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YEARBOOK



Yearbook of CRITICAL CARE 2024

HICS Initiative

Editors
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Desmopressin for Patients with Spontaneous Intracerebral Haemorrhage Taking Antiplatelet Drugs (DASH): a UK-based, Phase 2, Randomised, Placebo-controlled, Multicentre Feasibility Trial

Desborough MJR, Al-Shahi Salman R, Stanworth SJ, Havard D, Woodhouse LJ, Craig J, et al. Desmopressin for patients with spontaneous intracerebral haemorrhage taking antiplatelet drugs (DASH): a UK-based, phase 2, randomised, placebo-controlled, multicentre feasibility trial.

Lancet Neurol. 2023;22(7):557-67.

CLINICAL QUESTION OR PROBLEM

To recruit patients taking antiplatelets who develop intracerebral hemorrhage, give them desmopressin, and follow them up for 3 months to see if it reduces mortality or disability.

WHAT IS ALREADY KNOWN?

- Intracerebral hemorrhage is a medical emergency, caused by a blood vessel bleeding directly into the brain. Outcome is directly related to the amount of bleeding that occurs. Many patients die early and others are left with significant disability.
- A quarter of all people with intracerebral hemorrhage are taking an antiplatelet drug, which is associated with larger volumes of brain hemorrhage and significantly worse outcomes. 4–5 million people are taking antiplatelet drugs in the UK and use continues to rise in an aging population. Despite advances in treatment of ischemic stroke, there is no effective drug treatment for intracerebral hemorrhage.
- Desmopressin is a drug that reverses blood thinning effects of antiplatelet drugs, by indirectly increasing platelet adhesion, which we hypothesize will minimize the devastating consequences of intracerebral hemorrhage.
- Desmopressin is commonly used in patients with inherited platelet dysfunction disorders and is an appealing treatment for antiplatelet-associated intracerebral hemorrhage.
- Desmopressin is affordable, available and could be implemented clinically across the UK and worldwide in the next 5 years with immediate benefit for stroke patients, their families and society.

- There are no randomized trials comparing desmopressin with placebo for reversing antiplatelet drug effects in spontaneous intracerebral hemorrhage.

STUDY DESIGN

- It is a Phase 2, multicenter, randomized, and placebo-controlled feasibility study.
- Patients who were 18 years of age or older, using an antiplatelet medication, and having an intracerebral hemorrhage with stroke symptoms within 24 hours after randomization were eligible to be recruited from 10 acute stroke centers in the United Kingdom.
- Participants were assigned to receive a placebo or a single intravenous dose of desmopressin (20 μg) at random (1:1).
- All study participants, including staff and patients, were blinded about treatment allocation.

POPULATION STUDIED INCLUDING DEMOGRAPHICS

Inclusion Criteria

- Adult (aged ≥18 years),
- With intracerebral hemorrhage confirmed on brain CT, and
- Prescribed and thought to be taking a daily oral antiplatelet drug in the preceding 7 days (i.e., cyclooxygenase inhibitors, phosphodiesterase inhibitors, or $P2Y_{12}$ inhibitors).

Exclusion Criteria

- Known secondary causes of intracerebral hemorrhage,
- Patients at risk of fluid retention,
- Systolic blood pressure of <90 mm Hg,
- Known drug-eluting stent in previous 3 months,
- Allergy to desmopressin,
- Pregnant or breastfeeding,
- Life expectancy of <4 hours or planned for palliative care only,
- Glasgow Coma Scale score of <5, and
- Modified Rankin Scale score of >4.

OUTCOMES EVALUATED

- Analysis was done by intention to treat, and the primary outcome was feasibility, which was determined by the proportion of eligible patients approached and the number of eligible patients randomly assigned.
- The research revealed that,
  - Patients and their relatives were happy to take part
  - Desmopressin was simple to give
  - There were no safety concerns
  - Follow-up was completed for all patients at 3 months

AUTHORS' VIEWPOINT

- Given sufficient recruiting centers and pragmatic trial methodology, it should be feasible to conduct a definitive trial to determine if desmopressin improves outcomes in patients on antiplatelet drug therapy with intracerebral hemorrhage. Although this trial could be delivered as a standalone study, it might be more efficient as part of a platform trial or to embed in an existing intracerebral hemorrhage trial.
- Given the high mortality and morbidity after intracerebral hemorrhage in patients exposed to antiplatelet drugs, and the increased frequency of patients taking antiplatelet drugs, even a small reduction in morbidity or mortality could reduce the risk of death and leave tens of thousands of patients free from disability.

STRENGTH OF THE STUDY

- Antiplatelet-induced spontaneous intracerebral hemorrhage has a significant

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global mortality and morbidity burden, and treatment guidelines are not universally agreed upon. Therefore, the study is extremely important.
- It offers randomized data on desmopressin usage in cases of acute intracerebral hemorrhage.
- The trial's methodology was precise, and it was shown that the strategy being studied was feasible.

DRAWBACK OF THE STUDY

- The coronavirus disease-2019 (COVID-19) pandemic caused recruitment to be halted halfway through the experiment, and recruitment rates never recovered to their pre-pandemic levels. One significant change that had a significant impact on the trial's capacity to meet its goals and exceed the recruitment target was the extended recruiting period linked to the funding extensions.
- Although the hazards of unmasking were reduced by completely blinding treatment allocation from physicians, patients, and outcome assessors, the placebo was not identical to desmopressin.
- Additionally, data supplied by each study site was included in the screening logs; the central research team was unable to validate this data because they were collected locally.
- Since arriving after hours or >24 hours after the beginning of symptoms was one of the most frequent grounds for patient exclusion, the results of this research may not be typical of all patients.
- Future trials should shorten the period between imaging confirmation of intracerebral hemorrhage and desmopressin or placebo administration by streamlining trial procedures.
- The results were skewed because all six patients receiving dual antiplatelet medication were randomly assigned to placebo.
- Minimization of other prognostic markers, such as baseline stroke severity and dual antiplatelet medication, should be taken into account in a big definitive trial.

REVIEWERS' VIEWPOINT

Currently available guidelines from the different societies on use of desmopressin for patients on antiplatelet drugs with intracerebral hemorrhage are as follows:
- The Neurocritical Care Society and Society of Critical Care Medicine recommend a single dose of 0·4 μg/kg desmopressin for patients with intracranial hemorrhage who were exposed to antiplatelet agents[1] and planned for neurosurgical procedure. These guidelines recommend that desmopressin can be used in addition to platelet transfusion.
- The American Heart Association and American Stroke Association advise that further studies are necessary to determine if there is a subgroup of patients taking antiplatelet drugs with intracerebral hemorrhage who might benefit from desmopressin.[2]
- The Intercollegiate Stroke Working Party of the Royal College of Physicians guidelines[3] and British Society for Haematology guidelines[4] make no recommendations.

Thus, there is no consensus among the different societies and hence there is a definite need for a good trial. This is the first randomized trial in patients with intracerebral hemorrhage who are taking antiplatelet drugs comparing desmopressin with placebo.

There were no safety concerns or clinically relevant hyponatremia in the study group.

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IMPACT ON CURRENT PRACTICE AND TAKE-HOME MESSAGE

- For a feasibility study, this study has done justice in its good methodology and study design.
- The findings of this study support the need for a definitive, large-scale trial to determine if desmopressin could improve outcomes in patients with intracerebral hemorrhage on antiplatelet drug therapy.

Blood Pressure Management after Endovascular Therapy for Acute Ischemic Stroke: The BEST-II Randomized Clinical Trial

Mistry EA, Hart KW, Davis LT, Gao Y, Prestigiacomo CJ, Mittal S, et al. Blood pressure management after endovascular therapy for acute ischemic stroke: The BEST-II randomized clinical trial.

JAMA. 2023;330(9):821-31.

CLINICAL QUESTION OR PROBLEM

- Are moderately low systolic blood pressure (SBP) targets (<140 and <160 mm Hg) after successful endovascular stroke treatment harmful?
- In other words, will patients in whom systolic blood pressure targets were lowered for 24 hours post-endovascular therapy in an acute ischemic stroke, have a higher volume of stroke size at 36 hours and a higher disability at 90 days.
- The objective is to determine the futility of lower SBP targets after endovascular therapy (<140 mm Hg or 160 mm Hg) compared with a higher target (≤180 mm Hg).

WHAT IS ALREADY KNOWN?

- Endovascular therapy has changed the landscape in acute stroke treatment and patients do drastically better when they receive endovascular treatment in appropriate time window.
- Despite the enormous effectiveness of endovascular treatment, about 50% of patients remain disabled or die at 90 days.
- The current American Heart Association/American Stroke Association and European Stroke Organization guidelines recommend targeting systolic blood pressure (SBP) of 180 mm Hg or less after endovascular therapy based on prior thrombolysis trials.[5,6]
- Although higher systemic SBP is common in the setting of acute ischemic stroke due to cerebral autoregulation, observational studies have indicated that lower SBP after successful endovascular therapy may be associated with better functional outcomes.[7,8]
- A prospective multisite observational study identified that a maximal SBP of approximately 160 mm Hg in the first 24 hours after endovascular therapy delineated patients with good and poor functional outcomes.[9]
- Others showed that moderate SBP levels of between 140 and 160 mm Hg were associated with better patient outcomes.[10]
- However, a recent randomized trial among Chinese patients who had undergone successful endovascular therapy found that SBP lowered to <120 mm Hg was harmful.[11]
- In a 2017 survey of clinical practice, among 58 US sites, 69% of institutions

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practiced moderate SBP lowering and only 5% of institutions practiced extreme SBP lowering to <120 mm Hg for patients successfully treated with endovascular therapy.[12]

STUDY DESIGN

- Randomized
- Open-label
- Blinded end point
- Phase 2
- Futility clinical trial

POPULATION STUDIED INCLUDING DEMOGRAPHICS

Study enrolled 120 patients (average age, 70 years; 57% female) who had an acute ischemic stroke and successful endovascular treatment at one of three urban comprehensive stroke centers (Vanderbilt University Medical Center in Nashville, Tennessee; University of Cincinnati in Cincinnati, Ohio; and Hartford Health Medical Center in Hartford, Connecticut) between January 2020 and February 2022.

The inclusion criteria:

- Adult patients (≥18 years)
- With ischemic stroke
- Who had undergone successful endovascular therapy (defined as modified thrombolysis in cerebral ischemia, ≥2b-50–89% reperfusion; 2c-90–99% reperfusion; and 3-complete reperfusion)
- For an occlusion in an anterior cerebral circulation large vessel (specifically, internal carotid artery and M1 or M2 segments of the middle cerebral artery).

The exclusion criteria:

- A diagnosis of heart failure with ejection fraction <30%;
- On left ventricular assist device; or
- On extra corporeal membrane oxygenation
- Pregnant individuals and
- Patients enrolled in other clinical trials were excluded.

A total of 40 patients were randomly assigned to have their systolic blood pressure lowered to a target of ≤180 mm Hg, 40 patients were assigned to a systolic blood pressure target of <160 mm Hg, and 40 patients were targeted to reach a systolic blood pressure of <140 mm Hg. Patients were treated with nicardipine, an antihypertensive medication administered intravenously, started within 1 hour after endovascular treatment and given for 24 hours if their systolic blood pressure was above the target they were assigned.

It was assessed whether lowering BP causes harm to brain (particularly vulnerable during the 24 hours after a stroke) and to assess disability 90 days later.

OUTCOMES EVALUATED

- The main outcomes of the study were the size of stroke at 36 hours and degree of disability at 90 days. The study did not find significant evidence of an unequivocal harm due to lower blood pressure targets in terms of worsening size of stroke or increasing disability. But the trends indicated that there may be only marginal benefit on long-term disability by lowering blood pressure after endovascular treatment. In fact, there was an indication that lowering the blood pressure after thrombectomy may worsen patients' long-term disability.
  - In ≤180 mm Hg target group, average systolic blood pressure reached 129 mm Hg.
  - In <160 mm Hg target group, average systolic blood pressure reached 130 mm Hg.
  - In <140 mm Hg target group, systolic blood pressure lowered to an average of 123 mm Hg.

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- The mean follow-up infarct volume was:
  - 32.4 mL (95% CI, 18.0–46.7 mL) for the <140-mm Hg group,
  - 50.7 mL (95% CI, 33.7–67.7 mL), for the <160-mm Hg group, and
  - 46.4 mL (95% CI, 24.5–68.2 mL) for the 180-mm Hg or less group
  - Average 36-hour stroke volumes showed no conclusive evidence of harm.
- The mean utility-weighted Modified Rankin Score (mRS) was:
  - 0.51 (95% CI, 0.38–0.63) for the <140-mm Hg group,
  - 0.47 (95% CI, 0.35–0.60) for the <160-mm Hg group, and
  - 0.58 (95% CI, 0.46–0.71) for the high-target group
  - In the 90-day disability outcome, there was only a slight indication of harm.

AUTHORS' VIEWPOINT

Lower SBP targets of 140 mm Hg or 160 mm Hg following successful endovascular therapy did not meet predetermined criteria for futility as compared to an SBP target of 180 mm Hg or less in patients who had an acute ischemic stroke. However, the results indicated that, if attempted in a larger study in the future, there would be a small probability of benefit from reduced SBP targets following endovascular therapy.

STRENGTH OF THE STUDY

Robust methodology for a futility trial

The trial advances the knowledge regarding the feasibility of achieving SBP targets.

DRAWBACK OF THE STUDY

- The study is limited by enrollment at only three centers and a small sample size.
- Nicardipine was used as the first-line treatment for the majority of enrolled patients. Although nicardipine is commonly used in neurointensive care units within the US, it may not be readily available globally.
- Some baseline characteristics differed among groups. These may impact the generalizability of the results.
- Though the target SBP in the three groups were fixed (140, 160, and 180 mm Hg), the average SBP found to be reached in all the groups were between 120 and 130 mm Hg which was not the intended methodology to find out the difference between the groups.

REVIEWERS' VIEWPOINT

According to this study, patients' blood pressure should be allowed to autoregulate after endovascular treatment unless it is >180 mm Hg. However, physicians should exercise caution while aggressively lowering a patient's blood pressure because there may be chances of further worsening. Individualized decision-making is necessary in certain situations, such as when there are additional medical reasons for reducing blood pressure or when there are high possibilities of hemorrhagic transformation.

IMPACT ON CURRENT PRACTICE AND TAKE-HOME MESSAGE

If investigated in a bigger trial in the future it is thought that the results indicated that there was low probability of benefit from lower SBP objectives.

Still the criteria for futility were not met by lower SBP targets following effective endovascular therapy for acute ischemic stroke.

As of now based on the current available evidence including this trial it is better to maintain systolic BP <180 mm Hg and not aim for a further lower threshold.

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Effectiveness of Lumbar Cerebrospinal Fluid Drain among Patients with Aneurysmal Subarachnoid Hemorrhage: A Randomized Clinical Trial

Wolf S, Mielke D, Barner C, Malinova V, Kerz T, Wostrack M, et al. Effectiveness of lumbar cerebrospinal fluid drain among patients with aneurysmal subarachnoid hemorrhage: A randomized clinical trial.

JAMA Neurol. 2023;80(8):833-42.

CLINICAL QUESTION OR PROBLEM

In patients with aneurysmal subarachnoid hemorrhage (aSAH), does lumbar cerebrospinal fluid (CSF) drainage compared to standard therapy improve clinical outcomes as measured by the modified Rankin Scale (mRS) score at 6 months?

WHAT IS ALREADY KNOWN?

- Aneurysmal subarachnoid hemorrhage frequently leads to death or permanent disability due to both the initial insult and delayed cerebral ischemia (DCI).
- Delayed cerebral ischemia occurs predominantly due to vasospasm in patients with SAH may be related to blood degradation products in the CSF near the basal cisterns.
- Cerebrospinal fluid drainage via a lumbar drain may preferentially remove more of the blood degradation products due the effect of gravity and thus may decrease rates of vasospasm and DCI is a hypothesis.
- Retrospective data and meta-analyses of lumbar drain use in aSAH have demonstrated lower mortality, and reduced rates of clinical vasospasm, ischemic stroke and improved neurological outcomes[13,14]

LUMAS, a prospective single center RCT, including patients with aSAH [World Federation of Neurosurgical Societies (WFNS) grade 1–3], demonstrated reduced rates of delayed ischemia and better early neurological outcome but without difference in outcome at 6 months.[15]

STUDY DESIGN

- Parallel group, multi-center, open label randomized clinical trial
- Randomization – 1:1 to standard care or additional use of lumbar drain
  - Via internet randomizer – permutated blocks of 6
  - No stratification
- Blinded end-point evaluation
- Patients followed up to their death or 6 months post randomization
- Intention to treat analysis
- Protocol and analysis plan published prior
- Power calculation:
  - 300 patients would be required to detect a decrease in unfavorable outcome from 50 to 33% with 85% power and 5% α error
- 19 hospitals in Germany, Switzerland, and Canada
  - All provided 24 hours acute neurosurgical and neurocritical care with >30 aneurysm procedures/year
- Data collected from Jan 2011 to Jan 2016
- *Inclusion:*
  - ≥18 years, acute SAH with confirmed aneurysm origin via CT-angiography or DSA
  - Aneurysm treatment within 48 hours of SAH

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- *Exclusion:*
  - Presence of therapeutic anticoagulation
  - Contraindications for lumbar drain
  - Absent or compressed basal cisterns on admission CT-brain
  - Pregnancy
  - Reduced life expectancy
  - Participation in another interventional trial
  - Hemorrhage from non-aneurysmal origin
  - No hemorrhage present on initial CT-B (Fischer 1/modified Fischer grade 0)
- 307 patients randomized:
  - Lumbar drain >155 randomized (11 excluded)
  - Standard care >152 randomized (9 excluded)
- Baseline characteristics of lumbar drain versus standard care:
  - Similar between groups
  - *Median age:* 54 versus 56 years
  - *Female:* 68% versus 69%
  - *mRS score of 0 on admission:* 94 versus 93%
  - *Presence of intraventricular hemorrhage (IVH):* 63% versus 59%
  - *Presence of intracerebral hemorrhage (ICH):* 39% versus 35%
  - The World Federation of Neurosurgical Societies classification:
    - 1 = 37% versus 29%
    - 2 = 15% versus 15%
    - 3 = 5% versus 7%
    - 4 = 10% versus 11%
    - 5 = 33% versus 39%
  - *Modified Fisher score of 4:* 59 versus 55%
  - Location, size, and number of aneurysms similar

Intervention

- Insertion of lumbar drain with drainage of lumbar CSF at 5 mL/hour
- Commenced within 72 hours of aneurysmal SAH in addition to standard therapy
- Continued for least 4 days and up to 8 days
- *Safety:* If intracranial pressure (ICP) pressure >20 mm Hg or >5 mm Hg difference between ICP + lumbar drain – recommended to cease lumbar drainage
- Median CSF lumbar drainage of 108 mL in first 8 days

Control

No lumbar drainage

Management Common to Both Groups

- Treatment of aneurysmal SAH with endovascular coiling or clipping determined by local treating teams
- Local teams determined if external ventricular drain (EVD) or ICP monitor inserted
  - External ventricular drains inserted in 70.8% of lumbar drain group and 76.9% of control group
  - Median daily drainage via EVD lower in lumbar drain group (98 vs. 171 mL)
  - Total CSF drainage via both EVD +/– lumbar drains similar between groups
- *Local standard management for aSAH:*
  - Daily transcranial Doppler monitoring as per local protocol
  - Cerebral vascular imaging via computed tomographic angiography (CTA), magnetic resonance angiography (MRA), or digital subtraction angiography (DSA) for suspected vasospasm or routine day 7–10
  - Treatment for vasospasm at discretion of local investigators—not protocolized
- Rates of aneurysm treatment (53 vs. 50% coiled) and vasospasm prophylaxis (99

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vs. 99% nimodipine) use similar between groups
- Mean arterial pressure (MAP), fluid intake, and fever burden similar between groups

OUTCOMES EVALUATED

- *Primary outcome (lumbar drain vs. control):*
  - Rate of unfavorable neurological outcome measured at 6 months (defined as mRS 3–6)
  - *Statistically significant lower rate of unfavorable outcome*
    - 32.6% versus 44.8%
    - RR 0.73 (95% CI: 0.51–0.98; $p = 0.04$)
  - Adjustment for age, severity via Hunt-Hess grade, and presence of ICH and IVH:
    - RR 0.76 (95% CI: 0.54–1.00, $p = 0.047$)
  - Effect consistent across prespecified subgroups (age, sex, grade, Location, IVH/ICH, treatments provided, and center size)
- *Secondary outcomes (lumbar drain vs. control):*
  - *Significant difference in:*
    - Rate of secondary infarction following discharge
      - 28.5% versus 39.9% (RR 0.71, 95% CI: 0.49–0.99, $p = 0.04$)
    - GOS-E 1–4 at 6 months and Barthel Index <80 at 6 months
  - *No significant difference in:*
    - Mortality within 6 months
      - 13.2 versus 17.5%
    - Rate of vasospasm
      - *Clinical:* 29 versus 33%
      - *TCD:* 27 versus 25%
      - *Angiographic:* 46 versus 44%
    - Infection of any cause
      - 39 versus 36%
- *Adverse outcomes*
  - *Lumbar drain group:*
    - One patient developed elevated gradient >5 mm Hg between ICP + lumbar drain prohibiting drainage
    - One patient developed local skin infection—required surgical excision
    - One patient had lumbar drain torn off, requiring surgical removal

AUTHORS' VIEWPOINT

In patients with aSAH, prophylactic lumbar CSF drainage to lessen the burden of secondary cerebral infarction and unfavorable outcome is warranted.

STRENGTH OF THE STUDY

- Pragmatic as study design relies on local standard practice allowing easy translation to routine clinical care
- Meaningful patient-centered outcome
- Functional outcomes determined by blinded evaluators minimizing detection bias
- Included poor grades of aSAH which other trials have not, therefore increasing relevance for neurocritical care population

DRAWBACK OF THE STUDY

- Majority of patients randomized from only two of the centers
  - Possibly lower risk of adverse outcomes if lumbar drains more routinely used at these sites
- Clinicians may alter their "standard" therapy based on unblinded randomization
- Selection bias possible due to limited screening data available
  - Certain patient groups may have been excluded that would have changed outcome (e.g., a patient was excluded for poor grade)

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- 35 patients in lumbar drainage group were not treated as per protocol
  - 13 had no drain inserted, 22 had drain inserted but no relevant drainage performed
  - However, no difference in sensitivity analysis (per protocol and as treated)
- Potential for time-lag bias (trial enrolled from 2011 to 2016)
- A significant number of patients in the lumbar drain group did not receive the designated intervention, although the intention-to-treat analysis was consistent even when considering this discrepancy.
- The lack of blinding among patients, their relatives, and acute care clinicians introduced potential bias, though blinded assessments of outcomes tried to mitigate this.
- The study did not collect data on factors such as preexisting hypertension, initial CT scan details regarding clot thickness and blood quantity, or medical complications commonly seen in subarachnoid hemorrhage patients.
- Potential treatments such as clot thrombolysis or subarachnoid space irrigation were not explored, nor did the trial evaluate the benefits of higher drainage rates than the recommended 5 mL per hour, even though some patients exhibited higher lumbar drainage amounts.

REVIEWERS' VIEWPOINT

- In addition to standard care, use of lumbar CSF drainage may improve neurological outcomes in patients with aSAH is the basic hypothesis of the study.
- It was stated that although both groups had similar volumes of cerebrospinal fluid drainage, a striking visual difference was observed in the fluid color between the ventricular and lumbar drains. The lumbar drain's fluid appeared darker and more reddish, indicating a higher concentration of blood and its degradation products. This observation underscores the sedimentation of erythrocytes in the fluid, suggesting that lumbar drainage may be more effective at removing these components.
- But the complications associated with the intervention such as coning and infections are dreadful.
  - Hence, based on this study alone it might be difficult to change the existing practice.

IMPACT ON CURRENT PRACTICE AND TAKE-HOME MESSAGE

- Considering the high-risk nature of the intervention, it is advisable to wait for further studies to confirm the potential benefits of early lumbar drainage in aSAH.

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Trial of Early Minimally Invasive Removal of Intracerebral Hemorrhage - ENRICH trial.

Pradilla G, Ratcliff JJ, Hall AJ, Saville BR, Allen JW, Paulon G, et al. Trial of early minimally invasive removal of intracerebral hemorrhage.

N Engl J Med. 2024;390(14):1277-89.

CLINICAL QUESTION OR PROBLEM

In patients with spontaneous intracranial hemorrhage (ICH), does the use of early minimally invasive surgery with standard management compared to standard management alone, result in better functional outcomes at 180 days?

WHAT IS ALREADY KNOWN?

- Spontaneous ICH is a condition with high mortality, poor functional outcomes, and high costs of care.
- The mainstay of standard medical management for ICH has been the reversal of coagulopathy, blood pressure control and best supportive care.
- While showing mortality benefit, surgical intervention with craniectomy (STITCH, STITCH II)[16,17] and minimally invasive techniques (MISTIE III)[18] has failed to show long-term benefits in functional outcomes
- Data from these trials showed a trend toward benefit with early surgical intervention in superficial lesions and with greater clot evacuation
- The ENRICH trial was designed to investigate any benefit of early minimally invasive trans-sulcal parafascicular surgery (MIPS) in superficial ICH.

STUDY DESIGN

- Multi-center, two-arm, randomized, and adaptive design
- 1:1 block randomization stratified by:
  - ICH location (anterior basal ganglia vs. lobar)
  - Index GCS (<9 or ≥9)
- Interim analysis at 150 patients and then in blocks of 25 to determine if early stopping rules are met. If accrual stopped due to futility in one site (anterior basal ganglia or lobar) then this would lead to enrichment for the other site. Pre-specified stopping rules for both futility and success.
- Primary outcome defined as mean differences in utility weighted mRS (H_1: $\Delta > 0$). To demonstrate superiority, a Bayesian model-based posterior probability of MIPS benefit (i.e., $\Delta > 0$) was set to be ≥0.975

Intervention

- Early ICH evacuation (within 24 hours, ideally <8 hours) using MIPS + standard management
  - Standardized surgical approach with training provided
  - Imaging guided
  - BrainPath and Myriad device for minimally invasive technique (manufactured by NICO)
  - Video recording and independent review of surgeries at each site
- Pre-specified futility criteria for basal ganglion hemorrhage met at the interim analysis for 175 patients
  - Following this only lobar hemorrhages enrolled

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- Median time from last known well to surgery was 16.8 hours

Control

Standard management alone.

Management Common to Both Groups

Based on AHA/ASA guidelines:

- Aggressive resuscitation
- Blood pressure control
- Correction of bleeding diathesis
- Traditional surgical techniques permitted (EVD, craniectomy, etc.)

POPULATION STUDIED INCLUDING DEMOGRAPHICS

- 37 hospitals in the USA
- December 2016 – August 2022
- 59 treating neurosurgeons
- *Inclusion:*
  - Aged 18–80 years
  - Acute spontaneous, primary ICH with volume of 30–80 mL
  - Intervention within 24 hours of last known well
  - GCS 5–15
  - Previously mRS 0–1 before ICH occurred
- *Exclusion:*
  - Recurrent ICH or other underlying vascular abnormality
  - Primary thalamic or infratentorial intraparenchymal hemorrhage
  - NIHSS <5
  - Intraventricular hemorrhage (IVH) >50% of lateral ventricles
  - Uncorrected coagulopathy or a known clotting disorder
  - Anticoagulants not rapidly revisable or need for anticoagulation within 5 days of index admission
  - Not expected to recover, Do Not Resuscitate (DNR), and life expectancy <6 months
- *300 patients enrolled:*
  - 11,603 assessed for eligibility
  - 10,611 did not meet inclusion criteria/met exclusion criteria
  - 692 excluded with basal ganglion hemorrhage after adaptation of enrollment criteria
- Comparing baseline characteristics of surgery versus control group
  - *Age:* 64 versus 62 years
  - *Female sex:* 48 versus 52%
  - *Median score on NIH stroke scale:* 16 versus 18
  - *Glasgow Coma Scale (GCS) at randomization:*
    - *4 – 8:* 17% versus 19%
    - *9–14:* 83% versus 81%
  - *Median hematoma volume:* 54 versus 55 mL
  - *Intraventricular hemorrhage present:* 43% versus 39%
  - *ICH location:*
    - *Anterior basal ganglia (ABG):* 32% versus 29%
    - Lobar 68% versus 71%
  - *Median ICH score:* 2 versus 2
  - *Median APACHE II score:* 12 versus 12
  - *Medical history:*
    - *Cardiovascular disease (CVD):* 82% versus 78%
    - *Central nervous system (CNS) disease:* 30% versus 28%
    - *Endocrine or renal disorder:* 28% versus 26%
  - *Smoker (current/former):* 45% versus 40%
  - Time from last known well to randomization:
    - *≤8 hours:* 28% versus 25%
    - *≤12 hours:* 49% versus 46%

OUTCOMES EVALUATED

- *Primary outcome:*

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Yearbook of
CRITICAL CARE 2024
HICS Initiative

The field of intensive care is very dynamic, and new evidence emerges almost on a daily basis. Keeping pace with all the new information, analyzing and assimilating it, and implementing its gist is the key to the practice of evidence-based medicine. The Hyderabad Intensive Care Symposium (HICS) has been at the forefront of bringing such information into the midst of keen learners of intensive care every year. However, the time constraints of a didactic meeting make it impossible to convey every advance and guideline. The team therefore took upon itself the task of compiling all the major and interesting publications of the last 12 months and having them analyzed for publication. The end result is this *Yearbook of Critical Care*.

- Comprehensive review of all major publications from July 2023 to July 2024
- Experienced and seasoned teachers as reviewers
- Systemwise compilation
- Reviewers' opinion at the end of each section
- Handy format

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