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Canadian stroke best practice recommendations: *Management of Spontaneous Intracerebral Hemorrhage*, 7th Edition Update 2020

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Abstract

Spontaneous intracerebral hemorrhage is a particularly devastating type of stroke with greater morbidity and mortality compared with ischemic stroke and can account for half or more of all deaths from stroke. The seventh update of the *Canadian Stroke Best Practice Recommendations* includes a new stand-alone module on intracerebral hemorrhage, with a focus on elements of care that are unique or affect persons disproportionately relative to ischemic stroke. Prior to this edition, intracerebral hemorrhage was included in the Acute Stroke Management module and was limited to its management during the first 12 h. With the growing evidence on intracerebral hemorrhage, a separate module focused on this topic across the care continuum was added. In addition to topics related to initial clinical management, neuroimaging, blood pressure management, and surgical management, new sections have been introduced addressing topics

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surrounding inpatient complications such as venous thromboembolism, seizure management, and increased intracranial pressure, rehabilitation as well as issues related to secondary management including lifestyle management, maintaining a normal blood pressure and antithrombotic therapy, are addressed. The *Canadian Stroke Best Practice Recommendations* (*CSBPR*) are intended to provide up-to-date evidence-based guidelines for the prevention and management of stroke and to promote optimal recovery and reintegration for people who have experienced stroke, including patients, families, and informal caregivers.

Keywords
Stroke, spontaneous intracerebral hemorrhage, practice guidelines, treatment, prevention, rehabilitation

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Introduction

Hemorrhagic stroke is a particularly devastating type of stroke with greater morbidity and mortality compared with ischemic stroke.[1] While just under a third of strokes are hemorrhagic strokes, they account for 49% of the global burden of death from stroke.[2] Globally, there were 13.7 million new strokes in 2016, of which 4.1 million, or 30%, were hemorrhagic stroke.[2] Spontaneous intracerebral hemorrhage (ICH) is the most prevalent subtype of hemorrhagic stroke, accounting for about 75% of cases. In Canada, ICH accounts for 10–15% of all stroke cases presenting to hospitals, with mortality that is considerably higher compared with ischemic stroke (40% vs. 15%).[3] The economic burden associated with the treatment of ICH is aslo considerably higher than that of ischemic stroke.[4] In Canada, the median cost of treating spontaneous ICH was USD$10,500 per hospitalization per patient during the decade from 1999 to 2008,[5] with the majority of the cost incured during acute hospitalization (median of USD$7300). Surgery, comorbidity, and greater stroke severity were factors associated with increasing costs, while hypertension was the strongest predictor of ICH cost, mediated by a longer length of hospital stay.[6]

The 2020 update of the Canadian Stroke Best Practice Recommendations (CSBPR): *Management of Spontaneous Intracerebral Hemorrhage (sICH) is* a new addition for the 7th edition of the CSBPR. Prior to this edition, sICH, defined as bleeding within the brain parenchyma, was included in the Acute Stroke Management module and was limited to management provided within the first 12 h of the event. While much of the care associated with recovery following that time period is similar to that provided to people with acute ischemic stroke, there are some unique care aspects, which is the focus of this module (Figure 1). This module contains updates and additions to previously existing recommendations on acute management of ICH in the emergency department, including clinical assessment, neuroimaging, blood pressure management, and surgical management and supersedes all previous editions. Recommendations are also provided on topics surrounding inpatient complications such as venous thromboembolism (VTE), seizure management, increased intracranial pressure (ICP), and rehabilitation. Finally, recommendations are presented related to secondary prevention, addressing the most important risk factors of hypertension, the resumption of oral antithrombotics, statins and lifestyle factors, particularly those with the greatest associations with ICH (alcohol, smoking, and physical activity). A recent study highlights the positive impact that guideline-based practice can have on ICH outcome. The application of an evidence-based guideline care bundle including rapid reversal of anticoagulation, intensive lowering blood pressure, and prompt neurosurgical referral for appropriate patients was shown to reduce 30-day mortality by 10.8% compared with care received before the implementation of this protocol.[7]

The theme of this edition of the CSBPR is entitled "*Building connections to optimize individual outcomes*." Since people who have experienced a stroke often present to the healthcare system with multiple comorbid conditions, these conditions must be considered as treatment, and ongoing care planning is personalized and person-centred. In addition, there is strong evidence of the intrinsic connections between the heart and brain, and management of people following stroke should take heart health and possible association with vascular cognitive impairment into consideration. The healthcare system is often designed in siloes with different planning and organization for individual conditions that are not integrated across conditions, even related vascular conditions. As people transition across settings and phases of care following a stroke, they report experiencing anxiety and feeling quite overwhelmed. Individualized care and ensuring connections are made within the community have a significant impact on patient short and long-term outcomes.

The Canadian Stroke Best Practice Recommendations are intended to provide up-to-date

evidence-based guidelines for the prevention and management of stroke and to promote optimal recovery and reintegration for all persons affected including patients, families, and informal caregivers. This module is intended for use by all healthcare professionals across the continuum of care as well as people living with these conditions and their caregivers. Health system policy makers, planners, funders, senior managers, and administrators who are responsible for the coordination and delivery of health services within a province or region will also find this document relevant and applicable to their work. The goal of disseminating and implementing these recommendations is to optimize evidence-based integrated and coordinated stroke care across Canada, increase timely access to care, reduce practice variations in the care of stroke patients, and narrow the gap between current knowledge and clinical practice.

Guideline development methodology

The Canadian Stroke Best Practice Recommendations development and update process follows a rigorous framework adapted from the Practice Guideline Evaluation and Adaptation Cycle[7,8] and addresses all criteria defined within the AGREE Trust model.[9] The methodology has been used in previously published updates[6,10] and can be found on our Canadian Stroke Best Practices website at www.strokebestpractices.ca. An interdisciplinary group of experts was convened and participated in reviewing, drafting, and revising all recommendation statements. The writing group included stroke neurologists, epidemiologists, nurse practitioners, critical care physicians, neuroradiologists, and neurosurgeons. These recommendations were developed in collaboration with the Canadian Stroke Consortium.

Searches were conducted by experienced personnel to identify peer-reviewed literature that examined each topic area addressed in the current module. Systematic reviews, meta-analyses, randomized controlled trials, and observational studies were included, as available. The literature for this module was current to January 2020. Following a standardized abstraction format, evidence tables were constructed including content from selected studies and provided to the writing group for review. The writing group discussed and debated the strength, importance, clinical relevance, and applicability of the evidence and, through consensus, developed a draft set of proposed recommendations. During this process, additional literature may have been identified and used to develop a final set of proposed recommendations. All recommendations were assigned a level to indicate the strength of the evidence ranging from A to C (described below). The draft set of recommendations underwent an internal review conducted by each member of the writing group and the Canadian Stroke Best Practices and Quality Advisory Committee and were then sent for external review to several Canadian and international experts who were not involved in any aspects of the guideline development. All feedback received was given careful consideration during the editing process and was incorporated into the final version of the recommendations as appropriate. Definitions of terms used within the recommendations are available at: www.strokebestpractices.ca.

Assigning evidence levels

All recommendations were assigned a level indicating the strength of the evidence ranging from A to C according to the criteria adapted from Guyatt et al.[8] defined in Table 1. When developing and including "C-Level" recommendations, consensus was obtained among the writing group and validated through the internal and external review process. This level of evidence was used cautiously and only when there was a lack of stronger evidence for topics considered important system drivers for stroke care. An additional category for expert opinion statements has also been added in response to reasonable requests from a range of healthcare professionals who seek guidance and direction from the experts on specific clinical issues faced on a regular basis in the absence of any evidence on that topic. Since these statements did not meet the criteria to be stated as recommendations, they were included under the term, *clinical considerations*, with the goal of providing additional guidance or clarity in the absence of evidence.

Recommendations on the management of intracerebral hemorrhage

Section 1: Emergency management of intracerebral hemorrhage

Patients presenting with symptoms of suspected ICH, such as a depressed mental state, severe headache, nausea, vomiting, and weakness or paralysis (Box One), should undergo a non-contrast computerized tomography (CT) or magnetic resonance imaging (MRI) scan immediately to confirm the diagnosis. Both forms of imaging have been shown to accurately detect acute intracranial hemorrhage.[9,10] Given that an underlying macrovascular cause is responsible for 15–25% of spontaneous ICHs, further imaging studies should also be conducted using CT angiography, MR angiography, or digital subtraction angiography (DSA) to detect possible arteriovenous malformations,

Table 1. Summary of criteria for levels of evidence reported in the *Canadian Stroke Best Practice Recommendations* (Update 2020)

Level of evidence	Criteria[a]
A	Evidence from a meta-analysis of randomized controlled trials or consistent findings from two or more randomized controlled trials. Desirable effects clearly outweigh undesirable effects or undesirable effects clearly outweigh desirable effects.
B	Evidence from a single randomized controlled trial or consistent findings from two or more well-designed non-randomized and/or non-controlled trials and large observational studies. Desirable effects outweigh or are closely balanced with undesirable effects or undesirable effects outweigh or are closely balanced with desirable effects.
C	Writing group consensus and/or supported by limited research evidence. Desirable effects outweigh or are closely balanced with undesirable effects or undesirable effects outweigh or are closely balanced with desirable effects, as determined by writing group consensus. Recommendations assigned a Level-C evidence may be key system drivers supporting other recommendations, and some may be expert opinion based on common, new, or emerging evidence or practice patterns.

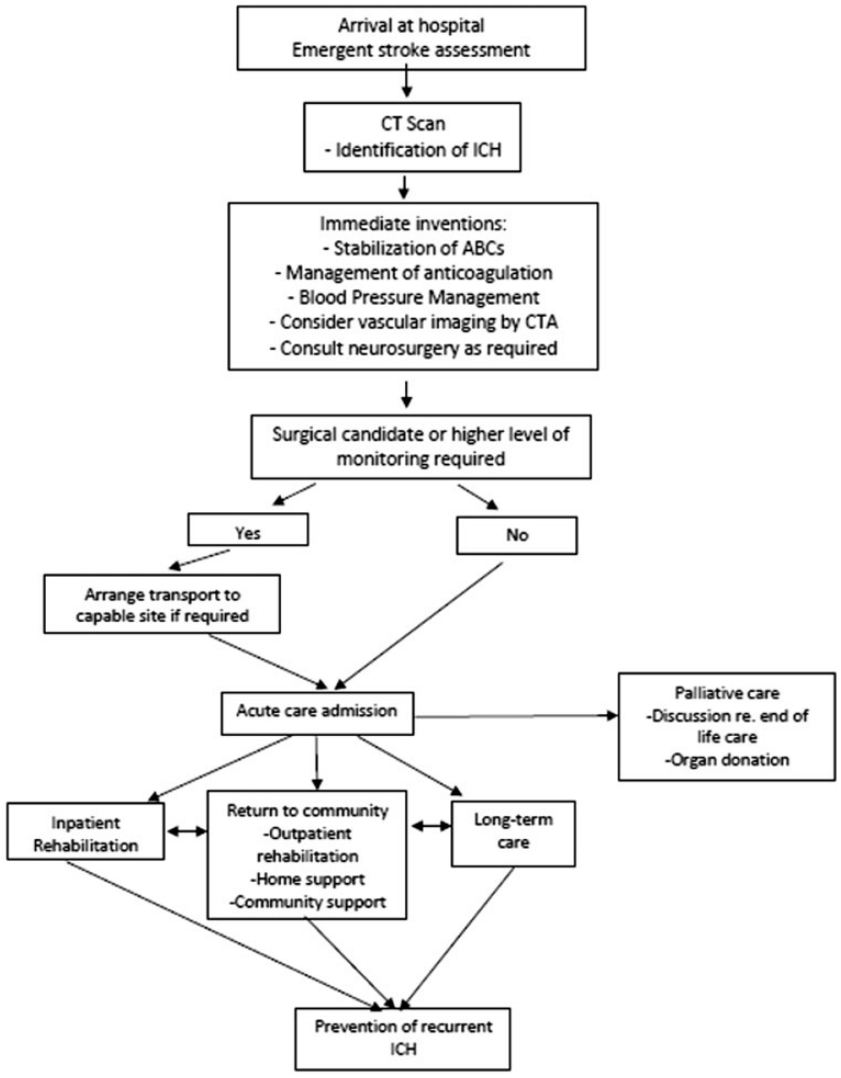
[a]Adapted from Guyatt GH, Cook DJ, Jaeschke R, et al. Grades of recommendation for antithrombotic agents: American College of Chest Physicians evidence-based clinical practice guidelines (8th ed) [published erratum in *Chest* 2008; 134: 473]. *Chest* 2008; 133 (6 Suppl): 123 S–131 S.

aneurysms, or cases of cerebral venous sinus thrombosis.[11,12] In the DIAGRAM study, younger age, lobar or posterior fossa location of ICH, absence of neuroimaging markers of cerebral small vessel disease, and a positive or inconclusive CTA were independent predictors for an ultimate macrovascular cause for the ICH being identified within one year of follow-up. In a separate retrospective single-center study, patients with an abnormal CTA, lack of microangiopathic findings, and absence of pre-existing history of hypertension had a 96% chance of having a macrovascular cause identified on DSA.[13] In addition to the above, predictors of a positive CTA additionally include female sex, associated intraventricular and subarachnoid hemorrhage, lack of impaired coagulation, associated enlarged vessels, or calcifications along the margin of the ICH.[12]

Following a confirmed diagnosis, one of the most important early therapeutic targets is aimed at limiting hematoma expansion, a factor which has been identified as a strong determinant of early neurological deterioration and poor clinical outcomes. Depending on the definition used, hematoma expansion occurs in up to 32% of ICH patients.[14] Risk factors for hematoma expansion include the presence of "spot sign" (contrast extravasation), heterogeneous hematoma density/border irregularity, early presentation, anticoagulation use, and initial hematoma volume.[15,16] Early blood pressure reductions are the mainstay of treatment to help prevent hematoma expansion.

While the optimal blood pressure targets for patients who have experienced a spontaneous ICH are not known, a systolic blood pressure (SBP) greater than 180 mm Hg is thought to increase the risks of rebleeding and hematoma expansion. Although this finding suggests that steps to lower blood pressure aggressively would be beneficial, the results from several large controlled trials on the topic are not conclusive. In the ATACH-2 trial,[17] intensive blood pressure management, with an SBP target of 110–139 mm Hg, did not reduce the risk of death or disability at 90 days (adjusted OR = 1.04, 95% CI 0.85–1.27, p = 0.72), or hematoma expansion within 24 h (adj OR = 0.78, 95% CI 0.58–1.03, p = 0.08), compared with standard treatment (target SBP of 140–179 mm Hg) in 1000 patients admitted acutely with an ICH. A subgroup analysis of the same trial suggested that patients with a basal ganglia hemorrhage may benefit from intensive treatment.[18] Results of the INTERACT-2 trial[19] also suggested no difference in the risk of a poor outcome or 90-day mortality among patients with a target SBP less than 140 mm Hg following ICH (52% vs. 55.6%, OR = 0.87, 95% CI 0.75–1.01, p = 0.06 and 11.9% vs. 12.0%, OR = 0.99, 95% CI 0.79–1.25, p = 0.96, respectively). However, there was a significant shift in the distribution of mRS scores toward less disability among patients in the intensive group (OR = 0.87, 95% CI 0.77–1.00, p = 0.04). The results of the ATACH-2 and INTERACT-2 trials were pooled using individual patient data ($n = 3829$).[20] Achieved target SBP during the first 24 h was associated with functional status, whereby each 10 mm Hg increase in SBP resulted in significantly reduced odds of a favorable shift in mRS scores (OR = 0.90, 95% CI 0.87–0.94, p < 0.0001), reduced odds of a good outcome (OR = 0.90, 95% CI 0.85–0.95, p = 0.0002), and increased odds of hematoma expansion, neurological deterioration, death at 90 days, and serious adverse events.

Figure 1. Intracerebral hemorrhage patient flow map.



Although not currently recommended for use in spontaneous ICH, another potential treatment that may help to optimize hemostasis and minimize hematoma expansion is recombinant-activated factor VII (rFVIIa). In a recent trial that included 69 patients with primary spontaneous acute ICH who were spot-sign positive and randomized to receive rFVIIa (80 μg/kg or placebo), there were no significant differences between groups in the change (increase) in median parenchymal ICH volume from baseline to 24 h (2.5 vs. 2.6 mL, $p = 0.89$) or in median total hemorrhagic volume (3.2 vs. 4.8 mL, $p = 0.91$).[21] Results of the FAST II[22] and FAST III trials[23] suggested that treatment with rFVIIa could help to blunt the increase in ICH volume at 24-h post treatment; however, the trials conflicted with respect to functional outcome. The FAST III trial[23] did not report a significant difference in the proportion of patients with death or severe disability at 90 days, while FAST II[22] reported a lower proportion in active treatment group patients. The authors of a recent Cochrane review stated that they could not draw firm conclusions of the benefit of blood clotting factors in the treatment of ICH, but noted ongoing research in subgroups (e.g. younger patients and earlier time windows).[24] Other hemostatic therapies are under investigation. The benefits of the antifibrinolytic agent tranexamic acid in major trauma have increased interest in its potential benefits in spontaneous ICH. In the TICH-2 trial, the use of tranexamic acid (1 g bolus, followed by 1 g infused over 8 h) was shown to be safe, seemed to reduce hematoma expansion and reduced early deaths, but ultimately did not

improve functional outcomes at 90 days in spontaneous ICH patients treated within 8 h of symptom onset.[25]

For patients who had been managed with warfarin prior to ICH, the results of the INCH trial[26] indicate that the treatment with prothrombin complex concentrate (PCC) is superior to intravenous fresh-frozen plasma. The trial was halted early due to safety concerns, after significantly more patients in the PCC group achieved anticoagulation reversal (INR ≤ 1.2) within 3 h after treatment (67% vs. 9%, OR = 30.6, 95% CI 4.7–197.9, p = 0.0003). There are other options when treating patients taking non-vitamin K oral anticoagulants. Treatment with idarucizumab has been shown to be effective in reversing anticoagulation for patients requiring surgery or other invasive procedures, who had been previously receiving treatment with the direct oral anticoagulation agent, dabigatran.[27] The ANNEXA-4 trial[28] included patients who had sustained acute major bleeding occurring while taking a factor Xa inhibitor. The primary site of bleeding was intracranial in 64% of 352 patients enrolled. Following treatment with andexanet, there was a median reduction of 92% in anti-factor Xa activity among the patients who had been taking apixaban or rivaroxaban, while 82% of all patients who could be evaluated had excellent or good hemostasis 12 h after infusion. The ongoing ANNEXA-I trial is assessing the clinical efficacy of random assignment to andexanet alfa compared with standard treatment (including PCC) in factor Xa inhibitor-related ICH.

The possible need for surgical decompression or hematoma evacuation should be urgently assessed by neurosurgical consultation.[29] While the role of surgical intervention for the evacuation of supratentorial ICH remains uncertain, patients with hematomas ≥ 3 cm, and those exhibiting signs of clinical deterioration or coma can be considered for craniectomy with and/or without clot evacuation. These procedures, typically performed using conventional craniotomy or minimally invasive surgery (MIS), can stop bleeding, prevent rebleeding, and prevent secondary brain damage by removing the mass effect.[30] Overall, while any form of surgical intervention was found to be associated with better outcomes compared with best medical management in a pooled analysis,[31] the proportions of patients who experienced a favorable outcome were not significantly higher in patients with primary supratentorial ICH, treated with conventional craniotomy in the STICH-1[32] and STICH-2[33] trials. MIS appears to be superior to conventional craniotomy.[34,35] The risk of death or dependence was shown to be reduced significantly in patients with supratentorial ICH treated with MIS compared with craniotomy or conservative management in two systematic reviews including the results of 12 and 15 high-quality trials.[35,36] Treatment with alteplase via the MISTIE technique significantly reduced hematoma size compared with standard care in 506 patients with supratentorial ICH of ≥ 30 mL, although there was no significant difference between groups in the proportion of patients who achieved a good functional outcome (mRS 0–3) at one year (45% vs. 41%, absolute risk difference 4% (95% CI −4–12); p = 0·33).[37] One-year and 180-day mortality were both significantly lower in the MISTIE group, but not 30-day mortality.

Section 1: Recommendations[a]

[a]These recommendations provide guidance in the management of spontaneous intracerebral hemorrhage (ICH), not hemorrhagic conversion of an ischemic infarction; These recommendations may not be applicable to ICH of secondary causes; These recommendations should be referred to once a confirmed diagnosis of ICH has been established following brain imaging; Prior to diagnosis of ICH, follow the Initial assessments and imaging guidelines defined in the CSBPR Acute Stroke Management module 2018 (Sections 2, 3, 4) for all patients who arrive at hospital with a suspected stroke and during prehospital management.

1.0. Intracerebral hemorrhage should be treated as a medical emergency. When intracerebral hemorrhage is suspected (or confirmed), patients should be evaluated urgently (Evidence Level B) by physicians with expertise in acute stroke management (Evidence Level C).

Note: For patients presenting in community or rural hospitals, Telestroke modalities could facilitate rapid access to stroke expertise for consultation and decision-making regarding transfer to a higher level of care.

1.1. Initial clinical assessment of intracerebral hemorrhage

i. A severity score based on neurological exam findings should be conducted as part of the initial assessment (Evidence Level B). The National Institute of Health Stroke Score is preferred for awake or drowsy patients or a Glasgow Coma Scale (GCS) in patients who are obtunded, semi or fully comatose (Evidence Level C).

Note: The GCS has been found to be a strong predictor of outcomes following ICH.

a. Patients with declining GCS and/or equal to less than 8 should be rapidly assessed for airway support by endotracheal intubation (Evidence Level B).
b. Patients with reduced level of consciousness (LOC), pupillary changes, and/or other signs of herniation should have temporizing maneuvers to manage presumed elevation in ICP, such as temporary hyperventilation, and hyperosmotics (e.g. mannitol or 3% saline) (Evidence Level C).

ii. Patients with suspected ICH should undergo CT immediately following stabilization to confirm diagnosis, location, and extent of hemorrhage (Evidence Level A). *Refer to CSBPR Acute Stroke Management module for additional information on initial brain imaging. www.strokebestpractices.ca.*
iii. In patients with confirmed acute ICH, intracranial vascular imaging is recommended *for most patients* to exclude an underlying lesion such as an aneurysm or arteriovenous malformation or cerebral sinus venous thrombosis (Evidence Level B).
   a. Factors that increase the yield of angiography include age $<$50 years, female sex, lobar, or infratentorial location of ICH, accompanying intraventricular hemorrhage, absence of neuroimaging markers of cerebral small vessel disease, and/or absence of hypertension or impaired coagulation (Evidence Level B).
   b. Where suspicion is high for an underlying vascular lesion, the vascular imaging should be performed at the same time as brain imaging (Evidence Level C).
iv. Evaluation of patients with acute ICH should include questions about medication history (Evidence Level C) and antithrombotic therapy, measurement of platelet count, partial thromboplastin time, and international normalized ratio (Evidence Level A).
v. Patients should be assessed for clinical signs of increased ICP such as pupil reaction and LOC (Evidence Level B).
vi. A GCS score and neurovital signs should be conducted at baseline and repeated at least hourly for the first 24 h, depending on stability of patient (Evidence Level C).
vii. If physicians with expertise in acute stroke management are not available onsite, protocols should be in place to contact appropriate experts through virtual telestroke technology (Evidence Level B) to expedite patient assessment and decisions regarding transport to a higher level of care (Evidence Level C).

Clinical considerations for Section 1.1

i. The resolution of CT angiography is preferred over MR angiography when screening for underlying vascular anomalies.
ii. Clinical signs of increased ICP include reduced LOC, dilated unresponsive pupils, new cranial nerve VI palsies, or other false localizing neurological signs, worsening headache and/or nausea/vomiting, and elevated blood pressure with reduced heart rate and irregular/decreased respirations (Cushing's reflex).
iii. Potential unstable patients requiring greater monitoring frequency (i.e. neurovital signs hourly for first 24 h) include patients with large ($>$30 cc) ICH volume, depressed or declining GCS ($<$12), worsening neurological disability, infratentorial location, associated intraventricular hemorrhage or hydrocephalus, refractory hypertension, and/or neuroimaging markers of ICH expansion (see Section 1.5).
iv. The use of tranexamic acid has been shown to be safe in a large phase 3 trial (TICH-2) but there was no effect on the primary outcome of functional status at 90 days. Post-hoc pre-specified subgroup analyses showed better functional status in patients with baseline SBP less than 170 mm Hg. However, this post-hoc finding has yet to be confirmed. Overall, the clinical role of tranexamic acid for spontaneous ICH remains unclear, and there is no evidence for its use in the setting of anticoagulant-related ICH.

1.2. Blood pressure management

i. Blood pressure should be assessed on initial arrival to the Emergency Department and every 15 min thereafter until desired blood pressure target is achieved and maintained for the first 24 h (Evidence Level C).
ii. SBP lowering to a target of $<$140 mm Hg systolic does not worsen neurological outcomes (relative to a target of 180 mm Hg systolic) (Evidence level A); however, clinical benefit has yet to be established (Evidence level A).
iii. Subsequent blood pressure monitoring should be tailored to the individual patients according to stability of the vital signs and ICP (Evidence Level C).
iv. There is a lack of strong evidence to guide choice of initial blood pressure lowering agents.

Clinical consideration for Section 1.2

i. A SBP threshold at an individual target of less than 140–160 mm Hg for the first 24–48 h post-ICH may be reasonable.
   a. Factors that may favor a lower target within this range (i.e. $<$140 mm HG) may include: presentation within 6 h of symptom onset; presenting SBP no greater than 220 mm Hg; anticoagulation therapy; presence of neuroimaging markers of expansion (see Section 1.5) and/or normal renal function.
ii. Parenteral labetalol, hydralazine, nicardapine, and/or enalipril (oral or intravenous) may be considered for acute blood pressure reduction.

1.3. Management of anticoagulation

i. Patients presenting with anticoagulant-related ICH should have their anticoagulation withheld and should be considered for immediate reversal, irrespective of the underlying indication for anticoagulation (Evidence Level B).
ii. Beyond initial investigations, further management should be tailored to the specific antithrombotic agent used (Evidence Level C).
iii. Warfarin should be reversed immediately with PCC dosed as per local protocols and in conjunction with intravenous Vitamin K 10 mg (Evidence Level B).
iv. For patients on direct oral anticoagulants (DOACs), most information about anticoagulation activity would come from establishing time of last dose, creatinine clearance, anti-factor Xa level, if available (Evidence Level C).

Note: Reversal should not be delayed while waiting for laboratory results, rather it should be based on clinical history.

v. Factor Xa inhibitors (apixaban, edoxaban, rivaroxaban) should be stopped immediately and PCC administered at a dose of 50 U/kg with a *maximum* dose of 3000 U (Evidence Level C).

Note: There are no targeted anti-Factor Xa reversal agents available in Canada at this time.

vi. Dabigatran should be stopped immediately and reversed with idarucizumab; patients should be given a total dose of 5 g, in two intravenous bolus doses of 2.5 g each, given no more than 15 min apart (Evidence Level B).

Note: The doses should be given successively. There is no requirement for time delay between doses.

   a. If idarucizumab is not available, use of FEIBA (anti-inhibitor coagulant complex; activated PCC) is recommended at 50 U/kg to a maximum of 2000 U (Evidence Level C).
   b. If both agents are not available, consider four-factor PCC at a dose of 50 U/kg to a *maximum* dose of 3000 U (Evidence Level C).
vii. If the patient has received therapeutic low molecular weight heparin (LMWH) within the past 12 h, consider administering protamine (Evidence Level C).
viii. If the patient is receiving intravenous heparin infusion at the time of ICH, infusion should be immediately discontinued and consider administering protamine (Evidence Level C).
ix. Antiplatelet agents (e.g. acetylsalicylic acid (ASA), clopidogrel, dipyridamole/ASA, and ticagrelor) should be stopped immediately (Evidence Level C).
x. Platelet transfusions are not recommended (in the absence of significant thrombocytopenia) and may be harmful (Evidence Level B).

Clinical considerations for Section 1.3

i. Dilute thrombin time can be used as a surrogate measure of anticoagulation in patients on dabigatran; however, we advise against delaying reversal to obtain these results.
ii. Andexanet alfa is not yet commercially available in Canada but has been shown to reverse the anticoagulant effect of Factor Xa inhibitors in a non-randomized single-arm clinical trial. It could be considered once commercially available.

1.4. Consultation with neurosurgery

i. Neurosurgical consultation can be considered as a life-saving intervention for large ICH that is surgical accessible or causing obstructive hydrocephalus. Smaller non-life-threatening ICH requires stroke unit care and does not necessarily require neurosurgical consultation (Evidence Level C).

Note: If neurosurgical services not available onsite, initial consultation should be initiated with nearest neurosurgical services without delay, using telephone or Telemedicine technology.

Clinical consideration for Section 1.4

i. Participation and enrollment in randomized trials should be considered where possible.

1.5. Neuroimaging

Note: For recommendations on initial neuro-imaging of all suspected acute stroke patients upon initial arrival to hospital refer to CSBPR Acute Stroke Management module, Section 3 and this module Section 1.1 (ii–iii) and Acute Stroke Management during Pregnancy module.

1.5.1. Recommended additional urgent neuroimaging to confirm ICH diagnosis

i. In cases where CTA is not obtained as part of the initial acute stroke protocol, non-invasive angiography (CTA or gadolinium enhanced MRA) of the intracranial circulation should be considered and, if proceeding, be performed promptly on most patients presenting with ICH to identify potential underlying vascular lesions or spot sign/extravasation (Evidence Level B).
   a. If suspected, CT venography can be performed to evaluate for cerebral venous sinus thrombosis (Evidence Level B).

Clinical considerations for Section 1.5.1

i. Hemorrhage volume (cc) can be quickly estimated using the formula ABC/2 where A is the greatest hemorrhage diameter in centimeters on an axial slice, B is the largest diameter perpendicular to A, and C is the approximate number of CT slices with hemorrhage multiplied by the slice thickness in cm (i.e. 5 mm slice thickness = 0.5).
ii. Urgent repeat CT should be performed in patients when there is clinical deterioration or worsening LOC. A repeat CT at 24 h may be considered even in the absence of clinical deterioration to document hematoma expansion (occurring in ~30% of acute ICH) and to identify extent of mass effect, new intraventricular hemorrhage, or evolution of hydrocephalus.
iii. Baseline clinical and imaging factors that are predictive of hematoma expansion and ensuing worse outcomes include short time from symptom onset to baseline imaging (i.e. 6 h), larger hematoma volume, and antithrombotic therapy. Additional imaging predictors of hematoma expansion including heterogeneous hematoma density or regions of intra-hematomal hypodensity, irregular hematoma shape and satellite hematomas, amongst others, on non-contrast CT as well as intra-hematomal contrast extravasation (Spot Sign) on CTA. However, these markers have yet to be proven useful for clinical interventions.
iv. Early marked vasogenic edema that is out of proportion to presumed timing of ICH may be suggestive of underlying hemorrhagic infarction, hemorrhagic tumor, or cerebral venous sinus thrombosis. CT hyperattenuation within a major dural venous sinus or cortical vein draining region of ICH is suggestive of cerebral venous sinus thrombosis.

1.5.2. Recommended additional etiological neuroimaging

i. MRI should be considered to evaluate potential underlying mass lesions, hemorrhagic transformation of an ischemic infarct, and cavernous malformations (Evidence Level B).

a. MRI can additionally provide information on microangiopathic changes to support the diagnosis of spontaneous ICH from underlying cerebral small vessel disease due to chronic hypertension and/or cerebral amyloid angiopathy (CAA) (Evidence Level B).
b. The optimal timing of initial MRI is uncertain (Evidence Level C).

ii. MRI with MR venogram and GRE/SWI may be considered to exclude cerebral venous thrombosis (Evidence Level B).
iii. DSA should be considered in select cases where there exists continued high suspicion of underlying vascular anomaly despite normal CTA and MRI, or non-invasive studies are suggestive of an underlying lesion (Evidence Level B).
a. The yield of angiography is higher in the presence of the following clinical and radiologic predictors: younger age <50 years, female sex, lobar/superficial or infratentorial location of ICH, associated intraventricular hemorrhage or subarachnoid hemorrhage, absence of prior history of hypertension or impaired coagulation, associated enlarged vessels or calcifications along the margin of the ICH, and absence of neuroimaging markers of cerebral small vessel disease (Evidence Level B).
iv. Where sufficient suspicion persists for an underlying lesion responsible for the index ICH, delayed repeat imaging with MRI and DSA following hematoma resolution (usually three months post-ICH) can be used to detect an underlying lesion that may have initially been unidentified, such as tumors, cavernous malformations, or small vascular anomalies initially compressed or obscured by the hematoma (Evidence Level B).

Clinical considerations for Section 1.5

i. The most prevalent cerebral small vessel diseases that contribute to spontaneous ICH are hypertensive arteriopathy and/or CAA. CT markers associated with these underlying microangiopathies include multiple chronic lacunes and brainstem, deep gray, periventricular, and subcortical white matter disease. Similar findings can be seen on MRI, with addition of enlarged perivascular spaces on T2-weighted imaging and cerebral microbleeds or cortical superficial siderosis on blood sensitive sequences (T2*-GRE and/or SWI). A strictly cortical/subcortical white matter distribution of these lesions, but with sparing of the brainstem and deep gray matter in older (≥55 years) patients with lobar or cerebellar ICH would favor CAA over hypertensive arteriopathy.
ii. The increased use of acute/subacute MRI has identified remote punctate DWI hyperintense lesions in up to 25% of spontaneous ICH patients. The underlying etiology of such lesions is currently under investigation, but seems to be strongly associated with the degree of underlying microangiopathy. An embolic workup could however still be considered in such cases, until their clinical significance becomes further elucidated.

1.6. Surgical management of ICH

i. External ventricular drainage (EVD) should be considered in patients with a reduced LOC and hydrocephalus due to either intraventricular hemorrhage or mass effect (Evidence Level B).
ii. Surgical evacuation is not recommended if symptoms are stable and there are no signs of herniation (Evidence Level B).
a. Intraventricular thrombolysis to treat spontaneous intraventricular hemorrhage with or without associated ICH is generally not recommended (Evidence Level B). Treatment may reduce the risk of death but does not increase the chances of survival without major disability (Evidence Level B).
iii. Acute surgical intervention may be considered in patients with surgically accessible supratentorial hemorrhages and clinical signs of herniation (e.g. decreasing LOC, pupillary changes) (Evidence Level C), particularly in the following subgroups:
a. Young patients (<65 years of age)
b. Superficial ICH location (less than or equal to 1 cm from the cortical surface)
c. Associated vascular or neoplastic lesion
iv. Patients with cerebellar hemorrhage may be considered for neurosurgical consultation, particularly in the setting of altered LOC, new brainstem symptoms, or diameter of 3 or more cm (Evidence Level C).
a. EVD placement should occur in conjunction with hematoma evacuation in the setting of concurrent hydrocephalus (Evidence Level C).
v. The clinical benefit of minimally invasive clot evacuation is yet to be established.

a. Routine use of stereotactic thrombolysis and drainage (MISTIE technique (tPA)) is not recommended based on current evidence (Evidence Level B).

Clinical considerations for Section 1.6

i. Patients with significant hydrocephalus and normal LOC should be monitored closely and could be considered for EVD at earliest signs of decreasing LOC.
ii. Intraventricular thrombolysis to treat spontaneous intraventricular hemorrhage with or without associated ICH may reduce the risk of death but seems to increase the chances of survival with major disability.
iii. Based on the findings of one RCT (MISTIE III), stereotactic thrombolysis appears to be safe and reduces mortality compared to medical management alone but does not improve functional outcomes. Successful hematoma volume reduction to <15 mL may be associated with functional outcome benefit.
iv. Endoscopic evacuation of deep and superficial ICH also decreases hematoma volume. Small randomized and non-randomized series have suggested benefit. The impact on functional outcomes is currently under assessment in larger randomized clinical trials.
v. Endoscopic evacuation without the use of thrombolysis is under ongoing investigations. Its routine use is not recommended outside the framework of a clinical trial.
vi. Confirmation of anticoagulation reversal should be obtained intraoperatively.
vii. Pneumatic compression devices should be placed preoperatively and maintained post operatively until pharmacologic DVT prophylaxis can be initiated.

Box One: Symptoms of intracerebral hemorrhage

Clinical assessment cannot reliably distinguish intracerebral hemorrhage from ischemic stroke; brain imaging is required. More frequent symptoms of ICH may include:

- Alteration in LOC (present in approximately 50% of patients)
- Nausea and vomiting (approximately 40–50%)
- Sudden, severe headache (approximately 40%)
- Seizures (approximately 6–7%)
- Sudden weakness or paralysis of the face, arm or leg, or numbness, particularly on one side of the body
- Sudden vision changes
- Loss of balance or coordination
- Difficulty understanding, speaking (slurring, confusion), reading, or writing

Presentation

- The classic presentation of ICH is sudden onset of a focal neurological deficit that progresses over minutes to hours with accompanying headache, nausea, vomiting, decreased consciousness, and elevated blood pressure.
- Patients may present with symptoms upon awakening from sleep. Neurologic deficits are related to the site of parenchymal hemorrhage.
- Thus, ataxia is the initial deficit noted in cerebellar hemorrhage, whereas weakness may be the initial symptom with a basal ganglia hemorrhage.
- Early progression of neurologic deficits and decreased LOC can be expected in 50% of patients with ICH.[38]

Section 2: Recommendations on acute inpatient care following ICH

While it is now well-accepted that patients with ischemic stroke admitted to a stroke unit featuring dedicated beds and staff have better outcomes compared with patients admitted to general or less-specialized units, there is also evidence that the subset of patients who have experienced ICH realize the same benefits. Patients with ICH treated on a specialized stroke unit have been shown to have reduced risks of death or dependency (RR = 0.81, 95% CI 0.71–0.92, $p < 0.0001$),[39] decreased in-hospital mortality (OR = 3.4; 95% CI 1.65–7.6),[40,41] and improved short and long-term survival[42] compared with care on non-specialized units.

In addition to the usual issues faced to prevent medical complications when managing a patient with

ischemic stroke, ICH presents some additional challenges, including the prevention of VTE, increased ICP, and seizures.

The frequency of VTE has been reported to be up to four times higher in ICH compared with ischemic stroke.[43] In the short term, use of intermittent compression stockings/devices (IPC) is a commonly used alternative to chemoprophylaxis until the hematoma has stabilized. The use of such devices was associated with a significantly decreased risk of any form of deep vein thrombosis (DVT) within 30 days in the CLOTs Trial (16.2% vs. 21.1%, OR = 0.72, 95% CI 0.60–0.87, p = 0.001),[44] as was the incidence of any DVT, death, or pulmonary embolism compared with the no IPC group (27.2% vs. 34.1%, OR = 0.72, 95% CI 0.61–0.84, p < 0.0001). The risk of these outcomes in the IPC group remained significantly lower at six months. Transition from IPC to LMWH can occur once the ICH has stabilized on repeat neuroimaging; however, the optimal timing of LMWH following acute ICH is uncertain. A systematic review and meta-analysis of observational and randomized controlled studies up to November 2010 demonstrated that early treatment with UFH and LMWH between one and six days following ICH led to a significant reduction in the rate of PE (1.7% vs. 2.9%; p = 0.01), without an increase in hematoma expansion.[45] In a small randomized trial of 68 patients with ICH, participants randomized to LWMH on day 2 following their ICH experienced less pulmonary emboli than those randomized to initiate treatment on days 4 and 10, without an apparent increase in rebleeding.[46] These results are supported by a prospective observational study demonstrating the absence of hematoma expansion with LMWH started within 48 h of ICH onset after hematoma stabilization compared to later initiation in 134 consecutive patients.[47] Similarly, in another observational study of 407 ICH patients, there was no increase in ICH expansion between those treated with LMWH (85% started within 48 h) or those receiving no chemoprophylaxis.[48]

Following ICH, patients are at increased risk of seizures. Early-onset seizure typically occurs at or near event onset, while late-onset seizures occur 6–12 months post event. The published estimates of early onset seizures vary widely depending on the patient population, timing, and whether clinical criteria or electroencephalography (cEEG) monitoring are used for detection. Within 14 days of ICH onset, the reported frequency of seizures ranges from 8[49] to 31.6%.[50] Patients presenting with new-onset seizures should be treated with an antiepileptic agent;[29] however, prophylactic use of antiepileptic drugs (AED) has not been shown to be effective at reducing the odds of recurrent seizure[51] and may be associated with poor outcome.[52]

While a wide variety of nonsurgical interventions are used commonly to lower ICP following ICH, including head elevation, hyperosmotic agents, hyperventilation, analgesia, and sedation, RCT evidence of their effectiveness is lacking. A notable exception is the HeadPoST[53] trial, which randomized over 11,000 patients following stroke to receive care in either a lying-flat position or a sitting-up position with the head elevated to at least 30°, which was initiated as soon as possible and maintained for 24 h. There were no significant differences between groups in any of the primary or secondary clinical outcomes (mRS scores, death, or major disability at 7 and 90 days). The results were similar in the subgroup of 8% of patients with ICH. Factors that may have potentially contributed to the null findings include the lack of ICP monitoring for patients with ICH, poor adherence to the trial protocol, and the inclusion of patients with mild stroke.[54]

Section 2: Recommendations

2.0. Inpatient care following an intracerebral hemorrhage

i. Medically stable patients with an acute intracerebral hemorrhage should be admitted to an acute stroke unit or neuro-intensive care unit (Evidence Level B) and undergo interprofessional stroke team assessment to determine their rehabilitation and other care needs (Evidence Level B). Refer to *CSBPR Acute Stroke Management Section 8* for more information on stroke unit care. Refer to the *CSBPR Rehabilitation and Recovery following Stroke* module for additional information regarding rehabilitation assessment.

ii. The goals of care and recovery should be established with patient and/or designated substitute decision-maker (Evidence Level B).

   a. Prognostication for the purpose of modifications to goals of care should generally be deferred for 48–72 h after time of presentation to determine the extent of deficits, response to medical therapy, and potential for worsening of condition (Evidence Level B). Refer to the *CSBPR Acute Stroke Management Section 10* on Palliative Care for additional information.

b. Exceptions to deferring prognostication and conservative goals of care may include patients with pre-existing wishes to avoid invasive life-sustaining therapies because of co-morbidities (e.g. dementia) or based on their own previously expressed values (Evidence Level C).

2.1. Venous Thromboembolism prophylaxis

i. In the acute phase of ICH, patients should be started on intermittent pneumatic compression devices, beginning the day of admission (Evidence Level A).
ii. Graduated compression stockings are not recommended for DVT prevention (Evidence Level A).
iii. Chemoprophylaxis (LMWH) can be initiated after 48 h and documentation of hematoma stabilization on neuroimaging (Evidence Level B).
   a. Documenting hematoma stabilization requires an additional scan that is separated by at least 24 h from the baseline scan.

2.2. Seizure management

i. People with ICH are at a greater risk of seizures at presentation (Evidence Level B) and should be monitored clinically.
ii. Consider continuous EEG for the diagnosis of nonconvulsive status epilepticus in patients with depressed LOC that is out of proportion to the size and location of ICH (Evidence Level B).
iii. New-onset seizures in patients admitted to hospital with ICH should be treated with antiepileptic medications if they are not self-limiting (Evidence Level C).
iv. A single, self-limiting seizure occurring at the onset or within 24 h after an ICH (considered an "immediate" post-stroke seizure) should not be treated with long-term anticonvulsant medications (Evidence Level C). Short-term anticonvulsant therapy can be considered in such cases on an individual basis (Evidence Level C).
v. Patients who have an immediate post-ICH seizure should be monitored for recurrent seizure activity during routine monitoring of vital signs and neurological status. Recurrent seizures in patients with ICH should be treated as per treatment recommendations for seizures in other neurological conditions (Evidence Level C).
vi. Prophylactic use of anticonvulsants in patients with ICH is not recommended (Evidence Level B).

2.3. Increased intracranial pressure (ICP)

i. In cases of suspected elevated ICP, conservative methods to decrease ICP (such as elevation of head of bed 30°, methods of neuroprotection (e.g. euthermia and euglycemia), analgesia, and mild sedation) are reasonable (Evidence Level C).
ii. In the absence of concerns regarding ICP, head of bed positioning does not seem to influence neurological outcomes or serious adverse events in stroke patients, including ICH (Evidence Level B).
iii. There is insufficient evidence to recommend the routine or prophylactic use of hyperosmotic agents in ICH (Evidence Level C).
   a. Hyperosmotic agents (mannitol and/or 3% normal saline) can be considered as a temporizing measure to decrease ICP in ICH patients with clinical signs of herniation prior to surgical intervention (Evidence Level C).
iv. Use of corticosteroids to treat ICP in ICH may cause harm, has no proven benefits, and therefore is not recommended (Evidence Level B).

Clinical considerations for Section 2.3

i. Hyperthermia and hyperglycemia have been associated with poor outcomes in ICH patients. In the absence of randomized controlled trial research evidence, it is advisable to target normothermia and normoglycemia in hospitalized ICH patients.
ii. In patients with elevated ICP ensure to avoid compression of neck vessels, particularly when securing endotracheal tubes.

2.4. Rehabilitation following intracerebral hemorrhage

Note: Rehabilitation assessment and management for people who have experienced an ICH generally follow the same approaches as for people with other causes of stroke. Therefore, the CSBPR Recommendations for Rehabilitation and Recovery Following Stroke module apply to this patient population. This includes early assessment during acute inpatient care.

i. Patients with ICH should have continued monitoring for rehabilitation readiness beyond conventional time frames used in ischemic stroke patients due to emerging evidence regarding their prolonged recovery trajectories (Evidence Level B).

Note: Early assessments for rehabilitation readiness may underestimate rehabilitation potential.

Section 3: Secondary stroke prevention in an individual with intracerebral hemorrhage

Certain lifestyle risk factors may increase the risk of ICH to a greater extent compared with ischemic stroke. Smoking, a sedentary lifestyle, and excessive alcohol consumption are of particular concern. In the second phase of the INTERSTROKE study,[55] the odds of ICH were increased to a greater degree compared with ischemic stroke among persons who consumed higher amounts of alcohol, defined as >14 drinks/week in women or >21 drinks/week in men, and in those who did not engage in at least 4 h of moderate or strenuous leisure activity, weekly. In the INTERSTROKE I study,[56] consuming >30 drinks/month or binge drinking was associated with an increased risk of ICH compared with never/former drinkers, and the risk of ICH was higher than ischemic stroke. In a systematic review that included the results of 27 prospective studies, Zang et al.[57] reported that while low-to-moderate alcohol intake was not associated with ICH risk, an intake of ≥45 g/day did.

In terms of treatment for secondary prevention, long-term intensive blood pressuring lowering can reduce the risk of ICH recurrence.[58] In the Secondary Prevention of Small Subcortical Strokes (SPS3) Trial,[59] lowering blood pressure to <130/80 mm Hg was shown to be safe and reduce the risk of future ICH (Hazard ratio = 0.37, 95% CI 0.15–0.95). This finding was reported among patients with lacunar stroke, who share a prevalent underlying pathophysiology (arteriolosclerosis or hypertensive arteriopathy) with ICH. Moreover, a mean blood pressure reduction of 9/4 mm Hg in participants within PROGRESS trial reduced the risk of CAA-related ICH by 77% and hypertensive arteriopathy-related ICH by 46%.[60]

Administration of statins, used for the prevention of recurrent ischemic strokes, may increase the risk of ICH.[61] In the Stroke Prevention by Aggressive Reduction in Cholesterol (SPARCL) trial,[62] after taking 80 mg of atorvastatin daily for an average of five years, while the risk of ischemic stroke was reduced significantly, the risk of ICH was increased (HR = 1.66 95% CI 1.08–2.55, p = 0.020). However, a meta-analysis including the results of 31 RCTs found that there was no increased overall risk of ICH or in subgroup analyses including primary and secondary prevention trials.[63] Similar results were reported in a more recent meta-analysis confined to secondary stroke prevention trials.[64] There does not appear to be an increased risk of ICH when statins are used for primary stroke prevention.[65] These discrepancies may reflect the nature of populations studied, as the greater risk of ICH in SPARCL seemed to have been driven by participants with baseline qualifying ICH or small vessel disease (lacunar) stroke who were at a four to fivefold increased risk of ICH with atorvastatin treatment.[66] These stroke subtypes were likely underrepresented in other lipid lowering trials. The ongoing SATURN trial is assessing the effect of statin continuation compared with discontinuation on recurrent ICH rates following lobar ICH.

The decision whether to resume antithrombotic therapy for patients following an ICH can be challenging due to the increased risk of bleeding. This risk must be balanced with the prevention of a future ischemic event, particularly for patients with nonvalvular atrial fibrillation. While the issue remains unresolved and is best approached on an individual basis, the evidence from recent studies suggests that the benefits may outweigh the risks.[67] The net benefit of continued antiplatelet therapy following a spontaneous ICH was recently tested in the randomized multicenter RESTART trial.[68] In 537 participants with spontaneous ICH, randomization to antiplatelet therapy (either aspirin, clopidogrel, and/or dipyridamole) compared to no antithrombotic therapy did not seem to increase the risk of recurrent ICH and led to a 35% (p = 0.025) relative risk reduction in the secondary composite outcome of non-fatal myocardial infarction, non-fatal stroke, and vascular death. Unexpectedly, there was a

statistically insignificant numerical trend for a reduction in recurrent ICH with antiplatelet therapy resumption (aHR 0.51, 95% CI 0.25–1.03, p = 0.06). Further reassurance is provided in the RESTART MRI subgroup analyses that did not demonstrate any treatment modification according to ICH location, or the presence and burden of MRI markers of cerebral small vessel disease, including cerebral microbleeds and cortical superficial siderosis.[69]

Pertaining to anticoagulation, after a median of 2.3 years, 6369 persons who had experienced a first-ever ICH and had resumed taking oral antithrombotics had significantly reduced risks of death and thromboembolic events without an increased risk of ICH (HR = 0.90, 95% CI 0.44–1.82) compared with persons who did not receive antithrombotic therapy.[70] Similar results have been reported.[71,72] Pooling the results from eight retrospective studies, Murthy et al.[73] reported that there was no significantly increased risk of recurrent ICH after resumption of anticoagulation therapy (RR = 1.01, 95% CI 0.58–1.77), while the risk of stroke or MI was significantly lower (RR = 0.34, 95% CI 0.25–0.45). Similar net benefit seems to generalize to higher risk patients with lobar ICH and may generalize to those with CAA.[74] However, confounding by indication limits the interpretation of these observational studies. In the Canadian-led NASPAF-ICH trial presented at the 2020 International Stroke Conference, there was only one primary outcome of recurrent ICH and/or ischemic stroke amongst 30 participants with atrial fibrillation and previous ICH randomized (2:1) to standard dosing non-vitamin K antagonist oral anticoagulant (NOAC) therapy or aspirin 81 mg daily over mean follow-up of 1.53 years (SD 0.54). This event was an ischemic stroke occurring in a patient with temporary discontinuation of assigned aspirin therapy due to a major genitourinary hemorrhage. There was no recurrent ICH in either arm of the study. All participants had close home blood pressure monitoring to ensure target <130/80 mm Hg. These preliminary results are being investigated further in ongoing randomized trials.[75]

The issue of timing of resumption of antithrombotics is not certain. Literature-based estimates on the ideal timing of resumption of anticoagulants have ranged broadly between 3 days and 30 weeks following ICH.[70,72,76] Literature supporting time windows beyond eight weeks come from datasets with overrepresentation of recurrent subdural hemorrhages and relatively few recurrent spontaneous ICH.[61]

Section 3: Recommendations

This section addresses secondary prevention management issues specific to individuals who have experienced an intracerebral hemorrhage (intraparenchymal and intraventricular hemorrhages). General principles of vascular health and risk reduction that are addressed in the CSBPR Secondary Prevention of Stroke Module may also apply to this population where they are non-specific to stroke type. The topics included here may overlap with the broader prevention module where they may have different levels of evidence available.

3.1. Risk assessment

i. Persons at risk of stroke and patients who have had an ICH should be assessed for vascular disease risk factors (such as diet, sodium intake, waist-to-hip ratio, sedentary lifestyle, alcohol intake, blood pressure, and smoking) (Evidence Level B). *Please refer to theCSBPR Secondary Prevention of Stroke Module for additional information.*

ii. Patients who experience an ICH should be assessed for underlying etiology and risk of recurrence (Evidence Level B).
   a. The assessment of recurrent risk for an ICH should be based on clinical factors (including age, hypertension, ongoing anticoagulation, and prior lacunar stroke) and neuroimaging (lobar location of index ICH suggestive of CAA, presence of associated convexal subarachnoid hemorrhage, and presence and number of cerebral microbleeds and/or cortical superficial siderosis on susceptibility weighted or gradient echo MRI sequences) (Evidence Level B).

Note: Validated risk assessment tools for intracerebral hemorrhage recurrence have not been published.

Clinical considerations for Section 3.1

i. In the absence of tissue diagnosis, probable cerebral amyloid angiopathy can be diagnosed in hospital populations based on the modified Boston criteria as follows: age ≥55 years; (and) clinical data and MRI

demonstrating multiple macro or microhemorrhages restricted to lobar, cortical, or corticosubcortical regions (cerebellar hemorrhage allowed), or a single lobar, cortical, or corticosubcortical macro- or microhemorrhage and cortical superficial siderosis; (and) absence of other cause of hemorrhage or cortical superficial siderosis.

3.2. Lifestyle management

i. For individuals with intracerebral hemorrhage, healthcare professionals should recommend increased physical activity, healthy diet, reductions of alcohol consumption, cessation of smoking, and cessation of cocaine/amphetamine use where relevant (Evidence Level C). *Refer to Section 2 CSBPR Secondary Prevention of Stroke Module for recommendations on lifestyle management after stroke*.

Clinical consideration for Section 3.2

i. There is no evidence to restrict air travel in patients' post-ICH above and beyond routine limitations following stroke.

3.3. Blood pressure management following intracerebral hemorrhage

i. Long-term, blood pressure should be aggressively monitored, treated, and controlled (Evidence level A) to sustain a target blood pressure consistently lower than 130/80 mm Hg (Evidence Level B).
ii. For specific agents to manage blood pressure, refer to *Hypertension Canada's* current blood pressure management guidelines.

Clinical considerations for Section 3.3

i. Home blood pressure monitoring devices should be encouraged to achieve blood pressure targets.

3.4. Antithrombotic therapy following intracerebral hemorrhage

i. In ICH patients with an indication for anticoagulant treatment, the decision to initiate or resume anticoagulation should be individualized according to the patient's risk of recurrent hemorrhage and thromboembolism (Evidence Level C).
ii. If anticoagulation is deemed necessary and where DOAC treatment is indicated (i.e. atrial fibrillation), DOAC therapy is favored over warfarin. This is based, however, primarily on their reduced rates of ICH in atrial fibrillation randomized trials where ICH patients were excluded (Evidence Level B).
    a. DOACs should not be used in patients with mechanical heart valves and intracerebral hemorrhage (Evidence Level B).
iii. Where indicated, antiplatelet monotherapy can be considered in patients deemed too high risk for anticoagulation (Evidence Level B).
iv. In patients with an indication for continued antiplatelet treatment, resuming antiplatelet therapy is reasonable (Evidence Level B).
v. The optimal timing and strategy regarding antithrombotic therapy (antiplatelet or anticoagulant) following an intracerebral hemorrhage is uncertain and should be individualized to the patient (Evidence Level C).

Clinical consideration for Section 3.4

i. Consultation with experts in cerebrovascular disease may assist in clinical decision-making regarding antithrombotic therapy following ICH.
ii. Randomized trials are ongoing regarding the net benefit and safety of DOAC therapy and left atrial appendage closure in patients with ICH and atrial fibrillation. These patients should be assessed by an expert in cerebrovascular diseases if possible to support decision-making on management.

3.5. Statin therapy in intracerebral hemorrhage

i. There is no role for statin therapy in the secondary prevention of ICH. Statin therapy should not be initiated for secondary prevention of intracerebral hemorrhage (Evidence Level C).
ii. For intracerebral hemorrhage patients who have a clear concomitant indication for cholesterol lowering treatment, statin therapy should be individualized and should take into account the patient's overall thrombotic risk as well as the possibility of increased ICH risk with statin therapy (Evidence Level C). *Refer to CSBPR Prevention of Stroke module section 4 on Lipid Management for additional information.*

Clinical considerations for Section 3.5

i. An ongoing clinical trial (SATURN) addressing this question may potentially inform clinical decision-making for these patients. Until these results are available, decisions regarding statin therapy should be made based on risk/benefit ratio in consultation with an expert in cerebrovascular disease.

3.6. Functional assessment

i. Following an ICH, patients should be assessed for neurological impairments and functional limitations when appropriate (e.g. cognitive evaluation, screening for depression, screening of fitness to drive, need for potential rehabilitation therapy, and assistance with activities of daily living), especially for patients who are not admitted to hospital (Evidence Level C). *Refer to CSBPR Rehabilitation Module Recommendations 5.1 and 5.6 for additional information.*
ii. Patients found to have any continued or new neurological impairments and functional limitations should be referred to the appropriate rehabilitation specialist for in-depth assessment and ongoing management (Evidence Level C).

Summary

Intracerebral hemorrhage is less common than ischemic stroke yet has a disproportionally higher rate of mortality. Among survivors, there is also a higher and longer-term burden of ongoing disability, leading to greater challenges with quality of life, mental health, social networks, and increased informal caregiver demands. Emerging research suggests that delayed recovery is possible in intracerebral hemorrhage survivors, suggesting a wider window for rehabilitation interventions.[37,77–80] Stroke systems of care need to take these differences into account and ensure that sufficient services are available in acute care, rehabilitation facilities, and in the community, with staff trained to anticipate and appropriately address challenges for this unique population.

The 2020 update of the *Canadian Stroke Best Practice Recommendations*: *Management of Spontaneous Intracerebral Hemorrhage* provides a set of evidence-based statements developed for healthcare professionals and system leaders to help guide the rehabilitation process post-stroke across settings and to ensure that the necessary structures and resources are in place. The Canadian Stroke Best Practice Recommendations continue to be a work in progress. They are regularly updated every two to three years, whereby new recommendations are created and old ones revised or deleted, in response to new evidence.

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Authors' contribution

Ashkan Shoamanesh (First author) and Laura C Gioia (Senior Author) are co-chairs of the *Management of Spontaneous Intracerebral Hemorrhage* expert writing group and lead authors contributing to all aspects of the development, evidence and data analysis, writing, editing, and final approval of this manuscript; M Patrice Lindsay is corresponding author, senior editor of the Canadian Stroke Best Practice Recommendations and of this manuscript, involved in all aspects of scientific literature review, writing group deliberations, external review process, manuscript preparation, and a writer of supplementary documentation. *Lana A Castellucci, Anne Cayley, Mark Crowther, Kerstin de Wit, Shane W English, Sharon Hoosein, Thien Huynh, Michael Kelly, Cian J O'Kelly, Jeane Teitelbaum, and Samuel Yip* are all members of *Management of Spontaneous Intracerebral Hemorrhage* expert writing group and contributed by reviewing, analyzing, and discussing the evidence and collectively finalizing the wording of all included recommendations. Norine Foley conducted the evidence searches and completed the evidence tables and evidence summaries supporting this guideline update and contributed to writing of this manuscript. Eric E Smith and Dar Dowlatshahi are senior leaders of the stroke best practices advisory committee and provided inputs throughout development of the recommendations and participated in development, preparation, and editing of this manuscript. Aleksandra Pikula provided external review to these guidelines and contributed content related to sex and gender considerations in ICH. Anita Mountain and Gord Gubitz provided inputs to sections of these guidelines and contributed to this manuscript.

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