

Time is Brain for Bleeds: Collaborative Strategies and New Horizons in Acute ICH Care

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Disclosures

- None

Objectives

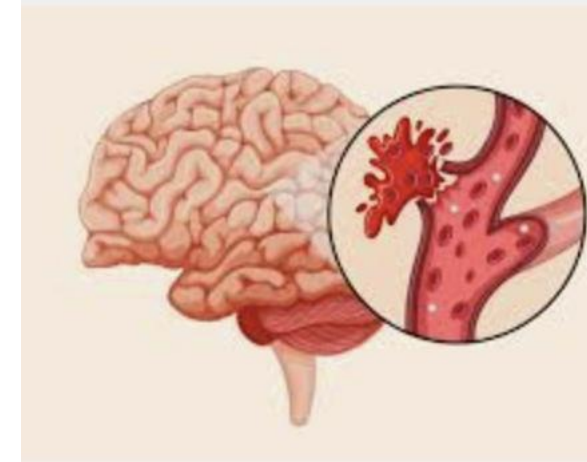
Recognize the Critical "Code ICH" Window: Understand the urgent pathophysiology of spontaneous intracerebral hemorrhage (ICH) and identify the high-risk signs of early hematoma expansion to optimize frontline recognition and rapid triage.

Deconstruct the Interdisciplinary Care Bundle: Define the essential components of hyperacute ICH management—including time-sensitive blood pressure stabilization, glycemic control, and reversal protocols—and understand how these interventions directly impact functional survival.

Explore the ICH Toolkit & I-CATCHER Framework: Gain insight into the direction of upcoming standardized Canadian care systems and learn how integrated protocols can reduce practice variation across the healthcare continuum.

Optimize Long-Term Care and Rehabilitation Pathways: Formulate evidence-based collaborative strategies for primary care and allied health professionals to support secondary prevention, manage post-stroke complications, and improve multi-disciplinary recovery outcomes

Intracerebral Hemorrhage- Scope of the Problem



- Acute spontaneous ICH is the **most devastating and disabling form of stroke**.
- In ICH, hematoma forms within the brain, destroying and disrupting the brain parenchyma underneath.
- ICH accounts **for 20% of strokes**.
- In Canada, there is **one ICH every 70 minutes**
- Approximately **40% of patients die within one month** of their ICH and many survivors remain disabled.
- The **median costs associated with the care of a patient with ICH are roughly 10 times** the median inpatient costs of any other patient in Ontario.

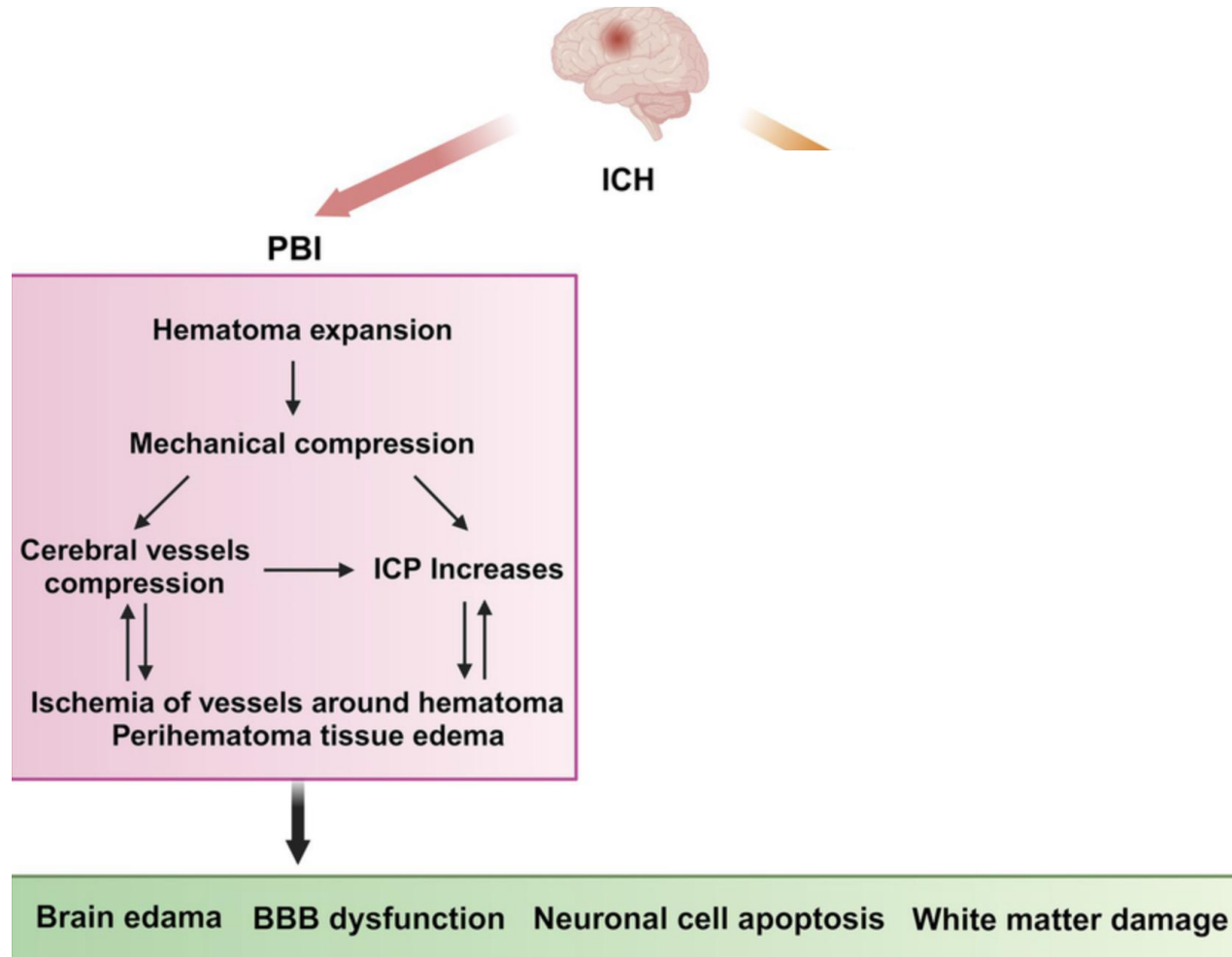


While advances in reperfusion therapies for thrombolysis and thrombectomy have transformed systems of care for acute ischaemic stroke, **no single intervention has been shown to have a major impact on outcomes in ICH**

Basis of Intervention Design in ICH → Understand the Pathophysiology

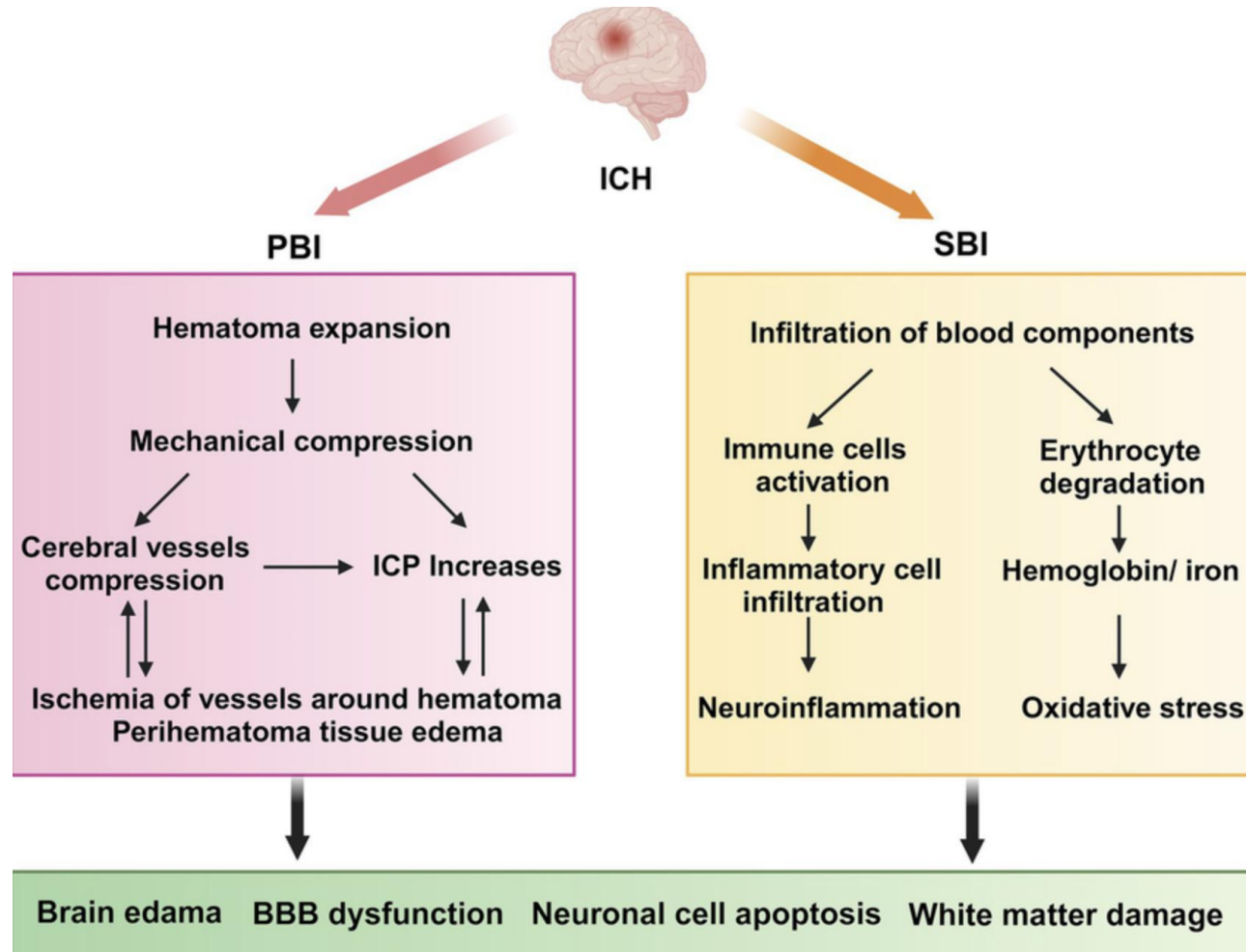
Pathophysiology of Spontaneous ICH

Understanding primary mechanical injury and secondary cellular cascades.



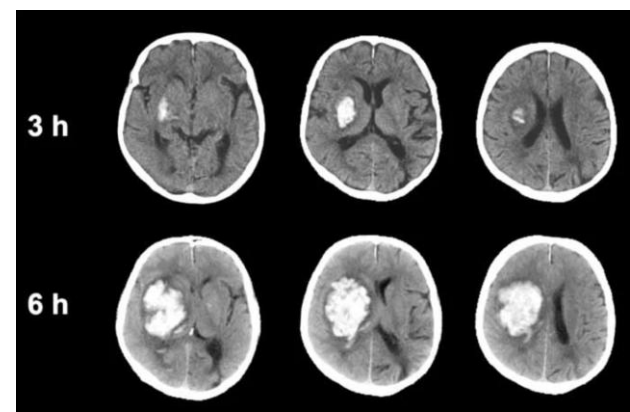
Pathophysiology of Spontaneous ICH

Understanding primary mechanical injury and secondary cellular cascades.



The Danger of Hematoma Expansion

HE is highly dynamic, most active early, and represents the primary modifiable focus.



0 – 1 Hour

Hyperacute Phase

Up to 26% of patients demonstrate massive expansion within 60 mins of onset. Active shearing of collateral microvessels is most severe.

1 – 3 Hours

Peak Therapeutic Window

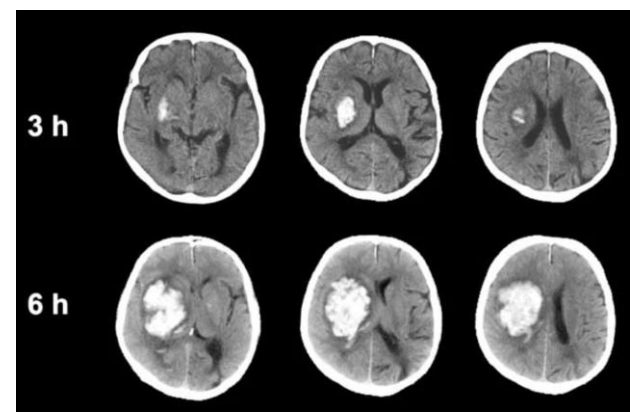
Primary target for hemostatic reversal and rapid blood pressure stabilization. Rapid screening prevents the 'avalanche effect'.

Avalanche Effect

- **The Initial Tear:** Spontaneous rupture of a single, fragile microvessel (weakened by chronic hypertension or cerebral amyloid angiopathy) forms the initial core hematoma.
- **Mechanical Mass Effect and Shearing:** As this initial pool of blood accumulates, it creates a localized mass effect, expanding and exerting high physical pressure on the surrounding brain parenchyma.
- **The Secondary Cascade:** This sharp mechanical expansion stretches and distorts adjacent microvessels, causing them to shear or tear under the localized stress.
- **Compounding Volumes:** These newly ruptured neighboring vessels add fresh blood to the hemorrhage matrix, which further amplifies the local pressure and triggers yet another wave of surrounding vessel failures—hence, an "avalanche" of secondary bleeding.

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Hyperacute Phase

Up to 26% of patients demonstrate massive expansion within 60 mins of onset. Active shearing of collateral microvessels is most severe.

3 – 6 Hours

Steady Progression

Stabilization window. Likelihood of fresh hematoma growth begins to decline but remains critically elevated in anticoagulated patients.

1 – 3 Hours

Peak Therapeutic Window

Primary target for hemostatic reversal and rapid blood pressure stabilization. Rapid screening prevents the 'avalanche effect'.

6 – 24 Hours

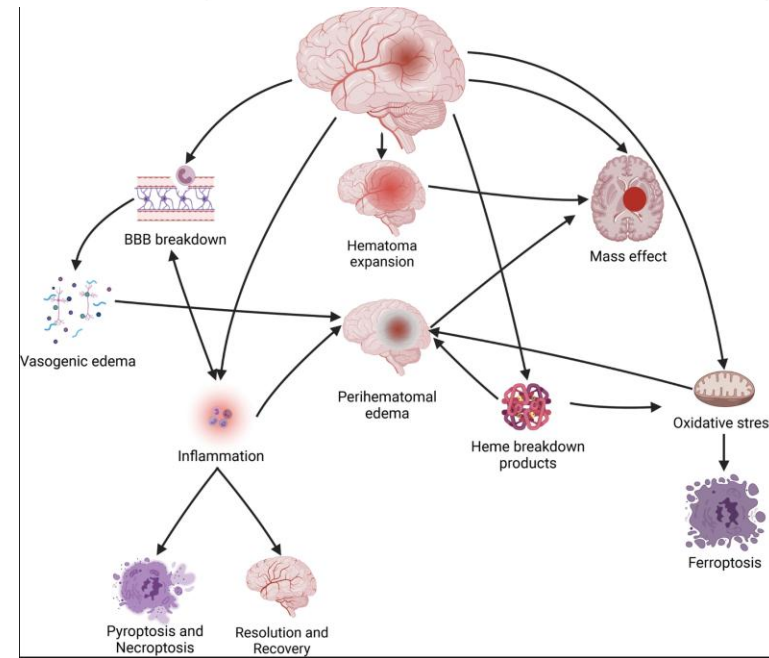
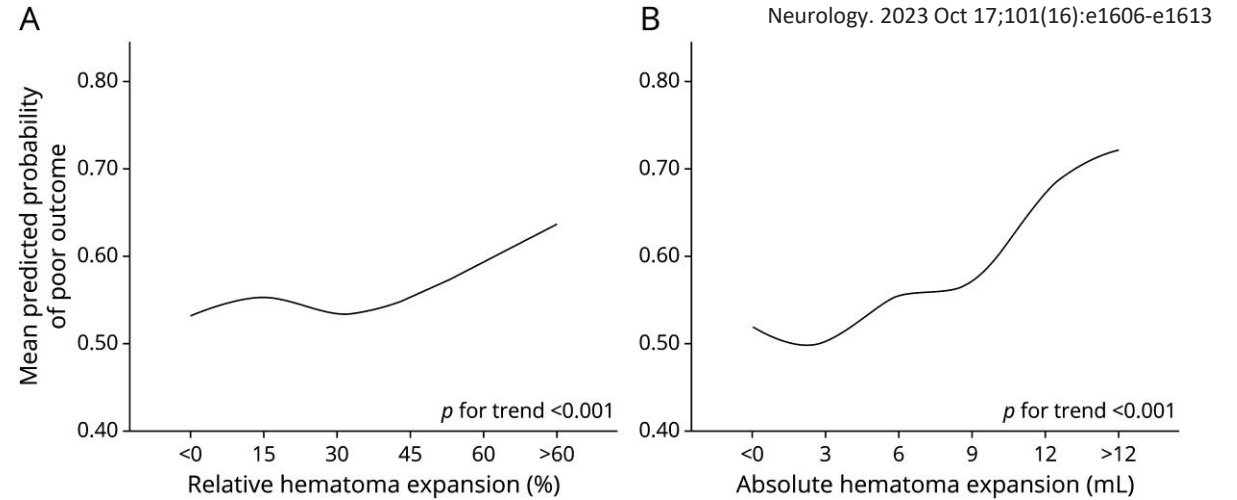
Subacute Expansion

Late expansion risk is often paired with peri-lesional edema formation, generating secondary mechanical peaks in ICP.

Hematoma Expansion

Why is it so important?

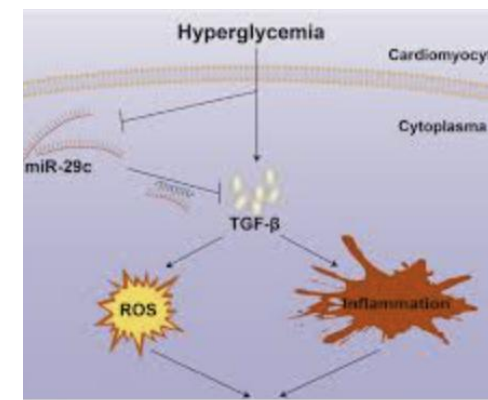
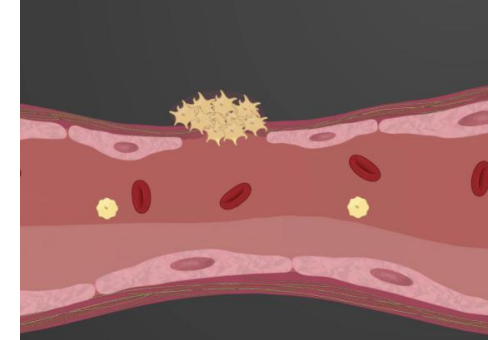
- It is associated with poor patient outcomes
- Causes secondary mass effect and increased ICP
- More blood → more inflammation/secondary cascade



Modifiers Hematoma Expansion

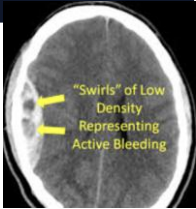
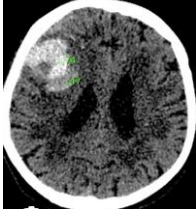
How can we help?

- **Systolic Blood Pressure (SBP):** Markedly elevated SBP (>160 mmHg) maintains a high pressure gradient at the site of vascular rupture, **preventing standard physiological platelet plugging** and clotting, thereby directly driving ongoing expansion.
- **Anticoagulation:** Prior use of oral anticoagulants (such as Warfarin or DOACs) severely **compromises the coagulation cascade**. Anticoagulant use is associated with a **6.2% fold increase** in the risk of hematoma expansion.
- **Hyperglycemia:** Up to 50% of acute stroke patients present with admission hyperglycemia. Excess serum glucose triggers local lactic acidosis and promotes free radical generation, compromising microvascular integrity.



High-Risk Imaging Markers

Qualitative Non-Contrast CT density markers provide expansion risk parameters.

NCCT Sign	Radiological Visual Criteria	Pathophysiological Basis	Predictive Value
Swirl Sign	Mixed hyperattenuating (clot) and hypo/isoattenuating areas within the hematoma. 	Visualizes fresh, un-clotted liquid blood flowing directly into the active hemorrhage.	High specificity (79%)
Black Hole Sign	Round/oval hypodense area completely enclosed within a hyperdense hematoma. 	Distinct multitemporal active bleeding episodes of different physical ages.	High specificity (91%)
Blend Sign	Hyperdense margin interfacing a distinct adjacent hypo-attenuating region. 	Zones of continuous active bleeding prior to solid cellular matrix formation.	High specificity (92%)
Island Sign	Detached satellite hematomas or protrusions sprouting off the primary bleed edge. 	Reflects multifocal collateral microvascular damage due to severe local shear stress.	Highest specificity (98%)

Emergency Mandate – CODE ICH

Ultra- early management and triage of ICH patients

The emergency management of ICH aims at reducing hematoma growth and improving patient outcome through the application of

- 1) Early intensive blood pressure (BP) lowering.
- 2) Reversal of anticoagulation.
- 3) The management of physiological variables such as fever and hyperglycemia.
- 4) Early targeted neurosurgical intervention is also recommended.

CODE-ICH: Introduction of Bundle Care

- Moving away from the 'single magic bullet' approach toward highly **synchronized, parallel interventions**.
- Bundle care for ICH patients based on the **Synergy Principle**: Combining hemodynamic, hemostatic, and metabolic interventions simultaneously to provide compounding clinical benefit.
- The Care Pillars:
 - Rapid SBP reduction
 - Immediate coagulopathy reversal
 - Aggressive metabolic defense



Pillar 1: Acute SBP Reduction – Evidence Benchmarks

INTERACT-2 Trial Blueprint

- Evaluated intensive SBP lowering (<140 mmHg within 1 hour of randomization (3.7h onset to randomization) vs. standard care (<180 mmHg).
- Results: Confirmed safety and demonstrated a significant statistical shift toward improved 90-day functional recovery (mRS scores).

ATACH-II Trial Refinements

- Tested an aggressive hyperacute target (110–139 mmHg) using IV Nicardipine within 4.5 hours.
- Results: Showed no added clinical benefit over standard targets and highlighted risks of severe blood pressure variability and renal adverse events.
- Clinical Consensus: Rapidly lower SBP to a stable target of 130–140 mmHg smoothly.

ORIGINAL ARTICLE



Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Authors: Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., , for the INTERACT2 Investigators* [Author Info & Affiliations](#)

Published June 20, 2013 | N Engl J Med 2013;368:2355-2365 | DOI: 10.1056/NEJMoa1214609 | [VOL. 368 NO. 25](#)

ORIGINAL ARTICLE



Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Authors: Adnan I. Qureshi, M.D., Yuko Y. Palesch, Ph.D., William G. Barsan, M.D., Daniel F. Hanley, M.D., Chung Y. Hsu, M.D., Renee L. Martin, Ph.D., Claudia S. Moy, Ph.D., , for the ATACH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network* [Author Info & Affiliations](#)

Published September 15, 2016 | N Engl J Med 2016;375:1033-1043 | DOI: 10.1056/NEJMoa1603460

Pillar 1: Acute SBP Reduction – Evidence Benchmarks

INTERACT-4 Trial Blueprint

- The earlier BP reduction occurs, the better.
- (BP control within 2 hrs of onset)

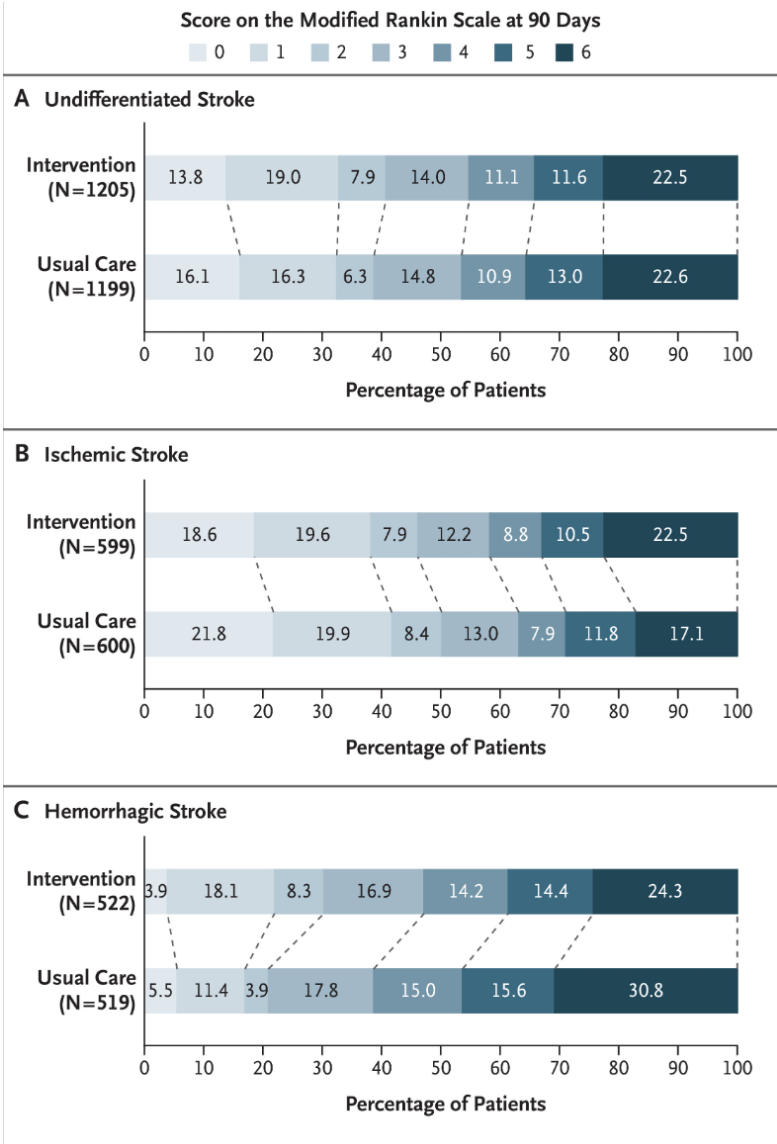
ORIGINAL ARTICLE



Intensive Ambulance-Delivered Blood-Pressure Reduction in Hyperacute Stroke

Authors: Gang Li, M.D., Ph.D., Yapeng Lin, M.M., Jie Yang, M.D., Ph.D., Craig S. Anderson, M.B., B.S., Ph.D. , Chen Chen, M.D., Feifeng Liu, M.M., Laurent Billot, M.Res. ,  , for the INTERACT4 investigators* [Author Info & Affiliations](#)

Published May 16, 2024 | N Engl J Med 2024;390:1862-1872 | DOI: 10.1056/NEJMoa2314741 | [VOL. 390 NO. 20](#)



Pillar 2: Immediate Reversal of Coagulopathy

Operational Mandate: Initiate reversal immediately upon hematoma confirmation on NCCT if history of anticoagulation is verified—do not wait for laboratory turnaround times.

Baseline Agent	Reversal Strategy	Trial / Clinical Objective
Warfarin (VKA)	4-Factor PCC + IV Vitamin K	Rapidly restore clotting factors to achieve INR < 1.3 (INCH Trial)
Dabigatran (DOAC)	Idarucizumab (Praxbind)	Immediate, specific antibody neutralization (RE-VERSE AD)
Factor Xa Inhibitors	Andexanet Alfa OR High-dose 4-Factor PCC	Rapidly reverse anti-Xa activity to restore thrombin generation (ANNEXA-4)

Pillar 3: Glycemic Control, Pyrexia & the INTERACT3 Breakthrough

The INTERACT3 Trial Blueprint (2023)

- Significance: A major international stepped-wedge cluster RCT evaluating a bundle protocol combining intensive BP control with strict physiological management.
- Outcome: Proved that structured, simultaneous care bundle execution results in significantly better 6-month functional outcomes.

Target Parameters for Metabolic Defense

- Hyperglycemia Management: Maintain serum glucose between 6.0 – 10.0 mmol/L using insulin protocols. Avoid neurotoxic hypoglycemia (<4.0 mmol/L).
- Pyrexia Control: Aggressively target core temperatures to maintain normothermia (<37.5°C) and limit secondary neuroinflammatory tissue cascades.

CODE-ICH: What about surgical intervention?

Trial	Surgical Approach	Timing Window	Why it didn't show improvement
STICH I & II (2005, 2013)	Traditional Open Craniotomy	Up to 48h	Surgical trauma to healthy brain tissue outweighed the benefit of removing the clot.

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MIND (2025)	Endoscopic MIPS	Up to 72h	Did not show improvement because of surgical timing (median 27.5h), deep brain clots and early study termination limiting power

CODE-ICH: What about surgical intervention?

- **Cortical bleeds**, not deep-seated bleeds
- **MIPS** (to avoid damage to surrounding brain)
- **Early intervention**- later, brain already exposed to toxic iron/Hb, initiating secondary cascade of damage and inflammation

CODE-ICH: What about surgical intervention?

Steep climb to implementation

- **Strict Tech Requirements:** Mandates specialized, costly equipment like the NICO BrainPath and stereotactic neuronavigation.
- **Financial Hurdle:** High capital costs limit adoption in smaller, resource-constrained community hospitals.
- **Steep Learning Curve:** Demands highly specialized training to safely clear clots through narrow tubular corridors.
- **Rapid Around the Clock Access to MRI (DTI-imaging)**
- **Tight 24-Hour Window:** Demands rapid surgical execution, frequently disrupted by real-world transfer and triage delays
- **Neurosurgeons** 😞

CODE-ICH- The Canadian Implementation Gap

✓ Ischemic Stroke Model

- Clear provincial benchmarks exist to prioritize hyperacute treatments
- Highly standardized targets for door-to-needle thrombolysis times
- Integrated, system-wide access protocols for Endovascular Thrombectomy (EVT)
- Established metrics lead to predictable, optimized clinical outcomes

⚠ Hemorrhagic Stroke Vacuum

- ICH accounts for 20% of stroke cases but carries disproportionately high costs
- No standardized provincial pathways or benchmarks exist for acute ICH
- High practice variation and clinical delays persist across Canada
- Evidence-based guidelines exist, but implementation remains highly incomplete

Introducing I-CATCHER

- **The International Care Bundle Evaluation in Cerebral Hemorrhage**
 - An international, multicentre, batched parallel stepped wedge cluster RCT of a multifaceted package of protocols (bundle care).
 - A Global Initiative: Staged rollout across high income countries including Canada, Australia, Sweden and the UK.
 - A Pragmatic Design: A cluster randomized trial mapping consecutive patient enrollment across 110 global sites (15 in Canada).
 - The Care Bundle: Operationalizes a multi-modal protocol targeting hemodynamic, hemostatic, and metabolic variables concurrently.

I-CATCHER: The Operational Pillars

- Currently, guidelines for each part of the race car pitstop exists. But specifics on the implementation of these are left at the discretion of the local clinical team.
- In I-CATCHER, the experimental group receives a **standardized time- and target-based Care Bundle** based on:

1) Early Physiological Control:

- Intensive blood pressure lowering targeting a **SBP of <140mmHg within 1 hour** (maintained for 24 hours),
- Normalize hyperthermia (**target <37.5 C**)
- Normalize hyperglycemia (**target blood glucose 7–10 mmol/L**).

2). Rapid Reversal of Anticoagulation:

- Rapid **administration of reversal agents within 30 minutes of hospital arrival** for patients on anticoagulants (e.g., PCC for warfarin to reach an INR <1.5, or formulary-approved agents for DOACs taken within 48 hours).

3). Avoidance of Early DNR Orders:

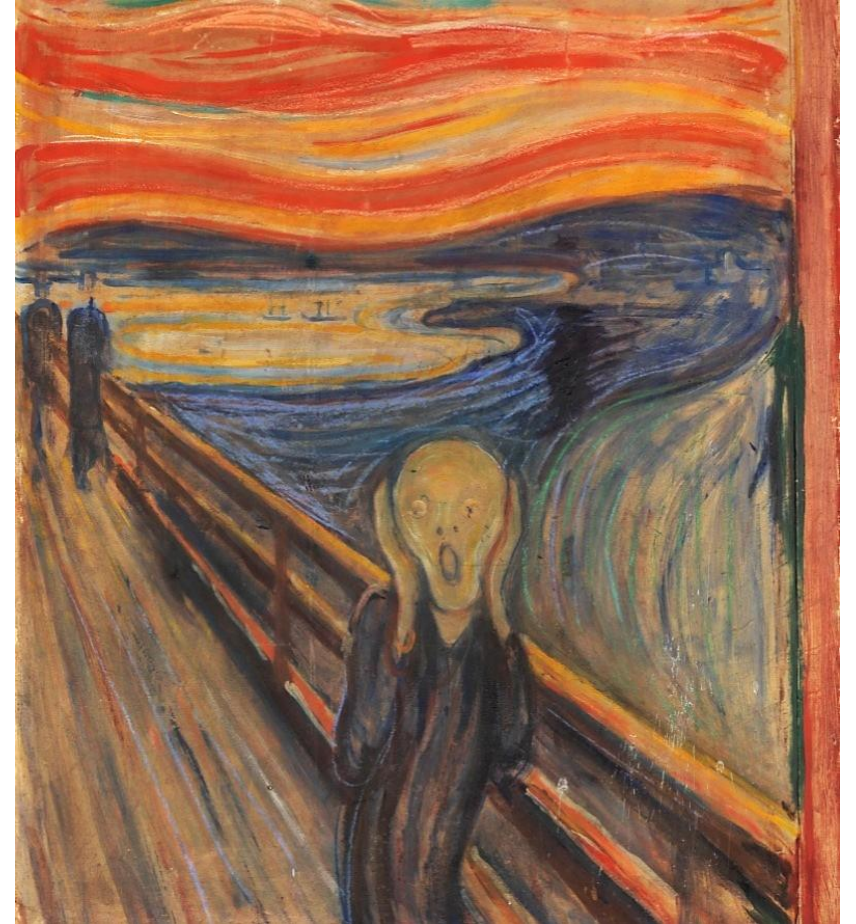
- Enforcing a strict restriction against Do-Not-Resuscitate (DNR) orders or withdrawal of care for the first 48 hours to prevent premature clinical nihilism (the "self-fulfilling prophecy")

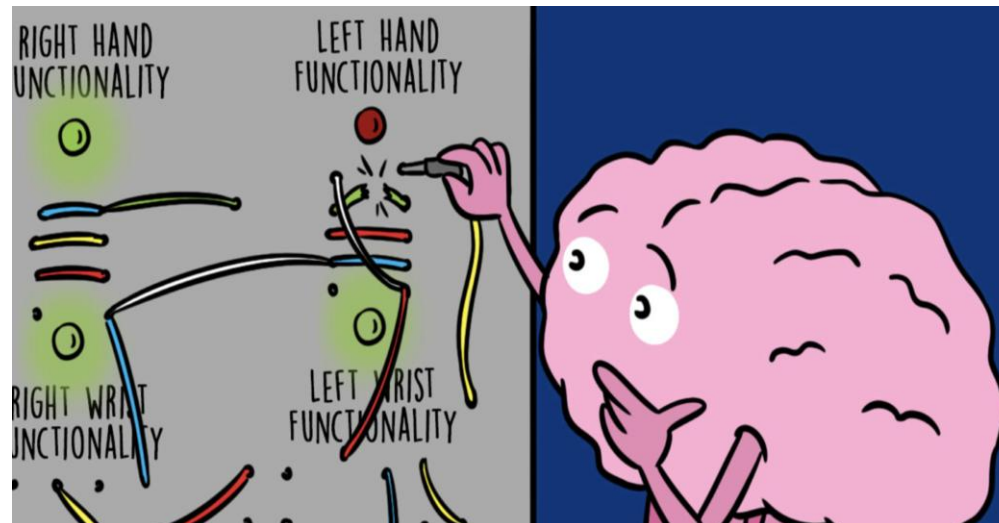
3). Structured Neurosurgical Referral Pathway

- Rapid <30min referral to neurosurgery if specific high-risk criteria are met, such as a large/evolving supratentorial ICH (>20ml), posterior fossa ICH, or intraventricular extension.

Dismantling Clinical Nihilism (The 48-Hour Rule)

- **Avoidance of the Self-Fulfilling Prophecy:** Multiple studies demonstrate that early clinical nihilism in acute ICH regularly becomes a self-fulfilling prophecy, where care is prematurely limited or de-escalated based on subjective clinician impressions, leading to worse patient outcomes
- **The 48-Hour Protocol Mandate:** To combat this practice variation and ensure hyperacute interventions have adequate time to take effect, the **I-CATCHER framework enforces a strict restriction against Do-Not-Resuscitate (DNR) orders or the withdrawal of active care for the first 48 hours**
- **Delaying Prognostication:** By delaying formal neuro-prognostication beyond this critical 48-hour stabilization window, clinical teams can significantly improve prognostic accuracy and prevent premature limitations of life-sustaining treatment.



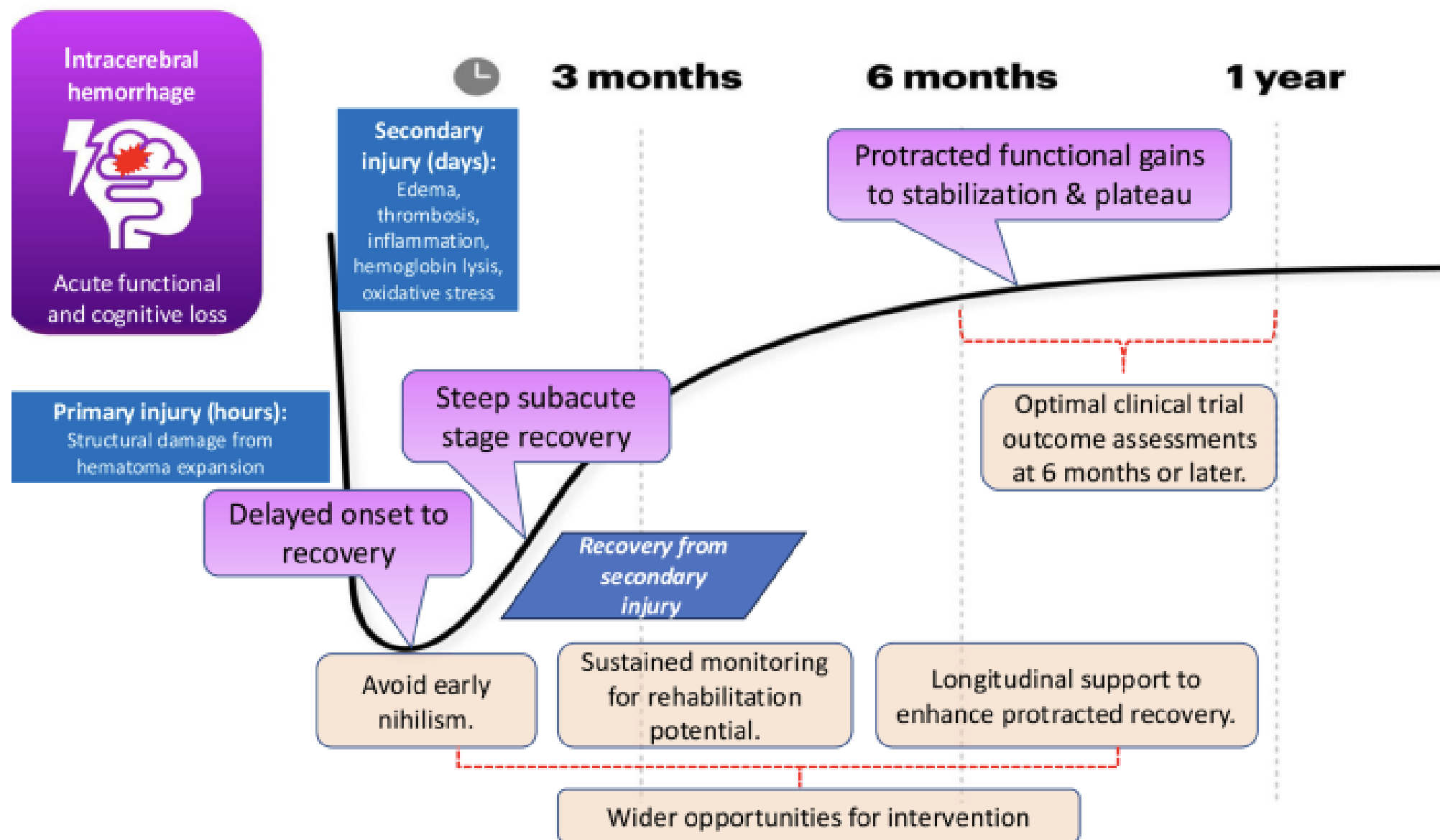


Recovery After ICH

- ICH and ischemic stroke both result in irreversible brain injury but the mechanism of injury, inflammatory response and tissue repair processes differ, with ICH recovery being relatively delayed when compared to ischemic stroke
- Understanding the patterns of functional improvement and stroke recovery in ICH, and pertinently, the differences from ischemic stroke, is important for several reasons:
 - Accurate prognostic information allows patients, and their caregivers, to plan for the future and make informed decisions about goals of care.
 - Knowing what to expect regarding timelines and potential outcomes allows the targeted delivery of health care, potential therapeutic interventions, and rehabilitation therapy to those who are likely to benefit
 - Understanding the general trends of when recovery reaches a plateau can inform the optimal timing of functional outcome ascertainment in the design of ICH clinical trials.

Recovery After ICH

Stroke. 2025;56:783–793. DOI: 10.1161/STROKEAHA.124.046130



Stroke Prevention after ICH

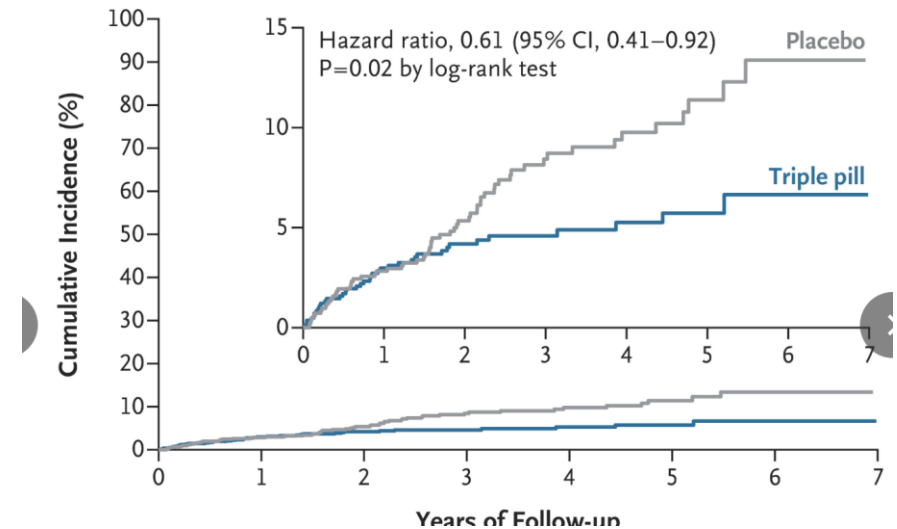
- The only proven treatment to prevent first and recurrent intracerebral hemorrhage is effective blood-pressure reduction.
- Although most survivors of stroke are discharged from the hospital with a prescription for medications to lower blood pressure, long-term blood-pressure control is generally inadequate
- This is due to:
 - poor adherence to treatment
 - uncertainty surrounding the degree of benefit
 - varying guideline recommendations
 - insufficient intensification of treatment when blood pressure remains elevated and therapeutic inertia

Three Low-Dose Antihypertensive Agents in a Single Pill after Intracerebral Hemorrhage

Author: The Trident Research Group [Author Info & Affiliations](#)

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DOI: 10.1056/NEJMoa2515043 | [VOL. 394 NO. 16](#) | [Copyright © 2026](#)



- International, double-blind, randomized, placebo-controlled trial
- Eligible if SBP 130-160 after ICH
- Single pill (telmisartan at 20 mg, amlodipine at 2.5 mg, and indapamide at 1.25 mg)
- At 6 months, blood-pressure control (defined as a systolic blood pressure of <130 mm Hg) was reached in 49.9% of the patients in the triple-pill group, as compared with 26.4% in the placebo group
- During a median follow-up of 2.5 years, recurrent stroke occurred in 38 patients (4.6%) in the triple-pill group and in 62 patients (7.4%) in the placebo group (hazard ratio 0.61, 95% confidence interval, 0.41 to 0.92; P=0.02)
- Meaningful blood-pressure control after intracerebral hemorrhage requires a coordinated, systemwide commitment that integrates team-based care, expanded access to medication, and real-time monitoring to bridge the gap between clinic visits and daily management. Therapeutic inertia remains our most modifiable (and neglected) barrier

Conclusions: ICH demands urgent, coordinated action — not therapeutic nihilism.

- ICH is the most devastating form of stroke, yet remains the most undertreated. **The window for meaningful intervention is measured in minutes, not hours.**
- **Hematoma expansion is the primary modifiable target.** Recognizing high-risk CT signs (Swirl, Black Hole, Blend, Island) enables rapid, informed triage at first contact.
- **Bundle care — not a single magic bullet — changes outcomes.** Simultaneous, time-targeted control of blood pressure (SBP <140 mmHg within 1 hour), anticoagulation reversal (within 30 minutes), glycemia (6–10 mmol/L) and normothermia (<37.5°C) yields compounding clinical benefit (INTERACT3).
- **Surgical innovation is evolving.** Early minimally invasive approaches (ENRICH) show promise for cortical bleeds — but require the right patient, the right technique, and the right timing.
- **The I-CATCHER framework operationalizes what we know.** Standardized, protocolized bundle care reduces practice variation and combats premature clinical nihilism through the 48-hour rule.
- **Recovery after ICH is delayed but real.** Accurate prognostication, targeted rehabilitation, and long-term BP control (triple-pill strategy, NEJM 2026) are essential pillars of the post-acute continuum.

Evaluation

For the **Provincial Stroke Rounds Planning Committee**:

To plan future programs

For quality assurance and improvement

For **You**: Reflecting on what you've learned and how you plan to apply it can help you enact change as you return to your professional duties

For **Speakers**: The responses help understand participant learning needs, teaching outcomes and opportunities for improvement.

[Time is Brain for Bleeds: Collaborative Strategies
and New Horizons in ICH Care – Fill out form](#)



Please take 2 minutes to fill the evaluation form out. Thank you!