drainage; GCS= Glasgow Coma Scale; ICH=intracerebral haemorrhage; ICP=intracranial pressure; IVH=intraventricular haemorrhage

GLOSSARY

AAEDD= average atorvastatin equivalent daily dose
ABW=adjusted body weight
ADL= activities of daily living
AEs= adverse events
AHA= American Heart Association
ANNEXA-I= Andexanet for Factor Xa Inhibitor–Associated ICH
ARIC= Atherosclerosis Risk in Communities
ASA= American Stroke Association
ASL= Arterial Spin Labeling
ASM= antiseizure medications
AVM= arteriovenous malformation
BE-FAST= Balance, Eyes, Face, Arm, Speech, Time
BG= basal ganglia
BP= blood pressure
BTX= Botulinum toxin
CAM= Confusion Assessment Method
CAM-ICU= Confusion Assessment Method for the Intensive Care Unit
CFS= Clinical Frailty Scale
CI= confidence interval
CLEAR III= Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase III
CLOTS-3= The Clots in Legs Or sTockings after Stroke
CPP= cerebral perfusion pressure
CT= computed tomography
CTA= computed tomography angiography
CTV= computed tomography venography
dAVF= dural arterio-venous fistula
DNAR= Do Not Attempt Resuscitation
DSA= Digital Subtraction Angiography
DVT= deep vein thrombosis
EANS= European Association of Neurosurgical Societies
EDH= extradural haemorrhage
ENRICH= Early Minimally Invasive Removal of Intracerebral Hemorrhage
ERICH= Ethnic/Racial variations of Intracerebral Hemorrhage
ESO= European Stroke Organisation
EVD= external ventricular drainage
EVT= endovascular treatment
FAST= face, arm, speech, time
FEES= Fibreoptic Endoscopic Evaluation of Swallowing
FFP= fresh frozen plasma
FUNC= Functional Outcome in Patients with Primary Intracerebral Haemorrhage
GCS= Glasgow Coma Scale
GOS-E= Glasgow Outcome Scale-Extended
HU= Hounsfield Unit
IBW=ideal body weight
ICH= intracerebral haemorrhage
ICH-GS= Intracerebral Haemorrhage Grading Scale
ICP= intracranial pressure
ICU= intensive care unit
INCH= INR Normalisation in Patients with Coumarin-related Intracranial Haemorrhages

INTERACT3= The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial
INR= international normalised ratio
IPC= intermittent pneumatic compression
IV= intravenous
IVH= intraventricular haemorrhage
LMWH= low molecular weight heparin
MAS= Modified Ashworth Scale
MgSO4= Magnesium Sulphate
m-ICH= Modified Intracerebral Haemorrhage
Mins= minutes
MISTIE III= Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation
MRA= magnetic resonance angiography
MRI= magnetic resonance imaging
mRS= modified Rankin Scale
NIHSS= National Institutes of Health Stroke Scale
NOAC= non-vitamin K oral anticoagulant
NP=nasal prong
NRHFM=non-rebreathing high flow mask
NS= non-significant
PATCH= Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy
PE= pulmonary embolism
OR= odds ratio
PCC= prothrombin complex concentrate
RACECAT= Direct Transfer to an Endovascular Center Compared to Transfer to the Closest Stroke Center in Acute Stroke Patients with Suspected Large Vessel Occlusion
RCT= randomised controlled trial
RSI= rapid sequence intubation
SAE= serious adverse events
SAH= subarachnoid haemorrhage
SBP= systolic blood pressure
SDH= subdural haemorrhage
SMD= standardised mean difference
SWITCH= Swiss trial of decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral hemorrhage
SYNAPSE-ICU= Intracranial pressure monitoring in patients with acute brain injury in the intensive care unit
TBW=total body weight
TED= thromboembolic deterrent
TICH-NOAC= Tranexamic Acid for Intracerebral Hemorrhage in Patients on Non-Vitamin K Antagonist Oral Anticoagulants
TOF= time-of-flight
UFH= unfractionated heparin
VFSS= Videofluoroscopic Swallow Study
VKA=vitamin-K antagonist
VTE= Venous thromboembolism

INTRODUCTION

Definitions, terminologies and scope

Intracranial haemorrhage refers to any accumulation of blood within the cranial vault[2] and should not be confused with intracerebral haemorrhage. Intracranial haemorrhage comprises of intracerebral haemorrhage (ICH), subdural haemorrhage (SDH), extradural haemorrhage (EDH) and subarachnoid haemorrhage (SAH)[3,4]. ICH refers to bleeding within brain parenchyma and may occur with or without intraventricular extension. Intracerebral bleed is another term synonymous with ICH, but is less often used in medical literature. ICH may occur after trauma or spontaneously. Spontaneous ICH and subarachnoid haemorrhage are two types of haemorrhagic strokes. This guideline covers only stroke caused by spontaneous ICH.

Epidemiology

ICH accounts for 3.4 million of the 12.2 million people worldwide who suffers from a stroke every year.[5] Spontaneous intracerebral haemorrhage has a median 30-day mortality rate of 40%.[6] In addition, between 70 to 80% of patients with intracerebral haemorrhage are dependent at one year after stroke.[6]

In Malaysia, there were approximately 48,000 incident stroke in 2019[5], with 18% of these ICH[7]. ICH affects younger population (mean age 55 years) compared to ischaemic stroke (mean age 63 years). The incidence of ICH had been increasing especially amongst people below 65 years.[7] ICH constitutes significant burden with a one-month mortality rate of 30-38%[7], higher readmission rate[8], with 56.8% of ICH patients being functional dependent at discharge[9,10] The economic cost of ICH is immense, with an estimated lifetime treatment cost of RM37,757 (USD$8,928) for each ICH patient in Malaysia.[11]

DIAGNOSIS OF INTRACEREBRAL HAEMORRHAGE

The symptoms of ICH depend on the location of the haematoma. The common locations of haematoma include basal ganglia (40-60%), thalamus (~30%), lobar/cortical (~20%), brainstem or cerebellum (<10%).[12] They are the results of direct damage to the involved region and compression of surrounding tissues. Putaminal haematoma presents as hemiparesis, facial weakness, dysarthria, hemi-sensory loss, gaze palsy and homonymous hemianopia. Thalamic haematoma causes hemi-sensory loss with expansion of haematoma to midbrain inferiorly causes gaze palsy, cranial nerves palsy and reduced level of consciousness. Cortical haematoma causes hemiparesis, hemi-sensory loss, dysarthria, dysphasia, homonymous hemianopia and other cortical signs depending on cortical area involved. Cerebellar haematoma manifests as ataxia, clumsiness and vertigo. Brainstem haematoma often leads to coma rapidly. In addition, quadriparesis, cranial nerves palsy and gaze palsy may occur with brainstem haematoma. Haematoma at any location can leads to reduced conscious level and coma if it causes raised intracranial pressure, hydrocephalus and cerebral oedema or disrupts the reticular activating system, the pathway responsible for consciousness.

Bleeding into the brain parenchyma *per se* do not cause headache, as brain tissues are devoid of pain receptors. However, headache occurs in half of patients with intracerebral haemorrhage due to stretching of meningeal pain fibres or irritation caused by blood in the cerebrospinal fluid and ventricles. Vomiting commonly occurs together with headache and may signify raised intracranial pressure. Neck stiffness is uncommon unless there is concurrent subarachnoid haemorrhage or extensive intraventricular haemorrhage. Seizures are more common in lobar/

cortical haemorrhage and occur in 4 to 14% of patients with acute intracerebral haemorrhage.[13-17]

Several scoring systems were design to discern supratentorial intracerebral haemorrhage from ischaemic stroke on clinical basis including the Siriraj stroke score and Guy's hospital score.[18,19] However, clinical scores are unreliable in the diagnosis of intracerebral haemorrhage.[20] Neuroimaging should be utilised in all cases.

Neuroimaging

CT and MRI

In patients presenting with stroke-like symptoms, neuroimaging is essential for distinguishing between ischaemic and haemorrhagic stroke. A computed tomography (CT) scan is regarded as the standard of care for such cases including detection of acute ICH due to its widespread availability in Malaysian hospitals and its practicality as the preferred neuroimaging modality. With regard to the use of magnetic resonance imaging (MRI), a multicentre, diagnostic study showed that MRI had good accuracy (ranging from 97.6% to 100%) in the detection of ICH.[21, level III] In a Cochrane systematic review, two moderate quality studies reported high accuracy of MRI in the diagnosis of haemorrhagic stroke (sensitivity ranged from 0.83 to 1.00, while specificity ranged from 0.98 to 1.00).[22, level I]

The American Heart Association/American Stroke Association (AHA/ASA) 2022 Guideline recommends rapid neuroimaging with CT or MRI in patients presenting with stroke-like symptoms to confirm the diagnosis of spontaneous ICH.[23] However, MRI should only be considered in the acute stroke workflow if centres are able to achieve speed and triaging efficiency similar to CT based imaging[24, level III] and availability of resources.

Recommendation 1

- Computed tomography scan or magnetic resonance imaging, depending on availability, should be used to confirm the diagnosis of intracerebral haemorrhage.

Non-Invasive Vascular Imaging

ICH may be caused by macrovascular causes e.g. arteriovenous malformation (AVM), intracranial aneurysm, dural arterio-venous fistula (dAVF), cavernoma and cerebral venous thrombosis. However, neuroimaging practice to detect these macrovascular causes varies depending on the availability of resources. Patients with the following features are at increased risk of having a macrovascular cause[25]:

- aged <45 years without hypertension
- ICH in non-classical locations (e.g. lobar ICH, or location outside of basal ganglia or thalamus)
- absence of signs of cerebral small vessel disease such as leukoaraiosis

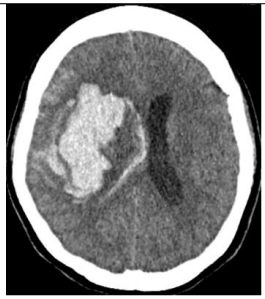
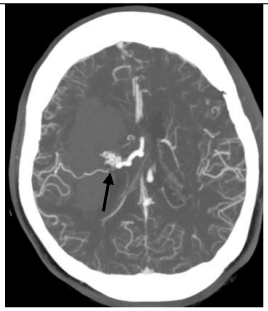
However, the CPG DG opines that patients not fulfilling the above criteria can also be recommended for further imaging based on clinical grounds. Consideration should also be taken into account of the age, haemodynamic status and pre-morbid status.

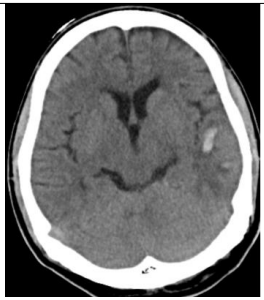
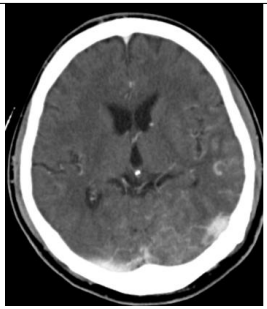
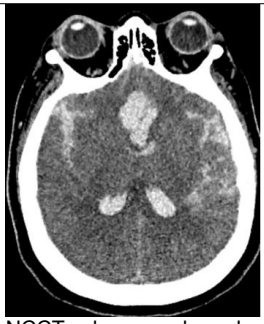
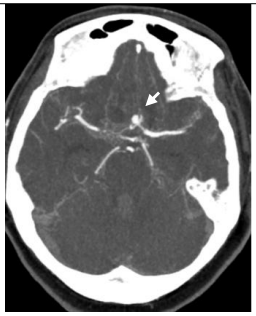
CT and MRI are widely used options in the investigation of ICH causes. CT angiography (CTA), a suitable first-line investigation, has a modest diagnostic accuracy in detecting underlying macrovascular cause with sensitivity of 74% (95% confidence interval [CI] 62 to 84) and specificity 91% (95% CI 86 to 94). Combining CTA with DSA improves detection rates with sensitivity of 100% (95% CI 80 to 100) and specificity 100 (95% CI 96 to 100). Despite having

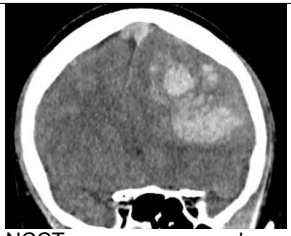
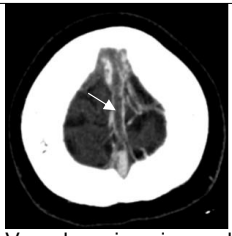
low sensitivity, a combination of CTA and MRI/Magnetic Resonance Angiography (MRA) gives a specificity of 94% (95% CI 90 to 97).[26, level III] MRA using time-of-flight (TOF) or ASL (Arterial Spin Labeling) protocols can visualise the blood vessels without the use of contrast. In addition, MRI may help to establish a non-macrovascular cause of ICH (e.g. cerebral amyloid angiopathy, deep perforating vasculopathy or malignancy).[23]

Digital Subtraction Angiography (DSA) remains the gold standard to evaluating for macrovascular cause of ICH but it carries a low risk of neurological complications (1.3 - 1.8%) and permanent neurological deficits (0.2 - 0.3%).[27] One advantage of DSA is endovascular intervention may be performed in the same setting. Timely endovascular therapy may prevent rebleeding, improve vasogenic oedema/ mass effect, and restore circulatory integrity. Table 1 illustrates imaging findings and endovascular management of specific macrovascular causes of ICH.

Table 1. Neuroimaging findings and endovascular treatment of specific macrovascular aetiologies of ICH

Macrovascular aetiologies	Non-Contrast CT Brain	Non-Invasive Neurovascular Imaging (e.g. CTA/CTV)	Endovascular Treatment Objectives
Brain AVM	 NCCT shows intraparenchymal haemorrhage. Possible to have associated foci of calcifications.	 Vascular imaging shows prominent, abnormal tangle of blood vessels (nidus, black arrow) within or adjacent to the haemorrhage, with early venous opacification.[28]	Targeted embolisation of angioarchitectural weak points responsible for the haemorrhage i.e. intranidal aneurysm, flow related aneurysm.[28]

Dural AVF	 NCCT shows intraparenchymal haemorrhage.	 Vascular imaging shows lack of vascular nidus, prominent venous sinus and tortuous cortical veins with early opacification.[28]	Embolisation of the arteriovenous shunt contributing for the venous hypertension and intracranial haemorrhage.[28]
Brain Aneurysm	 NCCT shows subarachnoid haemorrhage. Possible with intraparenchymal component if aneurysm is located near to brain parenchyma. Aneurysm may appear as “filling defect” within the haematoma.[29]	 Vascular imaging shows aneurysmal dilatation of the artery (white arrow) in the region of predominant subarachnoid haemorrhage.[29]	Embolisation of the ruptured aneurysm via endovascular coiling, with or without adjunctive procedure i.e. balloon assisted, stent assisted or flow diverter stenting.[29]

Cerebral Venous Thrombosis	 NCCT shows intraparenchymal haemorrhage. Hyperdense and dilated venous sinus/ cortical veins in keeping with thrombosis[4].	 Vascular imaging shows filling defects (white arrow) in the dural venous sinus/ with or without filling defects in the cortical veins.[30]	In worsening ICH and clinical deterioration despite anticoagulant, venous mechanical thrombectomy is a consideration for rescue treatment.[30]

(Images courtesy of Yuh Yang Leong, Universiti Kebangsaan Malaysia)

Ideally, all patients with ICH should have a vascular imaging to exclude vascular anomalies. However, considering that the majority of patients with ICH would have a normal vascular imaging, and the routine use of vascular imaging would increase clinical burden, the following recommendations are made:

Recommendations 2

- Patients who are suitable to undergo vascular imaging should be considered for advanced neuroimaging as the following:
  - computed tomography angiography (CTA) preferably within the same admission
  - in concomitant subarachnoid haemorrhage, CTA should be done emergently
  - if CTA is negative, referral to an interventional neuroradiologist for digital subtraction angiography may be considered
  - magnetic resonance imaging, when available, may be used to detect non-macrovascular causes
  - magnetic resonance angiography is an alternative to CTA in patients with renal impairment or contrast allergies.

Refer algorithm 1

Radiological Signs that Predict Haematoma Expansion

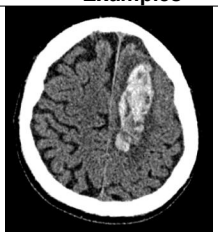
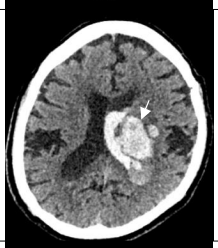
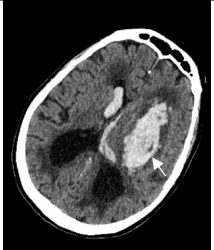
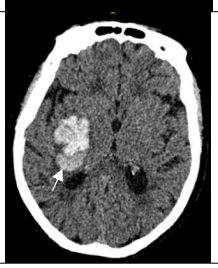
Haematoma expansion in ICH is linked to poor outcomes.[31] Identifying patients at risk of haematoma expansion is important as they may benefit from haemostatic therapies. In resource-limited settings, early recognition of such patients can aid in prognostication and optimal allocation of scarce resources e.g. ICU or high-dependency beds.

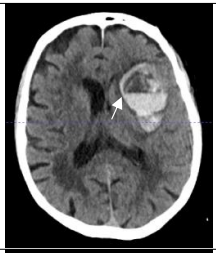
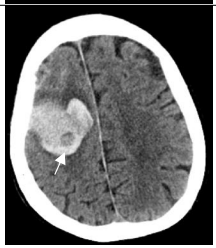
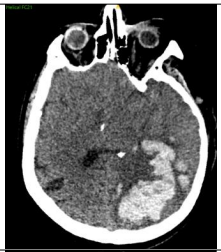
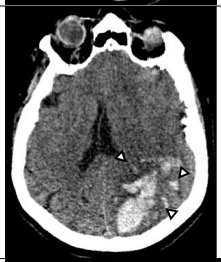
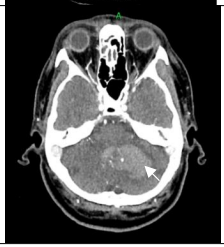
Non-contrast CT brain is the primary imaging modality for diagnosing ICH. It can also be used to identify haematoma expansion. Various imaging features on CT have been linked to an elevated risk of haematoma expansion and poor outcomes:[32, level II-2]

i. heterogeneous density
ii. hypodensities
iii. black hole sign

iv. blend sign
v. fluid level
vi. swirl sign
vii. irregular shape
viii. island sign

Table 2. Non-contrast CT and CT angiography signs predicting haematoma expansion

Signs	Definitions	Examples
Heterogeneous Density	Presence of ≥3 areas of hypodensity within the main ICH, in contrast to its overall density	
Hypodensity	Any hypodense region encapsulated within the haemorrhage, regardless of its shape, size or density (white arrow).	
Black Hole Sign	A hypodense area within the ICH showing a density difference greater than 28 HU compared with surrounding haemorrhage and not connected to external structures (white arrow).	
Blend Sign	A hypodense region adjacent to a hyperdense region within the ICH, marked by a clear, sharp boundary and a density difference exceeding 18 HU (white arrow).	

Fluid level	A distinct separation within the ICH, where a hypodense region lies above a hyperdense region, separated by a clear straight line (white arrow).	
Swirl Sign	An area of hypo- or isodensity, relative to brain parenchyma, that may or may not connect with structures surrounding the ICH (white arrow).	
Irregular Shape	Presence of ≥ 2 focal irregularities along the haematoma margin, either in contact or not with the edge of haematoma	
Island Sign	Characterised by ≥ 3 scattered small haematomas separated from primary ICH or ≥4 small haematomas, some or all of which may be connected to the main ICH (arrow heads)	
CT angiography spot sign	at least one element with either serpiginous or spot-like appearance, >1.5 mm in diameter (maximal dimension), at least double density (Hounsfield unit) compared to background hematoma, and located within the margin of the parenchymal hematoma without connection to outside vessels (white arrow).	

(Definition: taken from Morotti et al[32] and Ovesen et al.[33]
Images courtesy of Zhe Kang Law, Universiti Kebangsaan Malaysia)

Another modality commonly used to investigate potential macrovascular causes of ICH is CT angiography (CTA) where spot sign may be observed. The sign is a unifocal or multifocal contrast enhancement observed within an ICH and appears separated from adjacent normal or abnormal blood vessels. The presence of a spot sign on CTA also serves as a predictor for haematoma expansion and is associated with increased risk of death or poor outcomes.[34, level II-2]

- Specific signs on non-contrasted CT brain and/or CT angiography are useful to identify patients at risk of haematoma expansion.

PRE-HOSPITAL CARE AND MANAGEMENT IN EMERGENCY DEPARTMENT

Prehospital Care

According to a study in Malaysia, nearly 30% of patients with suspected acute stroke arrived to emergency department by emergency medical services,[35] thus it is crucial for prehospital care responders as the first point of medical contact to be familiar with standardised stroke assessment tool e.g. FAST (face, arm, speech, time) or BE-FAST (Balance, Eyes, Face, Arm, Speech, Time). Airway, breathing and circulation should be rapidly evaluated to identify and treat life-threatening conditions.[36] As it may be challenging to differentiate between haemorrhagic and ischaemic stroke clinically, patients should be transported to the nearest acute stroke ready hospital with CT scan facility as soon as possible to ensure timely diagnosis and management.[36]

Pre-hospital Bypass to Hospital with Neurosurgical Services

As a selected subgroup of patients with ICH may benefit from neurosurgical treatment, the question arises whether these patients are best treated in a tertiary centre with neurosurgical service from the outset. However, as ICH could not be clinically differentiated from ischaemic stroke without neuroimaging, there is no direct evidence comparing management in a hospital with neurosurgical services vs the nearest hospital.

The Direct Transfer to an Endovascular Center Compared to Transfer to the Closest Stroke Center in Acute Stroke Patients with Suspected Large Vessel Occlusion (RACECAT) trial which explored the effect of direct transport to an endovascular treatment (EVT)-capable stroke centre vs nearest local stroke centre provided indirect evidence. In the prespecified ICH subgroup analysis of this trial, direct transfer to an EVT-capable stroke centre resulted in:[37]

- delayed arrival to the hospital (58 mins vs 22 mins)
- worse functional outcome at day-90 (odds ratio [OR]=0.47; 95% CI 0.25 to 0.90)
- higher mortality (HR=1.76, 95% CI 1.05 to 2.95)
- greater risk of adverse events (AEs) (OR=2.77, 95% CI 1.26 to 6.07); these were mainly driven by increased vomiting and pneumonia

Delays in arrival also meant delays in implementing acute treatment e.g. care bundle. Only a minority of the ICH patients require neurosurgery (8.8% in EVT-capable stroke centre vs 3.6% in local stroke centre; NS) and thus direct transfer to EVT-capable stroke centre was not required in most cases.

In local setting, patients with suspected stroke are usually sent to the nearest hospitals with CT scan facility. If ICH is diagnosed, patients are referred to neurosurgical team for further management.

Recommendations 3

- Patients with suspected intracranial haemorrhage should be transported to the nearest stroke ready hospital with computed tomography scan.
  - Transfer to a centre with neurosurgical service should be considered when there is an indication for neurosurgery.

Management in Emergency Department

All patients arrived in emergency department (ED) will be appropriately triaged to different priority lanes based on Malaysian Triage Scale Protocol. The initial emergency management of ICH include the rapid assessment and stabilisation of the airway, breathing, and circulation. Patient will be sent for brain imaging after stabilisation to establish the diagnosis. Neurological examination should be performed whenever appropriate to allow monitoring of patient's progress. ICH care bundle will then be initiated in ED within the first hour of diagnosis, which consists of blood pressure reduction, control of body temperature, control of blood sugar, and reversal of anti-coagulation to optimise patients' outcome. (Refer subsection Acute Medical Care for execution of ICH Care Bundle and **Appendix 3** for choice of antihypertensive)

Securing a patent airway is the initial vital step in managing an acute ICH patient with impaired conscious level.[38, level III] The goal is to maintain adequate oxygenation and ventilation, to assist cerebral resuscitation and, to prevent aspiration and secondary brain insult. Airway manipulation during intubation can result in physiological changes that may increase intracranial pressure (ICP) and decrease cerebral perfusion pressure (CPP). Thus, rapid sequence intubation (RSI) is performed as it offers high-quality intubation condition in the emergency setting with appropriate pre-intubation optimisation.[39, level III]

Table 3. Rapid Sequence Intubation in Acute ICH

Time	Steps	Drugs	Dose	Remarks
Zero minus 10 mins	**P**reparation	-	-	Prepare patient, equipment and drugs
Zero minus 5 mins	**P**re-oxygenation	100% oxygen	15 L via NRHFM ± 15 L via NP*	Add on NP for obese patients
Zero minus 3 mins	**P**re-intubation optimisation (to give fentanyl ± esmolol/ lignocaine)	Fentanyl	1 - 2 µg/kg (TBW[40])	Attenuate the reflex sympathetic response of laryngoscopy
		Esmolol	0.5 mg/kg over 1 min (IBW[41])	
		Lignocaine	1.5 mg/kg (ABW[6])	May cause hypotension, lack of evidence on reflex sympathetic response[39,42]
		Induction (choose either one of the induction agents)		
Zero	**P**aralysis with induction	Etomidate	0.3 mg/kg (ABW[40]); 0.2 mg/kg if haemo-dynamically unstable[39]	Drug of choice because of haemo-dynamically stable[39] Adrenal suppression controversy[42]
		Propofol	1.5 mg/kg (ABW[40]); reduce to 1/3 or 1/2 if elderly or haemo-	May cause hypotension Safe to be used in

Time	Steps	Drugs	Dose	Remarks
			dynamically unstable[39]	soy/egg/ peanut allergy[43]
		Midazolam	0.2 - 0.3 mg/kg (TBW[40])	Slow onset, may cause dose-dependent hypotension Use only if no other superior agent available
		Paralysis (choose either one of the induction agents)		
		Succinylcholine	1.0 - 1.5 mg/kg (TBW[40])	May cause hyperkalemia
		Rocuronium	1.0 - 1.2 mg/kg[39] (IBW[40])	Reversal drug: sugammadex
Zero plus 20 - 30 secs	**P**ositioning	-	-	Bed at sufficient height Sellick manouvre
Zero plus 45 - 60 secs	**P**lacement with proof	-	-	Test the patient's jaw for flaccidity and then intubate
Zero plus 2 mins	**P**ost-intubation management	-	-	Mechanical ventilation Sedation and analgesia

All dosages are adapted from Brown CA, Sakles JC, Mick NW, editors. The Walls Manual of Emergency Airway Management. Lippincott Williams & Wilkins; 2018.

*NP=nasal prong: NRHFM=non-rebreathing high flow mask; ABW=adjusted body weight; IBW=ideal body weight; TBW=total body weight
Dosing for obese patients will follow TBW/ABW/IBW (in bracket)
Obesity: Body mass index (BMI) ≥30 kg/m^2 (6)0

Recommendation 4
- Rapid sequence intubation should be performed when intubating patients with intracerebral haemorrhage in acute settings.

ACUTE MEDICAL MANAGEMENT

Blood Pressure Reduction

There are three cardinal features to consider when managing the blood pressure (BP) of a patient presented with acute spontaneous ICH which are:
- intensity of initial treatment to achieve specific BP targets
- stability of BP throughout the acute-subacute event
- overall outcomes following treatment

A meta-analysis of four randomised clinical trials (RCTs) showed that the risk of 3-month mortality was NS between patients receiving intensive BP-lowering treatment within 24 hours and guideline BP-lowering treatment. There was also NS difference between the two interventions when analysed according to 3-month mortality or dependency rates (modified Rankin Scale grade 3 - 6). However, intensive BP reduction was associated with a greater reduction of absolute haematoma growth at 24 hours (standardised mean difference [SMD]= -

0.110, 95% CI -0.214 to -0.006). In terms of methodology, a low risk of bias was found within the primary studies. There was NS heterogeneity between the effect size.[44, level I]

The above findings were supported by a more recent meta-analysis of six RCTs in terms of mortality or dependency at 90 days. The target SBP in intensive treatment was 110 - 149 mmHg while it was 150 - 179 mmHg in conservative treatment. These were aimed to achieve from 1 - 24 hours but majority of the patients, based on two RCTs, had BP lowering aimed within one hour. Apart from that, there were NS differences in haematoma growth at 24 hours, neurologic improvement at 24 hours, hypotension at 72 hours and serious adverse events (SAEs) at 90 days between intensive and conservative BP lowering groups. In subgroup analysis of haematoma growth, significant reduction was seen intensive BP reduction in patients ≤62 years old (OR=0.66, 95% CI 0.51 to 0.86), time from symptoms onset to treatment ≤6 hours (OR=0.72, 95% CI 0.51 to 1.01), baseline hematoma volume ≤15 mL (OR=0.66, 95% CI 0.51 to 0.86) and combined intraventricular haemorrhage (IVH) ≤25% (OR=0.68, 95% CI 0.52 to 0.90) subgroups. Risk of bias was low in the included studies.[45, level I]

A post-hoc analysis of Antihypertensive Treatment of Acute Cerebral Hemorrhage-II trials on ICH patients with initial systolic blood pressure (SBP) of ≥220 mmHg, intensive SBP reduction (aiming for SBP of 110 - 139 mmHg) led to risk of neurological deterioration within 24 hours (RR=2.28, 95% CI 1.03 to 5.07) and kidney AE within seven days of discharge (RR=3.22, 95% CI 1.21 to 8.56). The lowest mean SBP after randomisation was 121 - 127 mmHg in the intensive group. However, there were NS differences in death or severe disability at 90 days, haematoma expansion, treatment-associated SAEs within 72 hours and kidney SAE within seven days of discharge.[46, level I]

Patients with spontaneous ICH in whom acute BP lowering is considered, treatment is initiated within two hours of ICH onset and reaching target within one hour to reduce the risk of haematoma expansion and improve functional outcomes.[23]

Recommendation 5

- The blood pressure in patients presenting with acute intracerebral haemorrhage should be treated intensively within one hour of presentation with target systolic blood pressure (SBP) of 130 - 140 mmHg.
  - More gradual reduction of blood pressure may be aimed for when initial SBP is ≥220 mmHg

Refer to **Appendix 3** for example for blood pressure lowering protocol

Hyperglycaemia

Hyperglycaemia had been associated with haematoma expansion, perihaematomal oedema, higher mortality and poor functional outcome[47]. Evidence for treating hyperglycaemia is provided by the INTERACT3 trial (The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial). Glycaemic control (targeting blood glucose of <7.8 mmoL in non-diabetic and 10 mmol/L in diabetic) as part of a care bundle which also include early intensive blood pressure lowering, fever control, and anticoagulation reversal—significantly improved functional outcomes (see Care bundle section)[48].

Fever

Fever occurs after ICH as a direct sequelae of brain damage and re-setting of thermostat centre in the hypothalamus or infection. Fever is an independent predictor of haematoma expansion, perihaematomal oedema, poor functional outcome and mortality[49]. Similar to hyperglycaemia,

evidence for treating pyrexia to achieve a body temperature of ≤37.5°C is provided by the INTERACT3 trial (see Care Bundle section)[48].

Haemostatic Therapies

ICH with concurrent use of anticoagulant

The use of anticoagulant increases the risk of haematoma expansion, death and disability after ICH[50,51]. With this respect, vitamin-K antagonist (VKA) carries a higher risk of haematoma expansion and worse outcomes compared with non-vitamin K oral anticoagulant (NOAC)[52-54]. In ICH with concurrent use of warfarin, a higher international normalised ratio (INR) is associated with haematoma expansion[55]. On the other hand, an INR of <1.3 is associated with lower rates of haematoma expansion[56]. Bleeding may be prolonged despite reversal of anticoagulation[55]. Care bundle which includes reversal of INR significantly improves functional outcomes in patients with ICH[48].

Reversal of vitamin K antagonist (VKA)

Intravenous (IV) vitamin K, prothrombin complex concentrate (PCC) and fresh frozen plasma (FFP) are several options of haemostatic agents in ICH with concurrent vitamin K antagonist use. In the INR Normalisation in Patients with Coumarin-related Intracranial Haemorrhages (INCH) RCT, 4-factor PCC was more effective in normalising INR to <1.2 within three hours compared with FFP (67% vs 9%, p=0.0003). Apart from that, haematoma expansion at three hours was higher with FFP (mean values of 23.7 mL vs 9.7 mL; p=0.023). However, 4-factor PCC was NS compared with FFP in reduction of death and dependency at day 90, and SAE. [57] On the other note, the effect of IV vitamin K takes up to 12 hours to peak and persists till 24 hours.[58]

In the AHA/ASA 2022 Guideline, the followings are recommended for patients with VKA-associated spontaneous ICH:[23]

- with INR ≥2.0, 4-factor PCC is preferred to FFP in achieving rapid correction of INR and limit haematoma expansion
- with INR of 1.3 to 1.9, PCC may be used to achieve rapid correction of INR and limit haematoma expansion
- IV vitamin K should be administered directly after coagulation factor replacement (PCC or other) to prevent subsequent increase in INR and subsequent haematoma expansion

In an RCT on care bundle, the INR target is <1.5 within one hour of anticoagulant reversal treatment in those taking warfarin.[48, level I]

Recommendation 6

- In patients with intracerebral haemorrhage and concurrent vitamin K antagonist (VKA) use, 4-factor prothrombin complex concentrate (PCC) or fresh frozen plasma (FFP) should be given as soon as possible to reverse anticoagulant effect of VKA.
  - PCC is the preferred choice.
  - An international normalised ratio (INR) of <1.5 should be targeted.
- Intravenous vitamin K should be given together with PCC or FFP to sustain the reversal of INR.

Refer to **Appendix 4** on Administration Protocol of Anticoagulation Reversal.

Reversal of Direct Oral Anticoagulant

Idarucizumab is a human monoclonal antibody fragment which reverses the anticoagulant effect of dabigatran, a direct thrombin inhibitor. In the Reversal Effects of Idarucizumab on Active

Dabigatran (RE-VERSE AD) prospective cohort study, 5 g of IV idarucizumab completely reversed elevated dilute thrombin time and ecarin clotting time.[59,60, Level II-2] There was no RCT testing the efficacy of idarucizumab.

Andexanet alfa is a reversal agent for Factor Xa inhibitors. In the Andexanet for Factor Xa Inhibitor–Associated ICH (ANNEXA-I) RCT, andexanet alfa was compared with usual care in patients with Factor Xa inhibitor-related ICH. The primary haemostatic efficacy end point after randomisation was defined as a combination of:

- a change in the haematoma volume of ≤20% (excellent haemostatic efficacy) or ≤35% (good haemostatic efficacy) within 12 hours
- an increase in the National Institutes of Health Stroke Scale (NIHSS) <7 points
- no rescue therapies e.g. andexanet, PCC or surgery to decompress the hematoma within 3 - 12 hours

Andexanet alfa was found to be superior to usual care (of which 86% received PCC) in haemostatic efficacy (67.0% vs 53.1%, p=0.003). However, there was higher risk of thrombotic events with it (10.3% vs 5.6%, p=0.048). A subgroup analysis comparing the dose of andexanet alfa showed that low dose medication (400 mg over 15 to 30 minutes followed by a continuous infusion of 480 mg over two hours) was superior than usual care, whilst high dose (800 mg + continuous infusion of 960 mg) was not.[61]

In the Tranexamic Acid for Intracerebral Hemorrhage in Patients on Non-Vitamin K Antagonist Oral Anticoagulants (TICH-NOAC) RCT, IV tranexamic acid at a dose of 1 g over 10 minutes followed by 1 g over 8 hours did not reduce the risk of haematoma expansion or death.[62]

The AHA/ASA 2022 Guideline recommend the followings as reasonable to be used for patients with direct factor Xa inhibitor-associated spontaneous ICH:[23]

- idarucizumab to reverse the anticoagulant effect of dabigatran
- andexanet alfa to reverse the anticoagulant effect of factor Xa inhibitors

Recommendation 7

- Patients with dabigatran-related intracerebral haemorrhage (ICH) may be considered to receive intravenous (IV) idarucizumab as reversal agent.
- Patients with factor Xa inhibitor-related ICH may be considered to receive IV andexanet alfa as a reversal agent, if available.
  - 4-factor prothrombin complex concentrate may be considered as an alternative.

Antiplatelet-associated ICH

Approximately 25% of patients with ICH are on antiplatelet treatment at the time of ICH.[63] Prior antiplatelet use is a known predictor of haematoma expansion.[50] Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH) was a large and multi-centre RCT. It compared platelet transfusion with standard treatment in patients with antiplatelet-related ICH who were not planned for neurosurgery. Majority of the patients (97%) were taking aspirin alone or in combination with other antiplatelet agent. The trial was terminated early as the odds of adverse events, death and dependency were higher in those receiving platelet transfusion (OR=2.05, 95% CI 1.18 to 3.56).[64,65]

The AHA/ASA 2022 Guideline recommends that for patients with spontaneous ICH being treated with aspirin and not scheduled for emergency surgery, platelet transfusions should not be administered due to its harmful effect.[23]

Recommendation 8
- In patient with intracerebral haemorrhage and concurrent use of antiplatelet agent, platelet transfusion should not be used.

Care bundle

- Care bundle refers to initial set of interventions aimed at optimising patients' outcomes. In the context of ICH, it consists of four different parameters:
  - blood pressure reduction
  - control of body temperature
  - control of blood sugar
  - reversal of anti-coagulation

Most patients with acute ICH present with elevated BP which is associated with increased risk of haematoma expansion, neurological deterioration, death and dependency.[66-68]

An Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3) was a pragmatic, international, multicentre, blinded endpoint, stepped wedge cluster randomised controlled trial at hospitals in nine low-income and middle-income countries and one high-income country. It compared care bundle and usual care in 7,036 patients with ICH presenting within six hours of onset. In the RCT, components of care bundle were:[48, level I]

i. early intensive BP management to achieve a target SBP of <140 mmHg within one hour of the initiation of treatment but not <130 mmHg
ii. intensive control of elevated blood glucose to achieve a glucose target of 6.1 - 7.8 mmol/L (for patients without diabetes) and 7.8 - 10.0 mmol/L (diabetic patients) as soon as possible after the initiation of treatment
iii. treatment of pyrexia to achieve a body temperature of ≤37.5°C within one hour of initiation
iv. reversal of abnormal anticoagulation in those taking warfarin using FFP or PCC to reach an INR of <1.5 within one hour of treatment

The findings were:
- the likelihood of a poor functional outcome at six months was lower in the care bundle group (OR=0.86, 95% CI 0.76 to 0.97)
- the care bundle group had fewer serious adverse events (16.0% vs 20.1%; p=0.0098)

Recommendation 9
- Care bundle, to be achieved within one hour of treatment initiation and consisting of the following, should be offered to patients with acute intracerebral haemorrhage:
  - Intensive blood pressure reduction to target systolic blood pressure of 130 - 140 mmHg
  - treating pyrexia to achieve a body temperature of ≤37.5°C
  - glycaemic control with a target of 6.1 - 7.8 mmol/L (non-diabetic) and 7.8 - 10.0 mmol/L (diabetic)
  - reversal of abnormal anticoagulation in those taking warfarin using prothrombin complex concentrates or fresh frozen plasma to reach an INR of <1.5.

Admission to an Organised Stroke Unit
An organised stroke unit is a geographically discrete, dedicated area for stroke patients, staffed by a coordinated multidisciplinary team with special expertise in stroke care.[69] An organised stroke unit may be a hospital ward by itself, or a part of another ward.

There are three cardinal features to consider when managing ICH with admission to a specialised stroke unit:

- multidisciplinary care coordination for comprehensive management
- early mobilisation and rehabilitation to optimise functional recovery
- systematic monitoring and treatment of secondary complications (e.g. hyperglycaemia, hypoxia, pyrexia)

A meta-analysis of seven RCTs demonstrated that stroke unit care reduced death or dependency (modified Rankin Scale [mRS] 3 - 6) compared with general ward care for ICH patients (RR=0.79, 95% CI 0.61 to 1.00). Mortality reduction was more pronounced in ICH (RR=0.73, 95% CI 0.54 to 0.97) than in ischaemic stroke (RR=0.82, 95% CI 0.61 to 1.09). The methodological quality of the included trials was high.[70, level I]

In a more recent and large Cochrane network meta-analysis reinforced the above findings. It showed that organised stroke unit reduced poor outcomes (mRS 3 - 6) in ICH patients (OR=0.37, 95% CI 0.21 to 0.65). Benefits were consistent across age, sex and stroke severity, with NS increase in hospital length of stay. The greatest benefits were observed in discrete stroke wards with dedicated multidisciplinary teams. Based on GRADE assessment, the outcomes were generally of moderate quality.[69, level I]

Recommendation 10

- All patients with acute intracerebral haemorrhage should be admitted to an organised stroke unit staffed by a multidisciplinary team.

Prognostic Scores in Predicting Mortality
There are a few validated prognostic scorings that is used widely for the mortality prognostication following the onset of ICH i.e.:

- Intracerebral Hemorrhage (ICH) score
- Modified Intracerebral Hemorrhage (m-ICH) score
- Functional Outcome in Patients with Primary Intracerebral Hemorrhage (FUNC) score
- Intracerebral Haemorrhage Grading Scale (ICH-GS) score

ICH Score is the earliest score developed in 2001 to predict mortality among patients with ICH.[71] This score has five parameters and provides fast assessment upon the initial onset of ICH. It is also feasible to be used at the emergency department due to its simplicity. ICH volume can be rapidly measured using the ABC/2 method with excellent reliability.[72] (Refer to **Appendix 5**)

In a meta-analysis, the above four prognostic tools were evaluated and compared. The findings were:[73, level III]

- ICH score was the most extensively validated tool for mortality (42 studies)
- ICH score showed the highest pooled discrimination for mortality (C-statistic=0.84) while the other scores had a C-statistic of 0.82 each

There was variable risk of bias of the primary studies and these were mainly related to the lack of blinding, insufficient length of follow-up and sample non-representativeness of the full spectrum of the disease.

In the AHA/ASA 2022 Guideline, the followings are recommended in patients with spontaneous ICH:[23]

- administering a baseline measure of overall haemorrhage severity is part of initial evaluation to provide an overall measure of clinical severity
- a baseline severity score might be reasonable to provide a general framework for communication with the patient and their caregivers
- a baseline severity score should not be used as the sole basis for forecasting individual prognosis or limiting life-sustaining treatment

Recommendation 11

- Intracerebral Haemorrhage (ICH) score may be used for mortality prognostication in patients with intracerebral haemorrhage.
- ICH score should not be used as sole indicator to decide on the direction of care in patients with ICH.

Refer to **Appendix 6** for the ICH score.

Avoidance of early Do Not Attempt Resuscitation (DNAR)

Early withdrawal of life-sustaining therapies in ICH patients often leads to in-hospital deaths. Early prognostication in ICH is frequently inaccurate, risking premature withdrawal of care for potentially recoverable patients. These are discussed below.

Evidence on avoidance of early DNAR showed the following:

- Early DNAR use within 24 hours was associated with increase in hospital mortality (OR=3.28, 95% CI 2.07 to 5.19).[74, level III]
- Early care limitations use within 24 hours were associated with doubling 30-day mortality (HR=2.17, 95% CI 1.38 to 3.41).[75, level II-2]
- Overall mortality at 30 days was 29.8% (95% CI 21.5 to 37.7) less than the ICH Score–predicted mortality in patients with no planned DNAR orders or withdrawal of support for the first five days of hospitalisation.[62, level II-2]
- DNAR orders within 24 hours were linked to limitations in various treatments, including escalation to critical care (OR=0.07, 95% CI 0.03 to 0.17) and commencement of palliative care within 72 hours (OR=8.76, 95% CI 4.76 to 16.61).[76, level III]

Based on the AHA/ASA 2022 Guideline, aggressive care, including postponement of new DNAR orders or withdrawal of medical support is recommended until at least the second full day of hospitalisation in patients with spontaneous ICH who do not have pre-existing documented requests for life sustaining therapy limitations.[23]

Recommendation 12

- Early Do Not Attempt Resuscitation (DNAR) decision should be avoided in the first 48 hours in patients with acute intracerebral haemorrhage who do not have pre-existing DNAR status.

Seizure Prophylaxis

Seizures is a common complication seen in patients presenting with spontaneous ICH, with cumulative incidence ranging from 1.7 - 31%. Majority of seizures occur during the first 72 hours of presentation and are usually subclinical. Seizures occurring after spontaneous ICH may reduce cerebral blood flow, worsen midline shift and increase metabolic demand in the hypoxic tissues, leading to secondary brain damage. It is also associated with haematoma expansion, death and disability.[77, level I; 78, level I]

Based on a meta-analysis, the usage of antiseizure medications (ASM) as a primary prophylaxis for seizures in spontaneous ICH was not associated with reduced incidence of poor outcomes during long-term follow-up. There was also no association between prophylactic ASM usage and seizures occurrence during follow-up.[78, level I]

In a small double-blind RCT on patients with mild to moderate ICH, levetiracetam was effective in preventing early electrographic seizures compared with placebo (OR=0.16, 95% CI 0.03 to 0.94). However, there were NS differences in mean haematoma volume change, midline shift at 72 hours, functional outcomes and quality of life between both groups.[77, level I]

Based on the AHA/ASA 2022 Guideline, prophylactic antiseizure medication is not beneficial in patients with spontaneous ICH without clinical evidence of seizures.[23]

Recommendation 13
- Prophylactic antiseizure medications should not be given in patients with spontaneous intracerebral haemorrhage without seizures.
- In patients with early clinical seizures, antiseizure medications should be considered.

Thromboembolism Prophylaxis
Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a significant cause of morbidity and mortality in patients with acute ICH. Patients with ICH are at increased risk of VTE due to prolonged immobility and systemic inflammatory responses. Balancing the risk of VTE against the risk of haematoma expansion is a critical challenge in the management of these patients.

Recent evidence from clinical trials highlighted the safety and effectiveness of both physical and pharmacological interventions in the prevention of VTE in stroke. Key findings included:
- The Clots in Legs Or sTockings after Stroke (CLOTS 3) trial demonstrated that intermittent pneumatic compression (IPC) significantly reduced the risk of DVT in patients with acute stroke, including those with ICH, compared with those not on IPC (absolute risk reduction= -3.6, 95% CI -5.8 to -1.4).[79, level I]
- In a meta-analysis of nine RCTs of mainly moderate quality, there were NS differences in haematoma enlargement, extracranial haemorrhage and death between heparin prophylaxis (low molecular weight heparin [LMWH] or unfractionated heparin [UFH]) and no heparin prophylaxis (physical prevention). In the primary studies, the heparin prophylaxis was initiated between day one to day seven.[80, level I]

The AHA/ASA 2022 Guideline recommends the following for non-ambulatory patients with spontaneous ICH[23]:
- IPC to be started on the day of diagnosis for VTE (DVT and PE) prophylaxis
- low-dose UFH or LMWH may be initiated in reducing the risk for PE; prophylaxis at 24 to 48 hours from ICH onset may be reasonable to optimise the benefits of preventing thrombosis relative to the risk of haematoma expansion
- graduated compression/ thromboembolic deterrent (TED) stockings of knee-high or thigh-high length alone are not beneficial for VTE prophylaxis

The CPG DG opines that pharmacological VTE prophylaxis may be initiated after considering individual risk profile post-24 hours of spontaneous ICH onset. Clinical and radiological monitoring for haematoma stability should be considered.

Recommendation 14

- The following venous thromboembolism (VTE) prophylaxis may be initiated in non-ambulatory patient with spontaneous intracerebral haemorrhage:
  - intermittent pneumatic compression on the day of diagnosis
  - heparin prophylaxis after 24 hours of admission
- Graduated compression/thromboembolic deterrent (TED) stockings alone should not be prescribed for VTE prophylaxis.

Swallowing Assessment

Dysphagia is a common complication following ICH, affecting 63.6% of patients in the acute phase.[81] It increases the risk of aspiration pneumonia, malnutrition, and prolonged hospitalization, emphasizing the need for prompt and accurate swallowing assessment to improve outcomes. Current evidence on Fibreoptic Endoscopic Evaluation of Swallowing (FEES) in stroke patients, lacks specificity to ICH populations.[82] Major stroke guidelines also provide general recommendations but lack detailed protocols for dysphagia assessment in ICH.[23] This highlights a gap in standardised, ICH-specific swallowing assessment protocols. The Malaysian Ministry of Health's Standard Operating Procedure (SOP)[83] offers a structured framework for swallowing disorder assessment and management, promoting standardized care and improved outcomes. This SOP provides clear criteria and procedures for adult swallowing assessment, addressing the need for consistency in dysphagia management. Based on the SOP, the criteria and procedures for swallowing assessment in adults include the following:

Table 4. Criteria and procedure for swallowing assessment

Criteria for Swallowing Assessment	
Patient Stability	• Awake and alert. • Respiratory rate: 12–20 breaths/min. • SpO_2 ≥ 95%. • Minimal, manageable secretions (no frequent suctioning required).
Risk Indicators	• Coughing/choking during meals. • Prolonged meal duration. • Difficulty with different food textures. • Wet/gurgly voice after swallowing. • Weight loss or recurrent chest infections. •
Procedures for Swallowing Assessment	
Initial Screening	• Review patient history. • Obtain consent. • Conduct Water Swallow Test. • Observe for aspiration signs (e.g., cough, wet voice).
	• If risk detected, proceed to detailed assessment.
Clinical Swallowing Examination	• Assess oral motor and cranial nerve function. • Observe swallowing with food textures. • Conduct bedside meal observation.
Instrumental Assessments	• FEES: Scope via nose to assess pharyngeal phase. • VFSS**:** X-ray swallow study to detect aspiration or residue.

Management & Documentation	• Plan intervention and dietary modifications based on findings. • Document all findings and outcomes.

Recommendation 15
- Swallowing assessments should be performed for patients with intracerebral haemorrhage using standardised protocols, such as the Ministry of Health Standard Operating Procedure.
- A structured, stepwise approach starting from screening to clinical and instrumental assessments ensures accurate diagnosis and effective management.

NEUROSURGERY

The decision to perform neurosurgery is complex and rests with the neurosurgical team in consultation with the patient and their family. A clinical indication for surgery does not invariably lead to an operation as factors such as the patient's or family's consent, operative risk, the perceived neurological prognosis, and prevailing local surgical expertise and protocols needs to be considered

Decompressive craniectomy
Decompressive craniectomy had been shown to reduce mortality in patients with malignant middle cerebral artery infarction by relieving raised intracranial pressure (ICP).[84] It is thought that this intervention may have similar mortality benefit in severe ICH.

This issue was explored in a large international Swiss trial of decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral hemorrhage (SWITCH). It compared decompressive craniectomy without evacuation performed within 72 hours of symptoms onset with best medical treatment in patients aged <75 years with deep supratentorial ICH (basal ganglia and thalamus), haematoma volumes of 30 - 100mL, NIHSS of 10 - 30 and GCS of 8 - 13. Patients in decompressive craniectomy had lower mRS 5 - 6 at 180 days (44% vs 58%; RR= 0.77, 95% CI 0.59 to 1.01). Decompressive craniectomy reduced the risk of mRS 5 - 6 by 13% (95% CI 0 to 26). There was NS difference in serious adverse events. The results provided weak evidence that decompressive craniectomy may be beneficial and harm was unlikely.[85]

The AHA/ASA 2022 ICH guideline states that decompressive craniectomy with or without haematoma evacuation may be considered for patients with large supratentorial ICH, midline shift, comatose or medically intractable raised ICP to reduce mortality.[23]

Recommendation 16
- In patients with severe and large supratentorial deep intracerebral haemorrhage decompressive craniectomy may be considered.

Haematoma evacuation
A meta-analysis of seven RCTs concluded that surgical hematoma evacuation did not significantly improve functional outcome measured by Glasgow Outcome Scale, modified Rankin Scale and Barthel index compared with conservative management in lobar ICH (OR=0.80, 95% CI 0.62 to 1.04). The analysis noted heterogeneity in surgical methods (endoscopic, stereotactic, craniotomy). Quality assessment showed moderate risk of bias of included studies.[86,level I]

The large Minimally Invasive Surgery Plus Alteplase for Intracerebral Hemorrhage Evacuation (MISTIE III) RCT compared image-guided catheter-based haematoma evacuation followed by thrombolysis with medical management in patients with supratentorial ICH ≥30 mL. While the trial failed to meet its primary endpoint (mRS 0 - 3 at 1 year: 45% vs 41%, p=0.33), it demonstrated reduced early mortality (1% vs. 4% at 7 days, p=0.02) and a dose-dependent relationship where a residual hematoma volume ≤15 mL correlated with better outcomes.[87,level I]

The recent and large Early Minimally Invasive Removal of Intracerebral Hemorrhage (ENRICH) RCT compared trans-sulcal parafascicular evacuation to medical management in patients with ICH volumes of 30 - 80 mL within 24 hours of symptoms onset. At 180 days, the surgery group had significantly superior functional outcomes (utility-weighted mRS: 0.458 vs. 0.374) and lower 30-day mortality (9.3% vs. 18.0%). Subgroup analysis confirmed benefit in lobar haemorrhages (mean mRS difference: 0.127, 95% Credible interval 0.035 to 0.219) but not in deep basal ganglia lesions. Post-operative re-bleeding rates associated with neurologic deterioration were low (3.3%).[88,level I]

The AHA/ASA 2022 ICH guideline states that craniotomy for haematoma evacuation may be a life-saving procedure in supratentorial ICH patients who are deteriorating. Minimal invasively surgery using stereotactic/endoscopic techniques with or without thrombolytics can be useful for patients with supratentorial ICH >20 – 30 mL and GCS of 5 - 12.[23]

Recommendation 17
- Haematoma evacuation for deep supratentorial intracerebral haemorrhage using open craniotomy may be considered for patients who are deteriorating as a life-saving measure.
- Minimally invasive surgery may be considered for patients with lobar intracerebral haemorrhage with a volume of 30 to 80mL within 24 hours of symptoms onset.

Posterior Fossa ICH

- The posterior fossa is a narrow, confined space containing the brainstem and cerebellum. Cerebellar haemorrhage may cause compression on the fourth ventricle resulting in obstructive hydrocephalus and on the brainstem causing herniation syndrome.

There is no RCT comparing haematoma evacuation with conservative management in cerebellar ICH. A large individual patient data meta-analysis of observational studies found that haematoma evacuation with or without EVD in patients cerebellar ICH:
- improved survival (74.5% vs 45.1%) in those with ICH volume ≥15mL
- lowered likelihood of good functional outcome (30.6% vs 62.3%) in those with ICH volume≤12mL[89,level II-2]

The AHA/ASA 2022 Guideline and European Stroke Organisation (ESO) and European Association of Neurosurgical Societies (EANS) 2025 guideline both recommended haematoma evacuation in patients with cerebellar ICH with volume of ≥15mL as a life-saving treatment. [23,90]

Recommendation 18
- In patients with cerebellar intracerebral haemorrhage with a volume of ≥15mL, haematoma evacuation with or without external ventricular drain should be considered.

Intraventricular haemorrhage

Intraventricular haemorrhage (IVH) is a serious neurological condition that is associated with high morbidity and mortality. The standard management of IVH includes external ventricular drainage (EVD) to relieve hydrocephalus, but recent studies have explored the use of thrombolytic agents to enhance clot clearance and improve patient outcomes.

A large RCT (Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase III-CLEAR III trial), compared EVD with intraventricular alteplase with EVD alone. The outcomes at 180 days showed that intraventricular alteplase resulted in:[91,level I]

- NS difference in functional outcomes of mRS 0-3 (48% vs 45%, p=0.554)
- Higher rate in functional outcome of mRS 5 (17% vs. 9%, p=0.007)
- Lower mortality rate (18% vs. 29%, p=0.006)
- Lower incidence of ventriculitis (7% vs. 12%, p=0.048)

A meta-analysis of 11 trials (5 randomized controlled trials and 6 observational studies)[92, level I] involving 680 patients demonstrated that neuroendoscopy combined with EVD when compared to EVD + intraventricular fibrinolysis:[92,level I]

- Reduced mortality (OR = 0.31; 95% CI 0.16 to 0.59)
- Higher hematoma evacuation rates (>60% clearance in 88.9% vs. 29.4%, p < 0.001)
- Improved functional outcomes (OR = 4.51; 95% CI 2.81 to 7.72)
- Lower ventriculoperitoneal shunt dependency (OR = 0.16; 95% CI 0.06 to 0.40)

Recommendation 19

- In patients with intracerebral haemorrhage complicated with intraventricular haemorrhage and hydrocephalus, external ventricular drain should be offered
  - Intraventricular fibrinolysis with alteplase may be considered
  - Neuroendoscopy may be considered

Recommendation 20

- In view of potential benefit of specific neurosurgical intervention, patients with the following conditions should be referred to the neurosurgical service for assessment and management:
  - Large and/or expanding supratentorial intracerebral haemorrhage (ICH) (>20 ml volume)
  - Any intraventricular extension
  - Posterior fossa ICH irrespective of volume
  - Deteriorating consciousness level and/or signs of raised intracranial pressure
  - Suspicion of a vascular malformation, independent of volume or location

Refer **Algorithm 2**

INTENSIVE CARE

Intracranial pressure monitoring in acute ICH

- Intracranial pressure (ICP) monitoring is established by insertion of an ICP probe into the brain parenchyma or an external ventricular drain (EVD) into the ventricles. It allows close observation of the ICP trend, which garners interest in its use in acute ICH management. This is despite the associated risks of intracranial bleeding and infection.

There are limited numbers of studies looking at the outcomes from ICP monitoring in acute ICH and they were either retrospective cohort in design[93,Level II-2] or secondary analysis of larger trials.[94-96. II-2]

In a single centre cohort study compared ICP monitoring (103 patients) and non-ICP monitoring (93 patients) for ICH patients over a period of seven years, [93,Level II-2] the adjusted results demonstrated a more favourable distribution of extended Glasgow Outcome Scale (GOS-E) scores in the ICP-monitored group (adjusted OR [aOR] 0.54 (95% CI 0.31 to 0.93). Subgroup analysis indicated that this favourable effect was observed in patients with Glasgow Coma Scale (GCS) scores of 9–12, but not in those with GCS scores of 3–8.

A large retrospective analysis of data from the Ethnic/Racial variations of Intracerebral Hemorrhage (ERICH) study between 2010 and 2015[94, Level II-2] showed no significant difference in the primary outcome of 90-day mortality between the matched ICP monitoring (420 patients) and no ICP monitoring (420 patients) cohorts with an adjusted OR of 1.174 (95%CI 0.875 to 1.575). Meanwhile a secondary analysis of the MISTIE III trial[95, Level II-2] revealed that patients with spontaneous ICH who had ICP monitors placed had significantly poorer neurological outcomes (OR=2.76, 95%CI 1.30 to 5.85) and recorded higher incidence of death (31.4% vs 21.0%).

The *SYNAPSE-ICU* study, a large international prospective cohort of ICU admissions for acute brain injury (traumatic brain injury, ICH, or subarachnoid haemorrhage), evaluated outcomes in spontaneous ICH patients. ICP monitoring was more frequently utilised in moderately severe cases (ICH score 3 or 4). Its use was associated with reduced in-hospital and 6-month mortality (HR=0.49, 95% CI 0.35 to 0.71), but no improvement in 6-month functional outcomes was observed.[95, Level II-2]

European Stroke Organisation (ESO) and European Association of Neurosurgical Societies (EANS) 2025 guideline states that there is uncertainty about the use of invasive ICP monitoring in patients with severe acute spontaneous space-occupying ICH and recommends recruitment into RCTs for these patients.[90]

Recommendation 21

- Intracranial pressure (ICP) monitoring in patients with acute intracerebral haemorrhage may not be routinely performed.

Ventilation and tracheostomy

Early Tracheostomy

- Tracheostomy is the airway procedure that is performed in prolonged ventilated patients. In the context of ICH, early tracheostomy is often considered in ICH patients with
  - poor Glasgow Coma Scale (GCS)
  - prolonged ventilation.

Tracheostomy is considered in patients with ICH, when the weaning process is difficult or extubation is not possible due to poor GCS recovery. The timing and safety of the procedure in ICH patients are still inconclusive.[96]

A meta-analysis of tracheostomy timing (early tracheostomy defined as <5 days and late tracheostomy as >10 days) in critically ill stroke patients included 13 studies with 17,346 patients, assessing its association with all-cause mortality and neurological outcomes (modified Rankin Scale, mRS), hospital length of stay (LOS), and intensive care unit (ICU) LOS. Among the reported cases, ICH, AIS and SAH accounted for 83%, 12%, and 5%, respectively. All 13 studies included were deemed to be good quality. Meta-regression analyses were performed to explore the association between tracheostomy timing and outcomes.
Findings showed :[96, level II-2]

- Early tracheostomy conferred no mortality benefit compared with late tracheostomy (7.8% vs. 16.4%, $p = 0.7$)
- Tracheostomy timing was not associated with improved neurological outcomes. There was no association between mean mRS score and time to tracheostomy on metaregression (β= 0.02, 95% CI = -0.12 to 0.16)
- Tracheostomy timing was not associated with reduced ICU LOS (β= 0.03, 95% CI = -0.76 to 0.82) or hospital LOS (β= 0.81, 95% CI =-0.68 to 2.31)

Recommendation 22

- Early tracheostomy in patients with intracerebral haemorrhage may not be routinely performed.

Pharmacological agents for cerebral oedema

A large cohort study, ERICH, explored the effect of hyperosmolar therapy (mannitol and hypertonic saline) on outcomes after ICH. The results showed that hyperosmolar therapy was associated with higher mRS (mean mRS was 0.33 higher, p=0.0174). Post hoc analysis revealed more brain oedema, herniation, and death at discharge in hyperosmolar therapy group.[97, level II-2]

Recommendation 23

- Hyperosmolar therapy may not be routinely administered for cerebral oedema in patients with spontaneous intracerebral haemorrhage.

REHABILITATION

Neurological rehabilitation aims to empower persons with stroke by guiding functional recovery and reducing effects and complications of stroke-related impairments. Persons with stroke will undergo a comprehensive, specialised, interdisciplinary assessment after which goals are set.

Strategies are used to educate and enable persons with stroke to participate in activities of daily living (ADL) and previous life roles. Persons with stroke have the potential for improvement using these strategies. This is based on neuroplasticity which is the brain's ability to reorganise and form new neural connections.
Following stroke, the impairments may affect physical, cognitive function, language and mood domains. Early initiation of stroke rehabilitation is important to reduce the complications and promote neuroplasticity.[98]

Early Rehabilitation Post-ICH

- Early rehabilitation typically involves early mobilisation within 72 hours of admission to the ward.

- Rehabilitation protocol needs to be individualised with complete assessment by multidisciplinary team to reduce disability and improve recovery.

A systematic review involving 13 studies concluded that intensive rehabilitation initiated in the acute phase, within 24 - 72 hours after the onset of ICH, improved patients' outcomes. Most intensive rehabilitation included occupational therapy, physical therapy, kinesiotherapy, task training, ADL training and gait training. Of the 13 studies, 5 were considered of fair to good quality whilst 8 were considered poor.[99]

Patients generally received between 30 minutes to two hours of therapy per day for five days a week. Early initiation of rehabilitation had shown improvements in ADLs, motor function, quality of life and neurological function. Late initiation of rehabilitation can result in prolonged hospitalisation, permanent disability and increased mortality.[99, Level I]

From the similar meta-analysis study above, results on mortality were available in approximately half of the 13 included studies and generally showed low or absent mortality. However, in a subgroup analysis of patients with ICH from the *A Very Early Rehabilitation Trial (AVERT)*, early and intensive intervention initiated within 24 hours of stroke onset when compared to usual care was associated with an increased risk of mortality at 14 days post-stroke (OR=3.21, 95%CI 1.13 to 9.07). Notably, most of the primary studies included in the meta-analysis scored low on methodological quality based on the PEDro assessment.[99, Level I]

The CPG DG opines that early rehabilitation is beneficial to the post-ICH patients, therefore it should be offered to them.

Recommendation 24
- Early initiation of rehabilitation should be offered within 24 - 72 hours of admission for patients with intracerebral haemorrhage (ICH).
  - However, very early intensive rehabilitation (<24 hours) should be avoided.

Neuropharmacological agents

Cognitive impairment is common after ICH, affecting 19-63% of patients at 6 months post-ICH.[100]

Cognitive rehabilitation refers to a set of interventions that aim to improve a person's ability to perform cognitive tasks by retraining previously learned skills and teaching compensatory strategies.[101]

- The mainstay of cognitive rehabilitation includes strategies to restore or compensate cognitive recovery. These are individualised tailored interventions done by occupational therapist and/or clinical psychologist.
- Neuropharmacological augmentation is used as an adjunct to the above strategies.

In a large RCT involving patients with vascular dementia of more than 3 months' duration, including those with recent stroke, donepezil 5 mg and 10 mg daily was shown to be more effective than placebo. At 24 weeks, both doses produced significant improvements in cognitive function measured by:[102,Level I]

- Alzheimer's Disease Assessment Scale–cognitive subscale (ADAS-cog): mean change from baseline – donepezil 5 mg: –1.90 ($p = 0.001$); donepezil 10 mg: –2.33 ($p < 0.001$)

- Mini-Mental State Examination (MMSE): mean change from baseline – donepezil 5 mg: +1.04 ($p < 0.05$); donepezil 10 mg: +1.49 ($p < 0.001$)

In an evidence-based CPG, the following medications shown in Table 5 were discussed on their effectiveness in the treatment of stroke-related cognitive impairments:[103]

Table 5. Medications for treatment of stroke-related cognitive impairment

Medication	Outcome
Anti-depressants	May be beneficial for improving learning and memory
Piracetam	May be beneficial for improving global cognition but not in improving aphasia-related outcomes post-stroke. Avoid in early ICH period due to antiplatelet effects.
Acetylcholinesterase inhibitors	May be beneficial for improving naming but not for improving cognitive rehabilitation and mixed result on improving neglect
Dopaminergic medication	May be beneficial for improving aphasia-related outcomes post-stroke but not for improving neglect, learning and memory, and motor rehabilitation
Memantine	May be beneficial for improving discourse, naming, social communication auditory comprehension and global speech, and language

Based on PEDro quality assessment, most of the RCTs used in the guideline scored ≥6. Apart from that, the various outcomes showed minimal effectiveness in the treatment of stroke-related cognitive impairment. Caution has to be exercised as the medications are used off-label setting.

Recommendation 25
- Neuropharmacological augmentation may be offered to post-intracerebral haemorrhage patients during rehabilitation phase.

Muscle spasticity
Spasticity is defined as an abnormal increase in joint rigidity, accompanied by an exaggerated, velocity-dependent rise in muscle tone. It results from hyperexcitability of the tonic stretch reflex in individuals with upper motor neuron lesions.[104] If not appropriately managed, spasticity can lead to pain, psychological distress, and significant functional disability.

While most studies on muscle spasticity have been conducted in post-stroke population, the similarity in the underlying pathology of brain injury following stroke and traumatic ICH suggests that the effects on interventions for muscle spasticity should likewise be comparable.

A structured referral framework known as the “traffic light system” may guide clinicians in identifying when specialist input is needed.[105]This system classifies post-stroke patients into low, medium, or high risk for developing spasticity.

Table 6 Risk of spasticity and referral strategies

Risk category	Referral strategies
Low risk	Patients have persistent dexterity difficulties without increased muscle tone and require monitoring every 3–6 months
Medium risk	Patients may present with moderate muscle stiffness (Modified Ashworth

	Scale [MAS] score ≈1) within 1–14 days post-stroke, left-sided weakness, involuntary contractions, sensory loss, visual inattention, or large brain lesions. Younger stroke patients may also fall into this category. They should be reviewed by a multidisciplinary team and referred to a spasticity specialist (e.g., Rehabilitation Physician) if symptoms persist.
High risk	Patients often have upper limb weakness, marked dexterity impairment, pronounced stiffness in one joint (MAS ≈2), or moderate stiffness in two or more joints within 4–12 weeks post-stroke. These individuals require immediate referral for urgent management.

- Management of post-stroke spasticity typically follows a stepwise approach:
  - The initial priority is to identify and eliminate noxious stimuli
  - Followed by optimal positioning strategies and the use of splints
  - Pharmacological treatment is considered once these factors are addressed
  - Choice of therapy depends on the severity and distribution of spasticity, comorbidities, and cost considerations
- Common noxious stimuli that can exacerbate spasticity include:
  - infection
  - pressure sores
  - deep vein thrombosis
  - bladder distension
  - bowel impaction
  - ingrown toenails
  - poorly fitting orthotics

Oral agents

Oral agents used for spasticity management include dantrolene, benzodiazepines, gabapentin, and baclofen. A systemic review of RCTs found that whilst oral muscle relaxants are effective in reducing spasticity and may improve ADL, they are associated with adverse effects such as weakness, sedation, cognitive impairment, and a lowered seizure threshold.[106, level I]

Recommendation 26

- Oral muscle relaxants such as dantrolene, benzodiazepines, gabapentin, and baclofen should be considered to treat spasticity after intracerebral haemorrhage.
  - This has to be balanced against possible adverse effects such as weakness, sedation, cognitive impairment, and a lowered seizure threshold.

Botulinum toxin (BTX) injection

Botulinum toxin (BTX), a locally administered muscle relaxant derived from *Clostridium botulinum*, acts by blocking neuromuscular transmission through inhibition of acetylcholine release, thereby inducing targeted muscle relaxation.[107]

A meta-analysis of RCTs among stroke patients showed that BTX:

- is effective in reducing spasticity compared with placebo (MD in MAS 0.51; 95% 0.19 to 0.83)
- facilitate functional recovery, including improvements in gait velocity (increase of 0.044 meter/second) and Fugl-Meyer Assessment score (MD=3.19; 95%CI 0.22 to 6.16)

Optimal timing is critical, with injections administered within 4 to 12 weeks after stroke demonstrating the greatest effectiveness. The overall quality of studies included were of moderate risk.[106, Level I]

Recommendation 27
- Botulinum toxin injection should be considered to treat muscle spasticity after intracerebral haemorrhage
  - The optimal timing for treatment is 4 to 12 weeks after stroke

Transcutaneous Electrical Nerve Stimulation (TENS)
High-frequency Transcutaneous Electrical Nerve Stimulation (TENS) as an adjuvant therapy has shown to reduce lower limb spasticity after stroke.[106, level I] It is a low-cost, self-administered treatment with minimal side effects, making it a practical option in clinical settings.

A meta-analysis of 10 RCTs including patients with chronic stroke (overall quality of studies was good) revealed that TENS, when used in conjunction with other physical therapy interventions, significantly reduced lower limb spasticity compared to placebo TENS, as measured by the Composite Spasticity Score and the Modified Ashworth Scale (SMD = -0.64; 95% CI: -0.98 to -0.31). Furthermore, TENS combined with other physical therapy treatments was more effective in reducing spasticity than physical therapy interventions alone (SMD = -0.83; 95% CI: -1.51 to -0.15).No studies reported adverse effect of TENS on spasticity. [108, level I]

Recommendation 28
- Transcutaneous Electrical Nerve Stimulation (TENS) should be considered as an adjunctive therapy for muscle spasticity after intracerebral haemorrhage.

In conclusion, early detection and risk-based referral are key to preventing post-stroke spasticity from becoming disabling. A stepwise, multidisciplinary approach which include removing triggers, optimizing positioning, and using targeted treatments like early botulinum toxin A offers the best chance for preserving function and quality of life.

Neuroprotection in ICH
Brain tissue injury following ICH is a complex process characterised by two main phases: primary and secondary injury. Primary Injury involves direct mechanical damage to surrounding brain tissue due to haematoma expansion and associated oedema. Secondary injury involves a multifaceted mechanism contributing to neuronal damage and worsening patient outcomes.[109]

Mechanisms include microglial activation, thrombin-mediated toxicity, red blood cell lysis and subsequent release of cytotoxic haemoglobin, iron, and heme. Iron and heme are particularly damaging as they drive the generation of reactive oxygen species. This oxidative stress, in turn, culminates in neuroinflammation, blood-brain barrier breakdown, vasogenic oedema, and ultimately, apoptosis of neurons and glia. Neuroprotective agents aim to ameliorate one or more of these mechanisms of brain injury. Several neuroprotective agents are described as follows:

Deferoxamine
In a multicentre, double-blind, phase-2 RCT, adults with primary supratentorial ICH randomised within 24 h to Deferoxamine (DFO) 32 mg/kg IV over 8 h daily for 3 days vs placebo showed no difference in the primary outcome (mRS 0–2 at day 90, 34% DFO vs 33% placebo). Ninety-day SAEs (27% vs 33%) and mortality (7% vs 7%) were similar.[110, Level I]

The European Stroke Organisation (ESO) and European Association of Neurosurgical Societies (EANS) 2025 guideline recommend against the use of deferoxamine in ICH due to lack of benefit on death and functional outcome.[90]

Intravenous Magnesium Sulphate (MgSO4)
A meta-analysis of randomised controlled trials evaluated the use of intravenous magnesium sulphate ($MgSO_4$) versus placebo/standard care in acute stroke, including a relevant subset of patients with ICH.[111,Level 1]

- Functional outcomes: No significant benefit of intravenous $MgSO_4$ compared with placebo/standard care (Barthel Index >60 at 90 days; OR=1.05; 95% CI, 0.92 to 1.19).
- Mortality at 90 days: No reduction with $MgSO_4$ (OR=1.10; 95% CI, 0.94 to 1.29).

Overall, the studies included in the meta-analysis were of good quality based on Cochrane Risk of Bias tool

Vitamin D
A systematic review explored the effect of various dose regimens of vitamin D supplementation on functional outcomes after stroke reported a low level of evidence primarily due to a high risk of bias and imprecision across the included studies. As such, authors concluded that there was insufficient evidence to recommend the routine use of vitamin D supplementation in patients with intracerebral haemorrhage (ICH).[112]

See **Appendix 7** for a non-exhaustive list of research of neuroprotective agents.
Based on current available evidence, there is no proven neuroprotective agent that improves the outcome of patients with ICH.

Recommendation 29
- Neuroprotective agents should not be routinely given to patients with intracerebral haemorrhage.

SECONDARY PREVENTION

Blood pressure control
Hypertension is a major risk factor for ICH, especially for those caused by hypertensive angiopathy. Therefore, blood pressure control after ICH is aimed at reducing stroke recurrence. Evidence for blood pressure control is provided by secondary analysis of one RCT and observational studies.

The PROGRESS trial is a large RCT that explored the benefit of blood pressure control amongst patients with previous stroke in reducing stroke recurrences. The study included 6105 patients (including 660 with ICH) who either received perindopril alone or in combination with indapamide, or placebo) achieving an average blood pressure reduction of 9/4 mmHg. Amongst patients with prior ICH, perindopril-based BP lowering:

- Reduced the risk of recurrent stroke by 50% (95% CI, 26% to 67%)
  - comparable effects were observed in ICH related to amyloid angiopathy (RRR=77%; 95% CI, 19% to 93%) and those to hypertension (RRR=46%; CI 95%, 4% to 69%).[113,114, level I]

Recommendation 30
- Long term strict BP lowering therapy should be initiated and maintained as a key secondary prevention management among intracerebral haemorrhage survivors
  - Systolic BP <130 mm Hg and diastolic BP <80 mm Hg should be aimed
  - A combination of angiotensin converting enzyme inhibitor and thiazide diuretic may be considered as antihypertensive agents of choice.

Resumption of anti-thrombotic agent

Patients with ICH often have co-morbidities e.g. ischaemic stroke, ischaemic heart disease or atrial fibrillation where anti-thrombotic agent of either anti-platelet therapy or anti-coagulant is indicated to prevent thromboembolic events. However, treatment with such agent may increase the risk of recurrent ICH, thus presenting a clinical dilemma of whether and when to resume antithrombotic agent after ICH.[115]

Resumption of anticoagulant in patients with atrial fibrillation (AF)

A meta-analysis of two RCTs and 18 cohort studies looked into the effectiveness and safety of oral anti-coagulation (OAC) in adults with AF who had survived a non-traumatic spontaneous ICH or had cerebral microbleeds. The results were:**116**, level I

- risk of thromboembolic events reduced in OAC vs no OAC (RR=0.51 95% CI 0.30 to 0.86) and non-vitamin K antagonist oral anti-coagulant (NOAC) vs warfarin (RR=0.65 95% CI 0.44 to 0.97)
- risk of recurrent ICH reduced in NOAC vs warfarin (RR=0.52 95% CI 0.40 to 0.67); however, there was NS reduction in risk between OAC vs no therapy
- risk of all-cause mortality reduced in OAC vs no therapy (RR=0.52 95% CI 0.38 to 0.71) and NOAC vs warfarin (RR=0.55 95% CI 0.41 to 0.74)

The quality of primary papers was moderate.

The optimal timing for resuming anti-thrombotic therapy has not been systematically studied, therefore treatment should be individualised to the patient. AHA/ASA 2022 Guideline recommends that in patients with AF and spontaneous ICH in whom the decision is made to restart anti-coagulation, initiation of anti-coagulation at about 7 - 8 weeks after ICH may be considered after weighing specific patient characteristics to optimise the balance of risks and benefits.[23] European Stroke Organisation Guideline 2014 suggests a time window of not earlier than 14 days up to 10 - 30 weeks for restarting anti-thrombotic after ICH.[117]

Recommendation 31

- In patients with intracerebral haemorrhage (ICH) and concomitant non-valvular atrial fibrillation, resumption of an oral anti-coagulant (OAC) may be considered.
  - Non-vitamin K antagonist OAC is preferred to warfarin.
  - Timing of resumption after ICH should be individualised based on patient's bleeding and thrombotic risks, preferably not earlier than two weeks.

Resumption of warfarin in patients with valve replacement

Based on a multicentre cohort study of patients with mechanical heart valve at high risk of thromboembolism, resuming therapeutic anti-coagulation, which include warfarin, within 13 days after ICH was associated with high risk of haemorrhagic complications (HR=7.06, 95% CI 2.33 to 21.37). The risk of haemorrhagic and thromboembolic events was high before day 6 post-ICH (HR=2.51, 95% CI 1.10 to 5.70). Therefore, for patients at high thromboembolic risk, it is safe to restart therapeutic anti-coagulation after day 6.[118, level II-2b] Regardless of the timing, ensure vigilant monitoring for both bleeding and thromboembolic complications upon resumption of anti-coagulation therapy.

- Risk of composite outcome (haemorrhagic and thromboembolic events) is high within six days of ICH occurrence. Thus, it is advisable to withhold anti-coagulant within that period.

Recommendation 32
- In patients with intracerebral haemorrhage (ICH) and mechanical heart valve requiring anti-coagulant, the earliest timing for resumption of anti-coagulant should be at least six days after ICH.
  - Ensure vigilant monitoring for both bleeding and thromboembolic complication upon resumption of the therapy.

Resumption of anti-platelet therapy
The RESTART (REstart or STop Anti-thrombotics Randomised Trial) looked into the resumption of anti-platelet therapy after an ICH. The trial found that resuming anti-platelet therapy did not significantly increase the risk of recurrent symptomatic ICH compared with avoiding anti-platelet therapy (8.2% vs 9.3%; HR=0.87, 95% CI 0.49 to 1.55). There was NS reduction in major vascular events (including ischemic stroke and myocardial infarction) between the two groups (26.8% vs 32.5%; HR=0.79, 95% CI 0.58 to 1.08).[119]

The AHA/ASA 2022 Guideline recommends that resumption of anti-platelet therapy may be reasonable for patients with spontaneous ICH who are indicated for anti-platelet therapy to prevent thromboembolic events based on risk and benefit analysis.[23]

Recommendation 33
- For patients with a history of intracerebral haemorrhage (ICH) who require anti-platelet therapy for secondary prevention of vascular events, resuming therapy may be considered based on individual risk assessment.
  - Any signs of recurrent bleeding or other complications should be closely monitored on the resumption of therapy.

Statins
A large meta-analysis of 31 RCTs showed no association between statin therapy and occurrence of ICH (OR=1.08, 95% CI 0.88 to 1.32).[120, level I] However, there was no report on the quality assessment of the primary studies. On contrary, in a community-based Atherosclerosis Risk in Communities (ARIC) cohort study in USA, the risk of ICH was strongly lower in statin users than non-statin users (HR=0.21, 95% CI 0.10 to 0.45). The study also showed that statin use was not associated with any cerebral microbleeds (CMBs), lobar CMB, subcortical CMB and deep CMB.[121, level II-2]

In a 10-year nationwide cohort study in Taiwan, hydrophilic solubility statins (pravastatin and rosuvastatin) had lower risk of recurrent ICH than lipophilic solubility statins (atorvastatin, cerivastatin, fluvastatin, lovastatin and simvastatin) with HR of 0.69 (95% CI 0.48 to 0.99). Analysis on three intensity of the statins showed NS differences in the recurrence of ICH.[122, level II-2] However, in a more recent and larger population-based retrospective cohort study, compared with those on average atorvastatin equivalent daily dose (AAEDD) <10 mg/d, the HR for ICH was 0.68 (95% CI 0.58 to 0.79) in those with AAEDD 10 - 19.9 mg/d and 0.62 (95% CI 0.47 to 0.81) in those with AAEDD ≥20 mg/d.[123, level II-2]

Recommendation 34
- Statin may be used to reduce cardiovascular risk in patients with intracerebral haemorrhage.
  - Hydrophilic solubility statins are the preferred choice.

ICH IN THE ELDERLY POPULATION

Assessment of frailty in older persons with ICH
Frailty is defined as a complex age-related decline in physiological reserves across different organ systems, resulting in increased vulnerability to stressors and poorer outcomes such as hospitalization, iatrogenic events and death.[124] Pre-morbid frailty is associated with mortality and poorer functional outcomes after a spontaneous ICH[125] and also after neurosurgical intervention post-spontaneous ICH.[126]

Frailty measures in use at present include:
- frailty phenotype measures based on clinical or physical assessments
- frailty indexes based on numerous parameters entered into a validated measure to generate a frailty index

The Clinical Frailty Scale (CFS) version 2 (2020) is a frailty scale for older persons that is user-friendly in daily clinical practice. Frailty status can be determined by a history of ability to perform ADLs and a physical examination.[127] It ranges from CFS 1 (very fit) to CFS 8 (very severely frail). It is important that the CFS is not used solely on its own to decide on treatment plans but to also consider the severity of other co-morbidities and physical attributes including body weight.

Pre-morbid frailty should be assessed in every older person admitted with an ICH when formulating an individualised treatment plan.[124,128] It should involve a multidisciplinary team that includes doctor, nurse, physiotherapist, occupational therapist, speech and language therapist, dietitian, medical social worker and pharmacist, where available and required.

Recommendation 35
- All older persons admitted with an intracerebral haemorrhage (ICH) should have their pre-morbid fitness/frailty status assessed.
- The frailty level of a person with ICH should be considered when formulating an individualised treatment plan with the multidisciplinary team.

Assessment for delirium in older persons with acute ICH
Delirium is characterised by a disturbance in attention, cognition and awareness that developed over a relatively short period of time (hours to days) secondary to an acute illness/event.[129]

Causes of delirium are:
- haematoma expansion
- perihaematomal oedema
- infection
- discomfort (pain, itch, room temperature etc.)
- constipation
- hunger/hypoglycaemia
- urinary retention etc.

Patients with delirium post-ICH in an ICU have been found to have longer length of stay, poorer outcomes and quality of life.[130] There are also additional challenges in rehabilitation and carer training in the setting of delirium.

Delirium assessment tools included the Confusion Assessment Method (CAM)[131], Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)[132] and 4AT.[133] It is recommended

that delirium be routinely assessed for in every ICH patient at every clinical encounter. Management of delirium should include treatment of underlying causes as listed above.

Non-pharmacological treatment includes:

- re-orientation
- avoiding multiple moves of ward bed
- a quiet environment
- familiar staff or carers

Pharmacological management with antipsychotics and sedatives are reserved for those with severe delirium and agitation that is distressing, affecting ability to receive treatment and possibly endanger to themselves and others. Adverse effects (AEs) of pharmacological treatment includes oversedation, extra-pyramidal side effects, cardiac arrhythmias with prolongation of QT interval and risk of falls.

Recommendation 36

- Assessment for delirium should be performed in patients with intracerebral haemorrhage.
- Underlying causes of delirium should be treated and management can include pharmacological and non-pharmacological methods.

Treatment of blood pressure in secondary prevention of ICH in older persons

An older person who recovered well from an ICH, is ambulant and fit may follow the conventional blood pressure targets for secondary prevention of ICH. However, frailer older persons may not tolerate very tight blood pressure targets.[134]

Every older person (not only frail) on treatment for hypertension should be assessed for:

- symptoms of postural hypotension which include unsteadiness, dizziness on getting up, falls and syncope
- drop in SBP >20 mmHg and/or DBP >10 mmHg[134]

Adjustment of dosage and change of medications should be done if there is presence of AEs of overtreatment of hypertension.

Recommendation 37

- The conventional blood pressure treatment target after intracerebral haemorrhage may not be strictly applied to frail older persons.
- All older persons on treatment for hypertension should be assessed for signs and symptoms of overtreatment.
  - Adjustment of dosage and change of medications should be done in the presence of adverse events due to overtreatment of hypertension.

Management of polypharmacy in older persons with ICH

Polypharmacy is common in older persons with multiple comorbidities. Appropriate polypharmacy can help prolong disability free life and improve quality of life. Inappropriate polypharmacy may result in AEs drug-drug interactions and drug-disease interactions. A medication review should be performed in older persons with ICH.[135]

When prescribing medications for the complex older person with ICH, adherence and compliance can be improved with once a day medications where possible. The older person's understanding of their medications and ability to take their own medications should be assessed.

If required, carer training should be done to assist the older person. An older person with dementia will require supervision from carers for their medications. An older person's swallow function should be considered when prescribing as some medications should not be crushed and administered via nasogastric or percutaneous endoscopic gastrostomy tube.

Drug-drug interactions can be checked by the pharmacist or using online drug interaction checkers together with clinical judgement. Drug-disease interactions should be checked for, with examples such as worsening of delirium and cognition with tramadol/morphine in persons with pre-existing dementia.

Recommendation 38
- Polypharmacy in older persons with intracerebral haemorrhage should be managed with:
  - medication review
  - involvement of carer in persons with dementia or other difficulties
  - deprescribing (stopping/reducing the dosage of medications) where required

Assessment of falls and fracture risk in older persons with ICH
A person with neurological deficits post-ICH can be at risk of falls and fracture. Other risks of falls and fractures in them include osteoporosis, malnutrition, sarcopenia, dementia, environmental hazards, polypharmacy and unsteady gait. The following guidelines may be referred to for management of falls and fracture:

- European position paper on polypharmacy and fall-risk-increasing drugs recommendations in the World Guidelines for Falls Prevention and Management: implications and implementation 2023[136]
- Falls Guideline for hospitalised older adults in the Ministry of Health. Ministry of Health Malaysia, 2019[137]
- Clinical Practice Guidelines - Management of Osteoporosis 3rd Edition. Ministry of Health Malaysia, 2022[138]

Recommendation 39
- An older person with intracerebral haemorrhage who is ambulant should be assessed for falls and fracture risk by a multidisciplinary team including doctors, nurses, physiotherapists, occupational therapists, and pharmacists.
- Osteoporosis should be screened for with:
  - blood tests - renal profile, serum calcium, vitamin D, bone turnover markers
  - bone mineral densitometry scan (DEXA)
- Patients with osteoporosis should be treated according to the Malaysian Osteoporosis Guideline.

IMPLEMENTING THE GUIDELINE

The management of ICH should be guided by an evidence-based approach, in order to provide quality care to the patients. Several factors may affect the implementation of recommendations in the CPG.

Facilitators and Barriers
Several existing factors may help to facilitate the implementation of the CPG recommendations:
- Increasing public awareness of stroke

- Increasing numbers of hospitals that provide round-the-clock acute stroke reperfusion service ("stroke call") in a timely manner
- Ongoing efforts by many hospitals to obtain World Stroke Organisation certification as advanced stroke centres and therefore a push for improving care quality.
- The National Stroke Registry records data on care quality for stroke, with an emphasis on acute reperfusion therapies.
- Robust professional and public societies in promoting stroke, including Malaysian Stroke Council/Malaysian Society of Neurosciences, Malaysian Stroke Academy, Neurosurgical Association of Malaysia, National Stroke Association of Malaysia , ANGELs initiative, World Stroke Organisation etc.
- Multi-disciplinary efforts to improve care quality in intracerebral haemorrhage, orchestrated by Ministry of Health, Ministry of Higher Education Hospitals and private hospitals.
- Most of the resources needed for implementation are already available.

Barriers to implementation of recommendations include:

- Therapeutic nihilism amongst health care professionals due to severe nature of ICH and for a long-time lack of effective treatment. Effective treatments are now available.
- Fragmented system of care where the primary team for ICH patients differ between hospitals and sometimes differ between patients leading to lack of standardisation of care process.
- Although a stroke call is available in stroke ready hospital with the intention to diagnosed ischaemic stroke and offer reperfusion therapy, ICH code is not. Stroke calls are often terminated when ICH is diagnosed leading to less attention and less timely care. Certain treatments in ICH such as blood pressure reduction and anticoagulation reversal are in fact needed more urgently than treatment of acute ischaemic stroke.
- Similarly, although CT angiography is now routinely performed in acute stroke to diagnose large vessel occlusion in ischaemic stroke, CT angiography is often deferred or not offered upon diagnosis of ICH on non-contrasted CT brain
- There is a lack of registry-based implementation of key performance indicators, including in the National Stroke Registry.
- Certain resources are not readily available in all hospitals, namely PCC, idarucizumab, andexanet alfa for anticoagulation reversal, devices for minimally invasive surgery, adequate number of stroke unit beds and IPC for DVT prophylaxis.

Potential Resource Implication

The recommendations in this CPG require additional resources in terms of funds, healthcare infrastructures and human resources/expertise for their successful implementation as discussed below.

Implementation of the care bundle requires hospital-level coordination of service and training of all health care providers. Continuing training programmes for healthcare providers are needed to ensure they are equipped with the latest knowledge and skills in ICH management. Additional health care provider may need to be assigned to ensure timely delivery of care bundle. Improving the care of ICH patients requires designation of an organised stroke care unit. This may require additional infrastructure or reorganisation of existing hospital beds. Furthermore, IPC will be required for DVT prophylaxis. Whilst only a small proportion of patients with ICH were on anticoagulant, reversal agents such as PCC and idarucizumab are considerably more costly than FFP which is most commonly used currently.

The CPG made recommendations for referral to neurosurgical services and conditions where neurosurgery may be beneficial. Equipment for minimally invasive surgery may not be already available in many hospitals. The cost vs benefit of acquiring new equipment and training of operators will need to be further deliberated.

Whilst there are resource implications in implementing the above-mentioned recommendations, some recommendations may indeed be cost-saving whilst ensuring high-quality care. Implementation of care bundle, admission to an organised stroke care unit, swallowing assessments and DVT prophylaxis prevents complications, reduce hospital length of stay and readmission as well as improves functional outcome. The CPG recommendations of avoiding primary prophylaxis with antiseizure medication, use of TED stoking, hyperosmolar therapy etc reduce unnecessary spending on ineffective treatments. Recommendations on indications for neurosurgical referrals avoid unnecessary referrals and reduce the burden of neurosurgical services.

In conclusion, a majority of the CPG recommendations can be achieved with reorganisation of existing resources.

Proposed clinical audit indicators
The DG proposed a clinical audit indicator as follows:

$$\text{Percentage of treatment with ICH care bundle} = \frac{\text{Number of ICH patients presenting within 6 hours with care bundle}}{\text{Total number of ICH patients presenting within 6 hours}} \times 100\%$$

Target=70%

Implementation and Monitoring Framework
Dissemination will utilise multi-tiered strategies:

(i) electronic dissemination via myMaHTAS and Academy of Medicine,
(ii) state-level Training of Trainers (TOT) for clinicians and allied health professionals, and
(iii) integration of audit indicators into hospital quality improvement systems

REFERENCES

1. Aziz ZA, Lee YY, Ngah BA, et al. Acute Stroke Registry Malaysia, 2010-2014: Results from the National Neurology Registry. *J Stroke Cerebrovasc Dis*. 2015;24:2701-2709
2. Caceres JA, Goldstein JN. Intracranial hemorrhage. *Emerg Med Clin North Am*. 2012;30:771-794
3. Kidwell CS, Wintermark M. Imaging of intracranial haemorrhage. *Lancet Neurol*. 2008;7:256-267
4. Al-Shahi Salman R, Labovitz DL, Stapf C. Spontaneous intracerebral haemorrhage. *BMJ*. 2009;339:b2586
5. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol*. 2021;20:795-820
6. van Asch CJ, Luitse MJ, Rinkel GJ, et al. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol*. 2010;9:167-176
7. Hwong WY, Ang SH, Bots ML, et al. Trends of Stroke Incidence and 28-Day All-Cause Mortality after a Stroke in Malaysia: A Linkage of National Data Sources. *Glob Heart*. 2021;16:39

8. Ang SH, Hwong WY, Bots ML, et al. Risk of 28-day readmissions among stroke patients in Malaysia (2008-2015): Trends, causes and its associated factors. *PLoS One*. 2021;16:e0245448
9. Tan KS, Venketasubramanian N. Stroke Burden in Malaysia. *Cerebrovasc Dis Extra*. 2022;12:58-62
10. Chen XW, Shafei MN, Aziz ZA, et al. Trends in stroke outcomes at hospital discharge in first-ever stroke patients: Observations from the Malaysia National Stroke Registry (2009-2017). *J Neurol Sci*. 2019;401:130-135
11. Lee YY, Shafie AA, Sidek NN, et al. Economic burden of stroke in malaysia: results from national neurology registry. *J Neurol Sci*. 2017;381:167-168
12. Steiner T, Kaste M, Forsting M, et al. Recommendations for the management of intracranial haemorrhage - part I: spontaneous intracerebral haemorrhage. The European Stroke Initiative Writing Committee and the Writing Committee for the EUSI Executive Committee. *Cerebrovasc Dis*. 2006;22:294-316
13. Woo KM, Yang SY, Cho KT. Seizures after spontaneous intracerebral hemorrhage. *J Korean Neurosurg Soc*. 2012;52:312-319
14. de Greef BT, Schreuder FH, Vlooswijk MC, et al. Early seizures after intracerebral hemorrhage predict drug-resistant epilepsy. *J Neurol*. 2015;262:541-546
15. Passero S, Rocchi R, Rossi S, et al. Seizures after spontaneous supratentorial intracerebral hemorrhage. *Epilepsia*. 2002;43:1175-1180
16. Bladin CF, Alexandrov AV, Bellavance A, et al. Seizures after stroke: a prospective multicenter study. *Arch Neurol*. 2000;57:1617-1622
17. De Herdt V, Dumont F, Hénon H, et al. Early seizures in intracerebral hemorrhage: incidence, associated factors, and outcome. *Neurology*. 2011;77:1794-1800
18. Poungvarin N, Viriyavejakul A, Komontri C. Siriraj stroke score and validation study to distinguish supratentorial intracerebral haemorrhage from infarction. *BMJ*. 1991;302:1565-1567
19. Sandercock PA, Allen CM, Corston RN, et al. Clinical diagnosis of intracranial haemorrhage using Guy's Hospital score. *Br Med J (Clin Res Ed)*. 1985;291:1675-1677
20. Weir CJ, Murray GD, Adams FG, et al. Poor accuracy of stroke scoring systems for differential clinical diagnosis of intracranial haemorrhage and infarction. *Lancet*. 1994;344:999-1002
21. Fiebach JB, Schellinger PD, Gass A, et al. Stroke magnetic resonance imaging is accurate in hyperacute intracerebral hemorrhage: a multicenter study on the validity of stroke imaging. *Stroke*. 2004;35:502-506
22. Brazzelli M, Sandercock PA, Chappell FM, et al. Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms. *Cochrane Database Syst Rev*. 2009:Cd007424
23. Greenberg SM, Ziai WC, Cordonnier C, et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke*. 2022;53:e282-e361
24. Vert C, Parra-Fariñas C, Rovira À. MR imaging in hyperacute ischemic stroke. *Eur J Radiol*. 2017;96:125-132
25. Hilkens NA, van Asch CJJ, Werring DJ, et al. Predicting the presence of macrovascular causes in non-traumatic intracerebral haemorrhage: the DIAGRAM prediction score. *J Neurol Neurosurg Psychiatry*. 2018;89:674-679
26. van Asch CJ, Velthuis BK, Rinkel GJ, et al. Diagnostic yield and accuracy of CT angiography, MR angiography, and digital subtraction angiography for detection of macrovascular causes of intracerebral haemorrhage: prospective, multicentre cohort study. *BMJ*. 2015;351:h5762

27. Chewning RH et al. Cerebral angiography. In: Carhuapoma JR MS, Hanley DF, ed. *Intracerebral Hemorrhage*. Cambridge: Cambridge University Press; 2009:139-148.
28. Geibprasert S, Pongpech S, Jiarakongmun P, et al. Radiologic assessment of brain arteriovenous malformations: what clinicians need to know. *Radiographics*. 2010;30:483-501
29. Chung CY, Peterson RB, Howard BM, et al. Imaging Intracranial Aneurysms in the Endovascular Era: Surveillance and Posttreatment Follow-up. *Radiographics*. 2022;42:789-805
30. Saposnik G, Bushnell C, Coutinho JM, et al. Diagnosis and Management of Cerebral Venous Thrombosis: A Scientific Statement From the American Heart Association. *Stroke*. 2024;55:e77-e90
31. Davis SM, Broderick J, Hennerici M, et al. Hematoma growth is a determinant of mortality and poor outcome after intracerebral hemorrhage. *Neurology*. 2006;66:1175-1181
32. Morotti A, Arba F, Boulouis G, et al. Noncontrast CT markers of intracerebral hemorrhage expansion and poor outcome: A meta-analysis. *Neurology*. 2020;95:632-643
33. Ovesen C, Jakobsen JC, Gluud C, et al. Tranexamic Acid for Prevention of Hematoma Expansion in Intracerebral Hemorrhage Patients With or Without Spot Sign. *Stroke*. 2021;52:2629-2636
34. Xu X, Zhang J, Yang K, et al. Accuracy of spot sign in predicting hematoma expansion and clinical outcome: A meta-analysis. *Medicine (Baltimore)*. 2018;97:e11945
35. Loh HC NN, Ganasegeran K, AziZ ZA, Looi I. Socio-demographics and clinical characteristics affecting pre-hospital delays in acute stroke patients: A 6-year registry study from a Malaysian stroke hospital. *Neurol Asia*. 2020;25:235-243
36. Malaysian Society of Neurosciences. *Clinical Practice Guidelines for Management of Ischaemic Stroke*. 3rd ed. Kuala Lumpur: Malaysian Society of Neurosciences; 2020
37. Ramos-Pachón A, Rodríguez-Luna D, Martí-Fàbregas J, et al. Effect of Bypassing the Closest Stroke Center in Patients with Intracerebral Hemorrhage: A Secondary Analysis of the RACECAT Randomized Clinical Trial. *JAMA Neurol*. 2023;80:1028-1036
38. Goldstein JN, Greenberg SM, Rosand J. Emergency management of intracerebral hemorrhage. *Continuum (Minneap Minn)*. 2006;12:13-29
39. Brown CA, III, Sakles JC, Mick NW. *The Walls Manual of Emergency Airway Management, 5e*. Lippincott Williams & Wilkins, a Wolters Kluwer bu; 2018
40. Eipe N, Jones SB, Crowley M. Anesthesia for the patient with obesity. In: Connor RF, ed. *UpToDate*. Wolters Kluwer https://www.uptodate.com.
41. Di Giacinto I, Guarnera M, Esposito C, et al. Emergencies in obese patients: a narrative review. *J Anesth Analg Crit Care*. 2021;1:13
42. Rincon F, Mayer SA. Clinical review: Critical care management of spontaneous intracerebral hemorrhage. *Crit Care*. 2008;12:237
43. Asserhøj LL, Mosbech H, Krøigaard M, et al. No evidence for contraindications to the use of propofol in adults allergic to egg, soy or peanut†. *Br J Anaesth*. 2016;116:77-82
44. Tsivgoulis G, Katsanos AH, Butcher KS, et al. Intensive blood pressure reduction in acute intracerebral hemorrhage: a meta-analysis. *Neurology*.83:1523-1529
45. Shi L, Xu S, Zheng J, et al. Blood Pressure Management for Acute Intracerebral Hemorrhage: A Meta-Analysis. *Sci Rep*.7:14345
46. Qureshi AI, Huang W, Lobanova I, et al. Outcomes of Intensive Systolic Blood Pressure Reduction in Patients With Intracerebral Hemorrhage and Excessively High Initial Systolic Blood Pressure: Post Hoc Analysis of a Randomized Clinical Trial. *JAMA Neurol*. 2020;77:1355-1365

47. Saxena A, Anderson CS, Wang X, et al. Prognostic Significance of Hyperglycemia in Acute Intracerebral Hemorrhage: The INTERACT2 Study. *Stroke*.47:682-688
48. Ma L, Hu X, Song L, et al. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial. *Lancet*. 2023;402:27-40
49. Balami JS, Buchan AM. Complications of intracerebral haemorrhage. *Lancet Neurol*. 2012;11:101-118
50. Al-Shahi Salman R, Frantzias J, Lee RJ, et al. Absolute risk and predictors of the growth of acute spontaneous intracerebral haemorrhage: a systematic review and meta-analysis of individual patient data. *Lancet Neurol*. 2018;17:885-894
51. Cucchiara B, Messe S, Sansing L, et al. Hematoma growth in oral anticoagulant related intracerebral hemorrhage. *Stroke*. 2008;39:2993-2996
52. Lioutas VA, Goyal N, Katsanos AH, et al. Clinical Outcomes and Neuroimaging Profiles in Nondisabled Patients With Anticoagulant-Related Intracerebral Hemorrhage. *Stroke*. 2018;49:2309-2316
53. Ahmed A, Ahmed R, Ali SS, et al. Intracerebral hemorrhage outcomes in patients using direct oral anticoagulants versus vitamin K antagonists: a meta-analysis. *Clin Neurol Neurosurg*. 2020;198:106146
54. Katsanos AH, Schellinger PD, Köhrmann M, et al. Fatal oral anticoagulant-related intracranial hemorrhage: a systematic review and meta-analysis. *Eur J Neurol*. 2018;25:1299-1302
55. Lee SB, Manno EM, Layton KF, et al. Progression of warfarin-associated intracerebral hemorrhage after INR normalization with FFP. *Neurology*. 2006;67:1272-1274
56. Kuramatsu JB, Gerner ST, Schellinger PD, et al. Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage. *JAMA*. 2015;313:824-836
57. Steiner T, Poli S, Griebe M, et al. Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial. *Lancet Neurol*. 2016;15:566-573
58. Lubetsky A, Yonath H, Olchovsky D, et al. Comparison of oral vs intravenous phytonadione (vitamin K1) in patients with excessive anticoagulation: a prospective randomized controlled study. *Arch Intern Med*. 2003;163:2469-2473
59. Pollack CV, Jr., Reilly PA, van Ryn J, et al. Idarucizumab for Dabigatran Reversal - Full Cohort Analysis. *N Engl J Med*. 2017;377:431-441
60. Pollack CV, Jr., Reilly PA, Eikelboom J, et al. Idarucizumab for Dabigatran Reversal. *N Engl J Med*. 2015;373:511-520
61. Connolly SJ, Sharma M, Cohen AT, et al. Andexanet for Factor Xa Inhibitor-Associated Acute Intracerebral Hemorrhage. *N Engl J Med*. 2024;390:1745-1755
62. Polymeris AA, Karwacki GM, Siepen BM, et al. Tranexamic Acid for Intracerebral Hemorrhage in Patients on Non-Vitamin K Antagonist Oral Anticoagulants (TICH-NOAC): A Multicenter, Randomized, Placebo-Controlled, Phase 2 Trial. *Stroke*. 2023;54:2223-2234
63. Thompson BB, Bejot Y, Caso V, et al. Prior antiplatelet therapy and outcome following intracerebral hemorrhage: a systematic review. *Neurology*. 2010;75:1333-1342
64. Baharoglu MI, Cordonnier C, Salman RA, et al. Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. *Lancet*. 2016
65. Eilertsen H, Menon CS, Law ZK, et al. Haemostatic therapies for stroke due to acute, spontaneous intracerebral haemorrhage. *Cochrane Database Syst Rev*. 2023;10:Cd005951

66. Qureshi AI. The importance of acute hypertensive response in ICH. *Stroke*. 2013;44:S67-69
67. Rodriguez-Luna D, Piñeiro S, Rubiera M, et al. Impact of blood pressure changes and course on hematoma growth in acute intracerebral hemorrhage. *Eur J Neurol*. 2013;20:1277-1283
68. Sakamoto Y, Koga M, Yamagami H, et al. Systolic blood pressure after intravenous antihypertensive treatment and clinical outcomes in hyperacute intracerebral hemorrhage: the stroke acute management with urgent risk-factor assessment and improvement-intracerebral hemorrhage study. *Stroke*. 2013;44:1846-1851
69. Langhorne P, Ramachandra S. Organised inpatient (stroke unit) care for stroke: network meta-analysis. *Cochrane Database Syst Rev*. 2020;4:Cd000197
70. Langhorne P, Fearon P, Ronning OM, et al. Stroke unit care benefits patients with intracerebral hemorrhage: systematic review and meta-analysis. *Stroke*. 2013;44:3044-3049
71. Hemphill JC, 3rd, Bonovich DC, Besmertis L, et al. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. *Stroke*. 2001;32:891-897
72. Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke*. 1996;27:1304-1305
73. Gregório T, Pipa S, Cavaleiro P, et al. Assessment and Comparison of the Four Most Extensively Validated Prognostic Scales for Intracerebral Hemorrhage: Systematic Review with Meta-analysis. *Neurocrit Care*. 2019;30:449-466
74. Hemphill JC, 3rd, Newman J, Zhao S, et al. Hospital usage of early do-not-resuscitate orders and outcome after intracerebral hemorrhage. *Stroke*. 2004;35:1130-1134
75. Zahuranec DB, Brown DL, Lisabeth LD, et al. Early care limitations independently predict mortality after intracerebral hemorrhage. *Neurology*. 2007;68:1651-1657
76. Minhas JS, Sammut-Powell C, Birleson E, et al. Are do-not-resuscitate orders associated with limitations of care beyond their intended purpose in patients with acute intracerebral haemorrhage? Analysis of the ABC-ICH study. *BMJ Open Qual*. 2021;10
77. Peter-Derex L, Philippeau F, Garnier P, et al. Safety and efficacy of prophylactic levetiracetam for prevention of epileptic seizures in the acute phase of intracerebral haemorrhage (PEACH): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2022;21:781-791
78. Angriman F, Tirupakuzhi Vijayaraghavan BK, Dragoi L, et al. Antiepileptic Drugs to Prevent Seizures After Spontaneous Intracerebral Hemorrhage. *Stroke*. 2019;50:1095-1099
79. Dennis M, Sandercock P, Reid J, et al. Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial. *Lancet*. 2013;382:516-524
80. Pan X, Li J, Xu L, et al. Safety of Prophylactic Heparin in the Prevention of Venous Thromboembolism After Spontaneous Intracerebral Hemorrhage: A Meta-analysis. *J Neurol Surg A Cent Eur Neurosurg*. 2020;81:253-260
81. Hess F, Foerch C, Keil F, et al. Association of Lesion Pattern and Dysphagia in Acute Intracerebral Hemorrhage. *Stroke*. 2021;52:2921-2929
82. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. 2016;47:e98-e169
83. Bahagian Sains Kesihatan Bersekutu, Kementerian Kesihatan Malaysia. *Prosedur Operasi Standard Penjagaan Pesakit dengan Kecelaruan Pengambilan Makanan (Feeding) dan Kecelaruan Penelanan*. Kementerian Kesihatan Malaysia; 2023.https://hq.moh.gov.my/alliedhealth/index.php/ms/penerbitan/prosedur-operasi-standard

84. Vahedi K, Hofmeijer J, Juettler E, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol*. 2007;6:215-222
85. Beck J, Fung C, Strbian D, et al. Decompressive craniectomy plus best medical treatment versus best medical treatment alone for spontaneous severe deep supratentorial intracerebral haemorrhage: a randomised controlled clinical trial. *Lancet*. 2024;403:2395-2404
86. Akram MJ, Zhao R, Shen X, et al. Surgical vs. Conservative Management for Lobar Intracerebral Hemorrhage, a Meta-Analysis of Randomized Controlled Trials. *Front Neurol*. 2021;12:742959
87. Hanley DF, Thompson RE, Rosenblum M, et al. Efficacy and safety of minimally invasive surgery with thrombolysis in intracerebral haemorrhage evacuation (MISTIE III): a randomised, controlled, open-label, blinded endpoint phase 3 trial. *Lancet*. 2019;393:1021-1032
88. Pradilla G, Ratcliff JJ, Hall AJ, et al. Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage. *N Engl J Med*. 2024;390:1277-1289
89. Kuramatsu JB, Biffi A, Gerner ST, et al. Association of Surgical Hematoma Evacuation vs Conservative Treatment With Functional Outcome in Patients With Cerebellar Intracerebral Hemorrhage. *JAMA*. 2019;322:1392-1403
90. Steiner T, Purrucker JC, Aguiar de Sousa D, et al. European Stroke Organisation (ESO) and European Association of Neurosurgical Societies (EANS) guideline on stroke due to spontaneous intracerebral haemorrhage. *Eur Stroke J*. 2025:23969873251340815
91. Hanley DF, Lane K, McBee N, et al. Thrombolytic removal of intraventricular haemorrhage in treatment of severe stroke: results of the randomised, multicentre, multiregion, placebo-controlled CLEAR III trial. *Lancet*. 2017;389:603-611
92. Li Y, Zhang H, Wang X, et al. Neuroendoscopic surgery versus external ventricular drainage alone or with intraventricular fibrinolysis for intraventricular hemorrhage secondary to spontaneous supratentorial hemorrhage: a systematic review and meta-analysis. *PLoS One*. 2013;8:e80599
93. Ren J, Wu X, Huang J, et al. Intracranial Pressure Monitoring-Aided Management Associated with Favorable Outcomes in Patients with Hypertension-Related Spontaneous Intracerebral Hemorrhage. *Transl Stroke Res*. 2020;11:1253-1263
94. Chen CJ, Ding D, Ironside N, et al. Intracranial pressure monitoring in patients with spontaneous intracerebral hemorrhage. *J Neurosurg*. 2020;132:1854-1864
95. Menacho ST, Grandhi R, Delic A, et al. Impact of Intracranial Pressure Monitor-Guided Therapy on Neurologic Outcome After Spontaneous Nontraumatic Intracranial Hemorrhage. *J Stroke Cerebrovasc Dis*. 2021;30:105540
96. Dallagiacoma S, Robba C, Graziano F, et al. Intracranial Pressure Monitoring in Patients With Spontaneous Intracerebral Hemorrhage: Insights From the SYNAPSE-ICU Study. *Neurology*. 2022;99:e98-e108
97. Shah M, Birnbaum L, Rasmussen J, et al. Effect of Hyperosmolar Therapy on Outcome Following Spontaneous Intracerebral Hemorrhage: Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) Study. *J Stroke Cerebrovasc Dis*. 2018;27:1061-1067
98. Coleman ER, Moudgal R, Lang K, et al. Early Rehabilitation After Stroke: a Narrative Review. *Curr Atheroscler Rep*. 2017;19:59
99. Marek K, Zielińska-Nowak E, Redlicka J, et al. Intracranial Hemorrhage-Is Very Early Rehabilitation Safe? A Narrative Review. *J Clin Med*. 2024;13
100. Potter T, Lioutas VA, Tano M, et al. Cognitive Impairment After Intracerebral Hemorrhage: A Systematic Review of Current Evidence and Knowledge Gaps. *Front Neurol*. 2021;12:716632

101. Tsaousides T, Gordon WA. Cognitive rehabilitation following traumatic brain injury: assessment to treatment. *Mt Sinai J Med*. 2009;76:173-181
102. Black S, Román GC, Geldmacher DS, et al. Efficacy and tolerability of donepezil in vascular dementia: positive results of a 24-week, multicenter, international, randomized, placebo-controlled clinical trial. *Stroke*. 2003;34:2323-2330
103. Marcus Saikaley, Jerome Iruthayarajah, Magdalena Mirkowski, et al. Chapter 12: Cognitive Rehabilitation. In: Teasell R, Salbach, N. M., Foley, N., Mountain, A., et al, ed. *Evidence-Based Review of Stroke Rehabilitation*. Heart and Stroke Foundation Canadian Stroke Network https://www.ebrsr.com. 2018.
104. Suputtitada A, Chatromyen S, Chen CPC, et al. Best Practice Guidelines for the Management of Patients with Post-Stroke Spasticity: A Modified Scoping Review. *Toxins (Basel)*. 2024;16
105. Bavikatte G, Subramanian G, Ashford S, et al. Early Identification, Intervention and Management of Post-stroke Spasticity: Expert Consensus Recommendations. *J Cent Nerv Syst Dis*. 2021;13:11795735211036576
106. Robert Teasell NH, Danielle Vanderlaan, Marcus Saikaley, Mitchell Longval, Jerome Iruthayarajah. 3. Lower Extremity Motor and Mobility Rehabilitation. In: Robert Teasell, Norhayati Hussein, Jerome Iruthayarajah, Marcus Saikaley, Mitchell Longval, Ricardo Viana, eds. *Stroke Rehabilitation Clinician Handbook*. Heart and Stroke Foundation Canadian Stroke Network https://www.ebrsr.com. 2020.
107. Wheeler A, Smith HS. Botulinum toxins: Mechanisms of action, antinociception and clinical applications. *Toxicology*. 2013;306:124-146
108. Mahmood A, Veluswamy SK, Hombali A, et al. Effect of Transcutaneous Electrical Nerve Stimulation on Spasticity in Adults With Stroke: A Systematic Review and Meta-analysis. *Arch Phys Med Rehabil*. 2019;100:751-768
109. Keep RF, Hua Y, Xi G. Intracerebral haemorrhage: mechanisms of injury and therapeutic targets. *Lancet Neurol*. 2012;11:720-731
110. Selim M, Foster LD, Moy CS, et al. Deferoxamine mesylate in patients with intracerebral haemorrhage (i-DEF): a multicentre, randomised, placebo-controlled, double-blind phase 2 trial. *Lancet Neurol*. 2019;18:428-438
111. Avgerinos KI, Chatzisotiriou A, Haidich AB, et al. Intravenous Magnesium Sulfate in Acute Stroke. *Stroke*. 2019;50:931-938
112. Fleet JL, McIntyre A, Janzen S, et al. A systematic review examining the effect of vitamin D supplementation on functional outcomes post-stroke. *Clin Rehabil*. 2023;37:1451-1466
113. Chapman N, Huxley R, Anderson C, et al. Effects of a perindopril-based blood pressure-lowering regimen on the risk of recurrent stroke according to stroke subtype and medical history: the PROGRESS Trial. *Stroke*. 2004;35:116-121
114. Arima H, Chalmers J. PROGRESS: Prevention of Recurrent Stroke. *J Clin Hypertens (Greenwich)*. 2011;13:693-702
115. Law ZK, Appleton JP, Bath PM, et al. Management of acute intracerebral haemorrhage – an update. *Clin Med (London)*. 2017;17:166-172
116. Ivany E, Ritchie LA, Lip GYH, et al. Effectiveness and Safety of Antithrombotic Medication in Patients With Atrial Fibrillation and Intracranial Hemorrhage: Systematic Review and Meta-Analysis. *Stroke*. 2022;53:3035-3046
117. Steiner T, Al-Shahi Salman R, Beer R, et al. European Stroke Organisation (ESO) guidelines for the management of spontaneous intracerebral hemorrhage. *Int J Stroke*. 2014;9:840-855
118. Kuramatsu JB, Sembill JA, Gerner ST, et al. Management of therapeutic anticoagulation in patients with intracerebral haemorrhage and mechanical heart valves. *Eur Heart J*. 2018;39:1709-1723

119. RESTART Colloboration. Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial. *Lancet*. 2019;393:2613-2623
120. McKinney JS, Kostis WJ. Statin therapy and the risk of intracerebral hemorrhage: a meta-analysis of 31 randomized controlled trials. *Stroke*. 2012;43:2149-2156
121. Sharma R, Matsushita K, Wu A, et al. Common Medications and Intracerebral Hemorrhage: The ARIC Study. *J Am Heart Assoc*. 2021;10:e014270
122. Tai SY, Lin FC, Lee CY, et al. Statin use after intracerebral hemorrhage: a 10-year nationwide cohort study. *Brain Behav*. 2016;6:e00487
123. Saliba W, Rennert HS, Barnett-Griness O, et al. Association of statin use with spontaneous intracerebral hemorrhage: A cohort study. *Neurology*. 2018;91:e400-e409
124. Dent E, Martin FC, Bergman H, et al. Management of frailty: opportunities, challenges, and future directions. *Lancet*. 2019;394:1376-1386
125. Ong SH, Tan AYX, Tan B, et al. The effect of frailty on mortality and functional outcomes in spontaneous intracerebral haemorrhage. *Clin Neurol Neurosurg*. 2024;246:108539
126. Imaoka Y, Kawano T, Hashiguchi A, et al. Modified frailty index predicts postoperative outcomes of spontaneous intracerebral hemorrhage. *Clin Neurol Neurosurg*. 2018;175:137-143
127. Rockwood K, Theou O. Using the Clinical Frailty Scale in Allocating Scarce Health Care Resources. *Can Geriatr J*. 2020;23:210-215
128. Dent E, Lien C, Lim WS, et al. The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty. *J Am Med Dir Assoc*. 2017;18:564-575
129. Lauretani F, Bellelli G, Pelà G, et al. Treatment of Delirium in Older Persons: What We Should Not Do! *Int J Mol Sci*. 2020;21
130. Naidech AM, Beaumont JL, Rosenberg NF, et al. Intracerebral hemorrhage and delirium symptoms. Length of stay, function, and quality of life in a 114-patient cohort. *Am J Respir Crit Care Med*. 2013;188:1331-1337
131. Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med*. 1990;113:941-948
132. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29:1370-1379
133. MacLullich AM, Shenkin SD, Goodacre S, et al. The 4 'A's test for detecting delirium in acute medical patients: a diagnostic accuracy study. *Health Technol Assess*. 2019;23:1-194
134. Ministry of Health Malaysia, Malaysian Society of Hypertension. *Clinical Practice Guidelines - Management of Hypertension, 5th Edition*. Ministry of Health Malaysia; 2018.https://www.malaysianheart.org/publication/clinical-practice-guidelines/p/clinical-practice-guidelines-management-of-hypertension-2018-5th-edition
135. All Wales Therapeutics and Toxicology Centre. *Polypharmacy in older people: A guide for healthcare professionals*. 2023.https://awttc.nhs.wales/medicines-optimisation-and-safety/medicines-optimisation-guidance-resources-and-data/prescribing-guidance/polypharmacy-in-older-people-a-guide-for-healthcare-professionals/
136. van der Velde N, Seppala LJ, Hartikainen S, et al. European position paper on polypharmacy and fall-risk-increasing drugs recommendations in the World Guidelines for Falls Prevention and Management: implications and implementation. *Eur Geriatr Med*. 2023;14:649-658
137. Ministry of Health Malaysia. *Falls Guideline for hospitalised older adults in the Ministry of Health*. Ministry of Health Malaysia,; 2019

138. Ministry of Health Malaysia, Malaysian Osteoporosis Society. *Clinical Practice Guidelines - Management of Osteoporosis 3rd Edition*. Ministry of Health Malaysia,; 2022.https://www.moh.gov.my/index.php/pages/view/3962?mid=1570
139. Fu Y, Hao J, Zhang N, et al. Fingolimod for the treatment of intracerebral hemorrhage: a 2-arm proof-of-concept study. *JAMA Neurol*. 2014;71:1092-1101
140. Zhang R, Yong VW, Xue M. Revisiting Minocycline in Intracerebral Hemorrhage: Mechanisms and Clinical Translation. *Front Immunol*. 2022;13:844163
141. University JH. Simvastatin for Intracerebral Hemorrhage Study. http://clinicaltrials.gov/ct2/show/NCT00718328. Accessed 13 September 2016.
142. Lee SH, Park HK, Ryu WS, et al. Effects of celecoxib on hematoma and edema volumes in primary intracerebral hemorrhage: a multicenter randomized controlled trial. *Eur J Neurol*. 2013;20:1161-1169
143. Tsang KS, Ng CPS, Zhu XL, et al. Phase I/II randomized controlled trial of autologous bone marrow-derived mesenchymal stem cell therapy for chronic stroke. *World J Stem Cells*. 2017;9:133-143
144. Lyden PD, Shuaib A, Lees KR, et al. Safety and tolerability of NXY-059 for acute intracerebral hemorrhage: the CHANT Trial. *Stroke*. 2007;38:2262-2269
145. Gonzales NR, Shah J, Sangha N, et al. Design of a prospective, dose-escalation study evaluating the Safety of Pioglitazone for Hematoma Resolution in Intracerebral Hemorrhage (SHRINC). *Int J Stroke*. 2013;8:388-396
146. Secades JJ, Alvarez-Sabín J, Rubio F, et al. Citicoline in intracerebral haemorrhage: a double-blind, randomized, placebo-controlled, multi-centre pilot study. *Cerebrovasc Dis*. 2006;21:380-385
147. Bajenaru O, Tiu C, Moessler H, et al. Efficacy and safety of Cerebrolysin in patients with hemorrhagic stroke. *J Med Life*. 2010;3:137-143
148. Tingyan H, Zhao Y, Hu Z, et al. Clinical Effects of Piracetam Plus Mannitol on Cerebral Edema, Neurological Function, and Vascular Endothelin-1 Levels Following Cerebral Hemorrhage. *Neurochemical Journal*. 2023;17:156-162
149. Kumar R, Fadzil F, Bee S, et al. Neuroaid use in intracranial hemorrhage (ICH). *J Neurol Sci*. 2021;429

APPENDICES

Appendix 1 Clinical Questions

Diagnosis of ICH
What is the accuracy of CT compared to MRI for diagnosis ICH?

What are the radiological signs that may predict haematoma expansion in ICH?

What are the accuracies of prognostic scores in predicting mortality after ICH?

Acute Medical Management
Is intensive blood pressure lowering safe and efficacious in acute ICH?

What are the safe and effective antihypertensive agents in acute ICH?

In patients with acute ICH what is/are the safe and effective haemostatic agents?

What are the safe and effective haemostatic agents in patients with acute ICH related to the followings:

- vitamin-K antagonist (VKA)
- non-vitamin K oral anticoagulant (NOAC)
- antiplatelet/platelet dysfunction

Are antiseizure medication(s) safe and effective in patients with acute ICH

- As primary prophylaxis?
- In patient with early seizures

Does admission to an organised stroke care unit improve outcomes in patients with acute ICH?

What physical/pharmacological interventions are safe and effective for prevention of venous thromboembolism in acute ICH?

Is an early do not attempt resuscitation (DNAR) decision safe in acute ICH?

What are the accuracies of swallowing assessments in patients with acute ICH?

Are neuroprotective agents are safe and effective in patients with acute ICH?

What are the safe and effective pre-medication and induction agent for intubating patients with acute ICH?

Acute Neurosurgical Management
Referral
Is routine transfer of patients to hospital with neurosurgical service safe and effective in acute ICH?

Haematoma evacuation
Is surgical evacuation of hematoma safe and effective compared to medical management in acute ICH?

IVH
Is IVH evacuation with EVD plus thrombolytics safe and effective compared to EVD alone in ICH patients with IVH?

Is IVH evacuation with neuroendoscopy safe and effective compared to EVD alone in ICH patients with IVH?

Craniectomy
Is decompressive craniectomy safe and effective in patients with ICH?

Neurocritical care, ICP monitoring and medical treatment of cerebral oedema
Is intracranial pressure monitoring safe and effective in acute ICH?

Are pharmacological agents safe and effective in reducing cerebral oedema in acute ICH?

Is early tracheostomy safe and effective in acute ICH?

Diagnosis of underlying aetiology in ICH
Is non-invasive vascular imaging (CTA/CTV or MRA/MRV), DSA and MRI accurate in diagnosing the aetiology of ICH?

Rehabilitation
Is early rehabilitation safe and effective post ICH?

Are neuropharmacological agents safe and effective for cognitive stimulation post ICH?

What are the safe and effective modalities for management of muscles spasticity post-ICH?

Secondary prevention
Is blood pressure control safe and effective in secondary prevention of ICH?

Is restarting antithrombotics, safe and effective in patients with ICH?

Are statins safe in patients with ICH?

Appendix 2 Example of Search Strategy

Clinical question: Is intensive blood pressure lowering safe and efficacious in acute ICH?

PICO	Initial term	MeSH term	Textwords
P	INTRA CEREBRAL HAEMORRHAGE	INTRACEREBRAL HEMORRHAGE/ BASAL GANGLIA HEMORRHAGE/ PUTAMINAL HEMORRHAGE/ Hemorrhagic stroke/	(Intracerebral h?morrhage or cerebral h?morrhage or intracerebral bleed or basal ganglia h?morrhage or basal ganglia bleed or putaminal h?morrhage or putaminal bleed or intraparenchymal bleed or intraparenchymal h?morrhage or h?morrhagic stroke or acute intracerebral h?morrhage or acute ICH).tw. ((supratentorial or infratentorial or intraventricular or lobar or pontine) adj3 h?morrhag*).tw.
I	Target Blood Pressure, optimal blood pressure, intensive blood pressure lowering/reduction, aggressive blood pressure lowering/reduction.	Blood pressure/ Hypertension/ Hypertension, malignant/ Essential hypertension/ blood pressure lowering/	((aggress* or vigor* or intens* or rigour*) adj3 (blood pressure manag* or blood pressure reduc* or blood pressure low* or blood pressure control* or blood pressure or BP)).mp. [mp=ti, bt, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, sy, ux, mx, tx, kw, ct, sh, cw]
C	-	-	-
O	Safe, effective, better, outcome, result	Treatment outcome/ Outcome assessment, health care/ Functional status/ Drug-related side effects and adverse reactions/	(safe* or efficac* or efficien* or effect* or outcome* or result*).tw.

Ovid MEDLINE(R) ALL <1946 to September 12, 2023>

1 INTRACEREBRAL HEMORRHAGE/ or BASAL GANGLIA HEMORRHAGE/ or PUTAMINAL HEMORRHAGE/ or Hemorrhagic stroke/
2 (Intracerebral h?morrhage or cerebral h?morrhage or intracerebral bleed or basal ganglia h?morrhage or basal ganglia bleed or putaminal h?morrhage or putaminal bleed or intraparenchymal bleed or intraparenchymal h?morrhage or h?morrhagic stroke or acute intracerebral h?morrhage or acute ICH).tw.
3 ((supratentorial or infratentorial or intraventricular or lobar or pontine) adj3 h?morrhag*).tw.

4	1 or 2 or 3
5	Blood pressure/ or Hypertension/ or "Hypertension, malignant"/ or Essential hypertension/ or blood pressure lowering/
6	((aggress* or vigor* or intens* or rigour*) adj3 (blood pressure manag* or blood pressure reduc* or blood pressure low* or blood pressure control* or blood pressure or BP)).mp. [mp=ti, bt, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, sy, ux, mx, tx, kw, ct, sh, cw]
7	5 or 6
8	Treatment outcome/ or "Outcome assessment, health care"/ or Functional status/ or "Drug-related side effects and adverse reactions"/
9	(safe* or efficac* or efficien* or effect* or outcome* or result*).mp. [mp=ti, bt, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, sy, ux, mx, tx, kw, ct, sh, cw]
10	8 or 9
11	4 and 7 and 10
12	limit 11 to "all adult (19 plus years)"
13	limit 12 to full text
14	limit 13 to (english or malay)
15	limit 14 to yr="2000 -Current"
16	limit 15 to humans
17	limit 16 to original articles
18	remove duplicates from 17

Appendix 3 Example of blood pressure lowering protocol in acute intracerebral haemorrhage

Initial therapy	
BP target	• Initial SBP 140-220: target SBP 130-140 mmHg within 60 minutes • Initial SBP ≥220: target SBP of 160 mmHg in 60 minutes. • Withold antihypertensive agent if SBP<130 mmHg during treatment
Monitoring	• Continuous HR monitoring • Record BP/HR q 5 mins during active treatment, then q 15 min for first hour, q 30 min for next 5 hours and then hourly to 24 h
Treatment	1st line- IV labetalol • IV bolus 10mg stat over 1 min • Repeat IV 20mg q 5 mins until target SBP reached (< 140mmHg) or HR <55 bpm; increase to 40 mg bolus if required • Maximum labetalol dose: 300 mg / 24 hours Or • IVI infusion start at 1–2 mg/min, • titrate q 5min up to 8 mg/min based on response. *If SBP target not achieved after cumulative dose of 50-60 mg labetalol, consider second line *skip to second line if contraindication to beta blockers (bradycardia HR<55/min, bronchial asthma)
	2nd line-IV infusion nicardipine • IV infusion initially 3-5mg/hour over 15 min • Increase q 15min by 2.5mg/hour until target SBP reached (< 140mmHg) • Max dose 15mg/hour Or 2nd line- IV hydralazine • IV Hydralazine with a test dose: 5 mg IV bolus over 1 minute • If SBP ≥ 140 mmHg, give another bolus in 5 minutes • If SBP still > 140mmHg, give 10 mg IV bolus q 5 mins until target SBP reached. Increase to 20 mg bolus if required • Maximum hydralazine dose = 240mg/24 hours
	3rd line-IVI GTN • Avoid if **<2 hours** of ICH onset • IV infusion initial 5μg/min, • increase q 3-5 min to 20μg/min • then increase q 3-5 min by 10-20μg/min • Max 400μg/min
Maintenance	
BP target	SBP 130-140 mmHg for 7 days
Monitoring	Once SBP is under target (confirmed by 4 readings 15 minutes apart): • Record BP/HR q 30 minutes for 5 hours and then q 1 h for 18h.
IV treatment prn	If SBP exceeds 140mmHg at any point: • Give IV Labetalol (20-40 mg) bolus
Oral medication	Start treatment by 24 hours (use nasogastric if required). • If not contraindicated and no other drug is specifically indicated, start

	combination therapy of ACEI + diuretics in addition to previous anti-hypertensives.

Adapted from the INTERACT-3 trial[48] and blood pressure management protocol for intracerebral haemorrhage of Hospital Canselor Tuanku Muhriz UKM.

Appendix 4 Recommended dose of 4F-PCC

Warfarin Anticoagulation Reversal

INR level is available

Intended INR	Initial INR				
	2.0 – 2.5	2.6 – 3.0	3.1 – 3.5	3.6 -10.0	> 10.0
≤ 1.2[1,2] (full reversal)	30 IU/kg	35 IU/kg	40 IU/kg	50 IU/kg	50 IU/kg

Note: single dose cannot exceed 3000 IU

INR level is not available, major/life-threatening bleeding

1st dose: 2000 IU (fixed dose)[3]

2nd dose: if the patient still has persistent bleeding and INR remains elevated

Repeated INR	1.5 – 1.9	≥ 2.0
Dose (fixed)	500 IU	1000 IU

Note: total dose cannot exceed 3000 IU within 6 hours

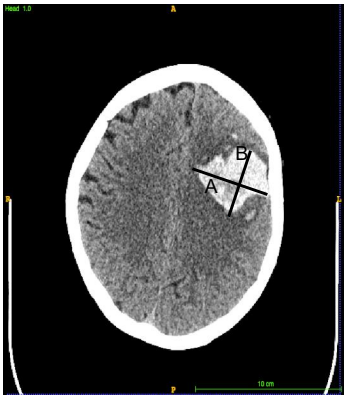
Non-Vit. K Oral Anticoagulants (NOACs) associated major/ life-threatening bleeding[3,4]

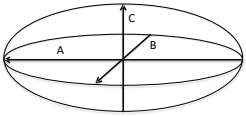
Apixaban Rivaroxaban Dabigatran (If Idarucizumab is not available)	1st dose: 2000 IU (fixed dose) 2nd dose: if persistent bleeding: 500 IU or 1000 IU (fixed dose) Note: total dose cannot exceed 3000 IU within 6 hours

References:

1. Octaplex® Package Insert (2018)
2. Lexicomp (2022). Prothrombin complex concentrate, 4-factor, unactivated, from human plasma: Drug information
3. Thrombosis Canada (2016) Anticoagulant-related Bleeding Management Order Set. https://thrombosiscanada.ca/wp-content/uploads/2016/07/Anticoagulant-Related-Bleeding-Mgmt_with-links.pdf
4. Majeed A, Ågren A, Holmström M, et al. Management of rivaroxaban- or apixaban-associated major bleeding with prothrombin complex concentrates: a cohort study. Blood 2017;130:1706–1712.

Appendix 5: ABC/2 method of measuring ICH volume





Haematoma volume=ABC/2
A=length (cm),
B=width (cm)
C=height (number of slices X slice thickness)

Images courtesy of Zhe Kang Law, Universiti Kebangsaan Malaysia

To calculate:

1) Scroll to the CT scan slice where the haematoma appears largest
2) Measure the longest diameter of haematoma at this slice (A=length in cm)
3) Measure the widest diameter of haematoma perpendicular i.e 90^{o} to A (B=width in cm)
4) Scroll through the CT, count the number of slices where the haematoma can be seen and multiply by slice thickness. E.g number of slices= 20, and slice thickness= 1mm or 0.1cm; C, the height=20 slices X 0.1cm=2cm
5) Calculate haematoma volume using ABC/2 formula. e.g A= 2.5cm; B=1.5cm, C=2cm; haematoma volume= 2.5X1.5X2/2=3.75 cm^3 or 3.75mL

Appendix 6 ICH score

Components	Score points
Glasgow Coma Scale	
3-4	2
5-12	1
13-15	0
ICH Volume (mL)	
≥30	1
<30	0
Infratentorial location	
Yes	1
No	0
Age (Years)	
≥80	1
<80	0

ICH score 0 to 6: 30-day mortality rate for score 0=0%; 1= 13%; 2=26%; 3=72%; 4=97%; 5=100%. No patient in the validation study scored 6 points

***Source**: Hemphill JC, 3rd, Bonovich DC, Besmertis L, Manley GT, Johnston SC. The ICH score:
a simple, reliable grading scale for intracerebral hemorrhage. *Stroke*. 2001;32:891-897

Appendix 7 List of neuroprotective agents researched in intracerebral haemorrhage

Neuroprotective agent	Phase of study	Results/Conclusion
Fingolimod[139]	I/II	neutral
Minocycline[140]	I/II	neutral
Statins[141]	I/II	inconclusive
Celecoxib[142]	I/II	neutral
Stem cell therapy[143]	I/II	neutral
NXY-059[144]	I/II	neutral
Pioglitazone[145]	I/II	Unpublished (only non-peer reviewed preprint)
Citicoline[146]	I/II	neutral
Cerebrolysin[147]	I/II	neutral
Piracetam[148]	I/II	Inconclusive (combined use with mannitol and only univariate analyses published)
NeuroAid[149]	Cohort study	inconclusive

ACKNOWLEDGEMENTS

The members of CPG DG would like to express their gratitude and appreciation to the following for their contributions:
• Panel of external reviewers who reviewed the draft
• Technical Advisory Committee of CPG for their valuable input and feedback
• Health Technology Assessment and Clinical Practice Guidelines Council for approving the CPG
• Mr Azlan Mohamad Hamzah (Hospital Canselor Tuanku Muhriz librarian) on retrieval of evidence
• Dr Teoh Chia Xuan on the design of CPG front cover
• All those who have contributed, directly or indirectly, to the development of the CPG

DISCLOSURE STATEMENT

The panel members of DG had completed disclosure forms. None held shares in pharmaceutical firms or acts as consultants to such firms. Details are available upon request from the CPG Secretariat.

SOURCE OF FUNDING

The development of the CPG on Management of was supported by the Malaysian Society of Neurosciences through the Malaysian Stroke Council

Malaysian Society of Neurosciences
Persatuan Neurosains Malaysia

Malaysian Society of Neurosciences
Neurology Laboratory,
6th Floor, South Tower
University of Malaya Medical Centre
50603 Kuala Lumpur
Malaysia

ISBN 978-629-96368-2-3