# Critical Care of Intracerebral Hemorrhage

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# Disclosures

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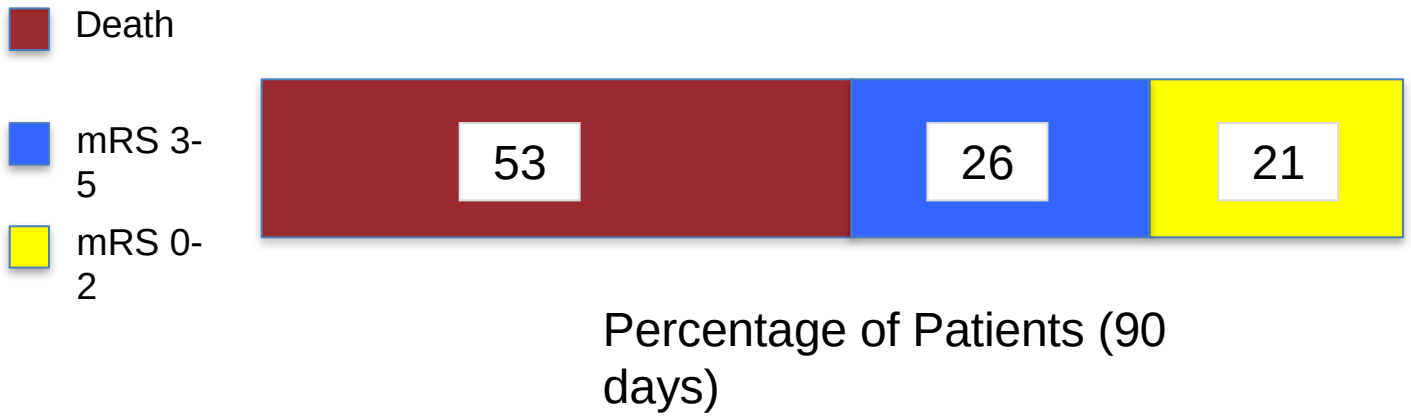
# Initial Assessment

- Vital signs, ABCs, with attention to airway
- GCS, NIHSS before intubation (or use ultra-short acting neuromuscular blockade or sedative-hypnotics agent to allow for rapid return of motor control and assessment of neurologic deficits).
- CT scan
- Co-morbid acute myocardial injury?
- Endotracheal intubation can cause transient elevation in ICP; etomidate is favored for induction when elevated ICP is a concern. The use of fentanyl may attenuate transient ICP elevation.

# Predicting outcome

- Proceed with caution
- Focus discussions with family members/loved ones on identifying patient preferences
- Recent key references
  - Hwang DY. Discussing Life-sustaining therapy with surrogate decision makers. Continuum (Minneap Minn). 2017 Feb. PMID: 28157753
  - Zahuranec DB, Fagerlin A, Sanchez BN, Roney ME, Thompson BB, Fuhrel-Forbis A, Morgenstern LB. Variability in physician prognosis and recommendations after intracerebral hemorrhage. Neurology. 2016;86(20):1864-71.
  - Hwang DY, Dell CA, Sparks MJ, Watson TD, Langefeld CD, Comeau ME, Rosand J, Battey TW, Koch S, Perez ML, James ML, McFarlin J, Osborne JL, Woo D, Kittner SJ, Sheth KN. Clinician judgment vs formal scales for predicting intracerebral hemorrhage outcomes. Neurology. 2016;86(2):126-33.

# Predicting Outcome: The FUNC score




## Predicting outcome

- Functional independence is what matters to our families and patients
- How to account for withdrawal of care in the model

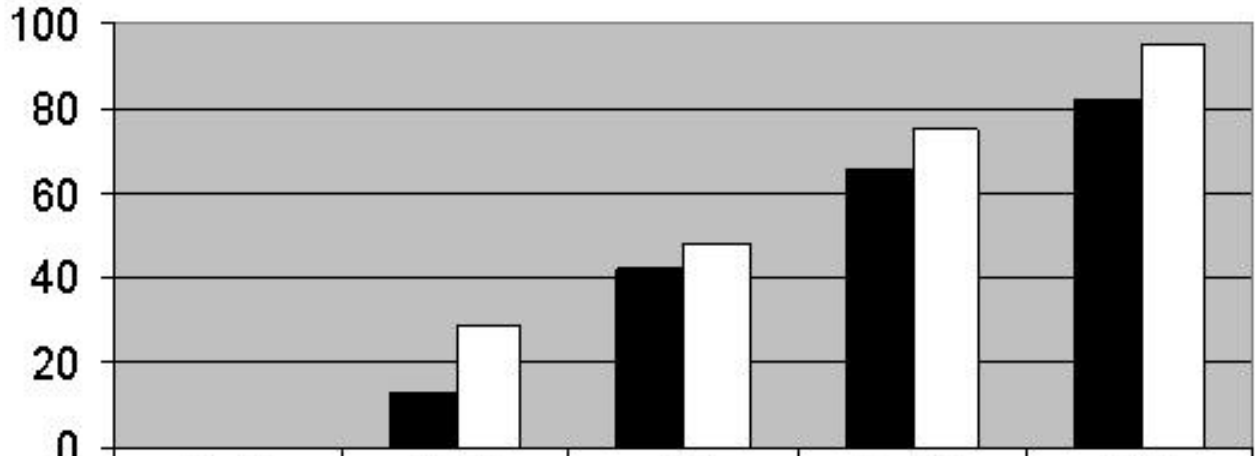
Rost et al. *Stroke* 2008;39:2304-9

Biffi et al. *Neurology* 2011;76:1581-88

# The FUNC score

## FUNC Score Prediction Tool

| | |
|---|---|
| ICH volume *(cc)* | |
| < 30 | 4 |
| 30-60 | 2 |
| > 60 | 0 |
| Age *(yrs)* | |
| < 70 | 2 |
| 70-79 | 1 |
| ≥ 80 | 0 |
| ICH Location | |
| Lobar | 2 |
| Deep | 1 |
| Infratentorial | 0 |
| GCS | |
| ≥ 9 | 2 |
| ≤ 8 | 0 |
| Pre-ICH cognitive impairment | |
| No | 1 |
| Yes | 0 |




| FUNC Score | [0-4] | [5-7] | [8] | [9-10] | [11] |
|---|---|---|---|---|---|
| ■ Entire Cohort | 0 | 13 | 42 | 66 | 82 |
| □ Survivors Only | 0 | 29 | 48 | 75 | 95 |

**% functionally independent at 90 days**

www.stopstroke.org

# CT angiography

- MR angiography can also be considered, but CTA is faster and provides greater vascular resolution.
- Ensure no contraindication to contrast use (i.e. renal failure or contrast allergy)
- Presence of a spot sign on CTA can help predict hematoma expansion

(A) Left deep ICH on NCCT, with baseline volume of 45 mL; (B) CTA showing presence of spot sign (arrow); (C) follow-up NCCT at 19 hours showed significant hematoma growth to a volume of 192 mL with severe midline shift and massive intraventricular extension.

*Demchuk et al. Lancet Neurol 2012*
*Goldstein et al. Neurology 2007*

# MRI

- For ICH secondary to possible underlying neoplasm, amyloid angiopathy or other degenerative process, or cavernous malformation.
- The most helpful sequences are GRE or SWI
- Contrast MRI or contrast CT can also be considered (see Lunder 6 MRI protocols).
- This imaging may be useful initially and should be repeated 6-12 weeks later if clinical suspicion is high, once hemorrhage products have undergone reabsorption.
- MRI is also invaluable if hemorrhagic conversion of an ischemic infarct is suspected (DWI and GRE sequences)
- → If acute ischemic stroke is suspected (onset less than 12 h), contact acute stroke team (Beeper 34CVA).
- MRV: for hemorrhage secondary to venous sinus thrombosis or cortical vein thrombosis. CT venography provides more limited tissue information.

Right lobar ICH and multiple lobar microbleeds, SWI sequence

# Digital subtraction angiography

- Digital subtraction angiography (DSA) may be useful in any setting where an underlying lesion is suspected but not confirmed by non-invasive imaging, or where better vascular detail is needed for diagnostic or treatment purposes.

# Laboratory evaluation

**Send the following lab tests (STAT):**

- PT/INR
- PTT
- CBC with platelets,
- Fibrinogen,
- Electrolytes, BUN/Cr,
- Glucose,
- Liver function tests,
- Type and screen to blood bank.

# Blood Pressure Management

- All patients who require treatment with continuous intravenous antihypertensive therapy should undergo urgent placement of an intra-arterial catheter for blood pressure monitoring.
- Consider central venous catheter for central venous pressure monitoring as well as administration of IV antihypertensive medications.
- Once a physician determines that a patient requires treatment with IV antihypertensive therapy, he/she must designate an individual who will remain at the bedside and monitor effectiveness of therapy until blood pressure is controlled.
- Elevated blood pressure (suggested medications in approximate order of preference):
  1. Labetalol: 5-100mg/hr by intermittent bolus doses of 10-40mg or continuous drip (2-8mg/min)
  2. Nicardipine: 5 mg/hr increased by 2.5 mg/hr q15 minutes to max 15 mg/hr
  3. Esmolol: 250 mcg/kg as a load; maintenance use, 25-300 mcg/kg/min
  4. Enalapril: 0.625-5mg IV Q6h

# Blood Pressure Targets

- For patients presenting with severely elevated blood pressure (>220mmHg), consider a 25% reduction initially.
- For patients presenting with SBP <220mmHg, consider acute lowering of systolic BP to 140 mmHg for 7 days
- Any clinical deterioration in association with reduction of BP should prompt reconsideration of BP management strategy.
- Patients who are placed on multiple high dose BP medications in the acute setting frequently require fewer medications at lower doses in the sub-acute setting (days to weeks) and vigilance is required to avoid risk of hypotension.

# Avoid Hypotension!

- Etiology of hypotension must be established.
- Volume replenishment is the first approach. Isotonic saline or colloids can be used and monitored with central venous pressure.
- If hypotension persists after correction of volume deficit, continuous infusions of vasopressors should be considered, particularly for low systolic BP (>90mmHg).
    1. Phenylephrine: 2-10mcg/kg/min
    2. Dopamine: 2-20mcg/kg/min
    3. Norepinephrine: 0.05-0.2mcg/kg/min

# Correct coagulopathy - Warfarin

- If patient is on warfarin and INR is elevated: Administer vitamin K 10mg IV over 10 minutes and EITHER prothrombin complex concentrates (4F-PCCs) or FFP. PCC should be considered as first line for all patients with warfarin-associated ICH FFP may be preferred in patients with concomitant extracranial bleeding requiring volume replenishment.

**4F-PCC dosing**

- INR > 6: 50U/kg (not to exceed 5,000 units total)
- INR 4-6: 35 U/ kg (not to exceed 3500 units total)
- INR 2-3.9: 25 U/kg (not to exceed 2500 units total)

**FFP dosing:**

- INR > 6: 15 mL/kg
- INR 4-6: 12 mL/kg
- INR 2-3.9: 10 mL/kg

# Considerations in Warfarin-associated ICH

- INR should be repeated 15 minutes after infusion of 4F-PCC or FFP.
- Goal INR is < 1.4
- Intravenous vitamin K associated with a small risk of severe allergic reaction. When administered intravenously, the rate should not exceed 1mg/minute.
- Reversal of anticoagulation by any means (vitamin K, FFP, or PCCs) is associated with a risk of thrombosis depending upon the patient's underlying indication for anticoagulation.
- Follow-up monitoring and therapy
  - STAT PT/INR q 4 hrs x 24; then q 6 hrs x 36; then as needed.
  - If the INR is greater than 1.3 at 4 hours, administer second dose of Vitamin K 10 mg IV. Additional administration of fresh frozen plasma (FFP / PCC) can be considered. Evaluate the patient for disseminated intravascular coagulation and consult Hematology.
  - Patients with anticoagulant-related ICH are at high risk for prolonged bleeding and hematoma expansion. Consider repeating a non-contrast cranial CT scan every 6 +/- 2 hours from time of initial CT scan until ICH volume is stable. In addition, CT scanning should be repeated when any neurologic deterioration occurs.

# Correct coagulopathy - Direct Oral Anticoagulants (DOACs)

- Direct Oral Anticoagulants (DOACs), Target Specific Oral Anticoagulants (TSOACs), or Novel Oral Anticoagulants (NOACs) (dabigatran, rivaroxaban, apixaban, edoxaban).
- Unlike warfarin, DOACs have relatively short half lives and their plasma concentration follows a peak-trough format. No currently available laboratory test is validated for this purpose, but anti-Xa activity can be ordered at MGH which may provide some gauge for both LMWHs and Factor Xa inhibitors.
- When determining whether any treatment is necessary, always consider the time from last intake and renal function 15–17.
- Half lives in healthy subjects (likely longer in the elderly and with poor renal function):
  1. Dabigatran: 12-14 hours
  2. Rivaroxaban: 5-9 hours
  3. Apixaban: 9-14 hours
  4. Edoxaban: 10-14 hours

# Considerations in DOAC-associated ICH

**Dabigatran (Pradaxa) Reversal**:

- A specific reversal agent (idarucizumab, or Praxbind) is available
  1. Order 5 grams given as two separate 2.5 gram consecutive infusions.
  2. Prior to administration, flush preexisting IV line with sodium chloride 0.9%.
  3. Administer dose undiluted as an infusion by hanging the vials. Infusion of each vial should take no longer than 5 to 10 minutes with the second vial of 2.5 grams administered no later than 15 minutes after the end of the first 2.5 gram vial.
  4. Begin administration within 1 hour of spiking the vial.
  5. Following administration of the second 2.5 gram vial, administer 100mL of sodium chloride 0.9% within the same IV line to ensure complete administration of the dose.

**Factor Xa inhibitors (Rivaroxaban, apixaban, edoxaban) Reversal:**

- It is not clear whether any currently available option reverses these agents.
- Clinical trials ongoing
- Some hospitals have adopted a protocol using 4F-PCC

# Antiplatelet Agents and Platelet Disorders

**Antiplatelet Agents**

- Platelet transfusion may be associated with increased mortality in ICH patients taking antiplatelet drugs and therefore is not recommended. For perioperative use, transfusion can be considered in consultation with neurosurgery.

**Platelet disorders**

- Platelet transfusion is recommended for patients with thrombocytopenia (platelet count less than 100,000/uL)—Give 6-12 units (1-2 doses) of platelets. Consult blood bank fellow on call to discuss whether a goal platelet level should be targeted.
- Von Willebrand syndromes: Phone consult with a staff member of hematology or transfusion medicine for dosing of VWF factor concentrate. Treat with 0.3 mcg/kg DDAVP given IV over 30 minutes.

DDAVP may also benefit patients with:

1. Uremic platelet dysfunction.
2. Congenital platelet function disorders.
3. Recent ingestion of combinations of antiplatelet agents such (e.g. ASA and clopidogrel).

# Correct coagulopathy - Heparin

**Standard (Unfractionated Heparin)**

- Discontinue the heparin infusion and administer Protamine sulfate 25 to 50 mg intravenously at a rate not exceeding 5 mg/min.
- Monitor for signs of anaphylaxis; the risk higher in diabetics who have received insulin.

Follow-up therapy

- STAT PTT q1 hour for the next 4 hours, then q4 hours through 12 hours of hospitalization.

**Low Molecular Weight Heparin**

- Protamine sulfate only partially reverses anti-factor Xa activity of low-molecular-weight heparin.
- Enoxaparin: 1 mg protamine for each mg of enoxaparin; if PTT prolonged 2-4 hours after first dose, consider additional dose of 0.5 mg for each mg of enoxaparin.
- Dalteparin or tinzaparin: 1 mg protamine for each 100 anti-Xa IU of dalteparin or tinzaparin; if PTT prolonged 2-4 hours after first dose, consider additional dose of 0.5 mg for each 100 anti-Xa IU of dalteparin or tinzaparin.
- Ongoing clinical trials of andexanet as a specific LMWH reversal agent

# Correct coagulopathy - Thrombolytic Agents

Check STAT labs: CBC, PT, PTT, platelets, fibrinogen and D-dimer.

If hypofibrinogenemia present, treat with anitfibrinolytic or cryopreciptate (or both) as follows:

- Give anti-fibrinolytic: eg, amicar 5 gram bolus i.v. over 15-30 min
- If fibrinogen less than 100 mg/dL, then give cryoprecipitate 10 units. If still bleeding at 1 hr and fibrinogen level still less than 100 mg/dL, repeat cryoprecipitate dose.
- Empiric administration of cryoprecipitate 10 U followed by further administration until normalization of fibrinogen levels can also be considered 18.
- Institute frequent neurochecks and therapy of acutely elevated ICP, as needed.

# DVT prevention, glycemia, seizures, fever

- **Thromboprophylaxis.** For prevention of venous thromboembolism, intermittent pneumatic compression should be applied. Consider initiation of subcutaneous low molecular weight heparin for DVT prophylaxis between 1-4 days following ICH [9], generally at 48 hours after stability of the hemorrhage.

- **Glycemic Control.** For glucose greater than 140 - 180 mg/dl institute insulin therapy either in the form of a sliding scale dose regimen or continuous IV drip. Avoid hypoglycemia.

- **Seizures.** Anti-epileptic therapy should always be used for treatment of known clinical or electrographic seizures. Continuous EEG monitoring should be considered for ICH patients with depressed or fluctuating mental status. There is no data to suggest prophylactic anti-epileptic therapy decreases incident seizure risk.

- **Temperature.** Maintain temperature less than or equal to 38 degrees using PO/PR acetaminophen 650 mg q6h. In the setting of poor airway control or if temperature remains elevated despite acetaminophen, consider external cooling.

# Dysphagia and MI screening

- **Dysphagia screening.** A screening for dysphagia should be performed in all ICH patients to reduce the risk of pneumonia.

- **Screening for myocardial ischemia.** Eletrocardiogram and cardiac enzyme testing should be performed. Resumption of antiplatelet agents should be considered in patients with high risk for coronary ischemia.

# Neurosurgical consultation

**Current and future clinical trials are likely to alter the role of surgery for ICH**

**Until these trials are completed, we suggest the consulting neurosurgery for:**

1. Traumatic intracranial hemorrhage (EDH, SDH, etc)
2. SAH or other suspected hemorrhage from cerebral aneurysm
3. ICH from suspected vascular malformation
4. ICH with clinical or CT signs of significant mass effect or midline shift
5. Cerebellar ICH. Indications for surgery include clinical deterioration, hematoma greater than 3cm in diameter, brainstem compression, and hydrocephalus 3.
6. Patients with lobar ICH who demonstrate progressive clinical deterioration. For ICH in a superficial lobar distribution without intraventricular extension, there may be a small survival benefit to early surgical evacuation when compared to standard conservative medical management based on results of the STICH2 (Surgical Trial in Intracerebral Hemorrhage 2) trial.
7. Minimally invasive surgery, based on local practices

# EVD placement and ICP monitoring

**EVD and ICP monitor placement**

- Limited data exists regarding indications for monitoring and treatment of ICP in ICH.
- In cases where CSF drainage may be necessary to control hydrocephalus and/or ICP, EVD should be considered.
- Reverse coagulopathy if possible prior to EVD/ICP monitor placement.

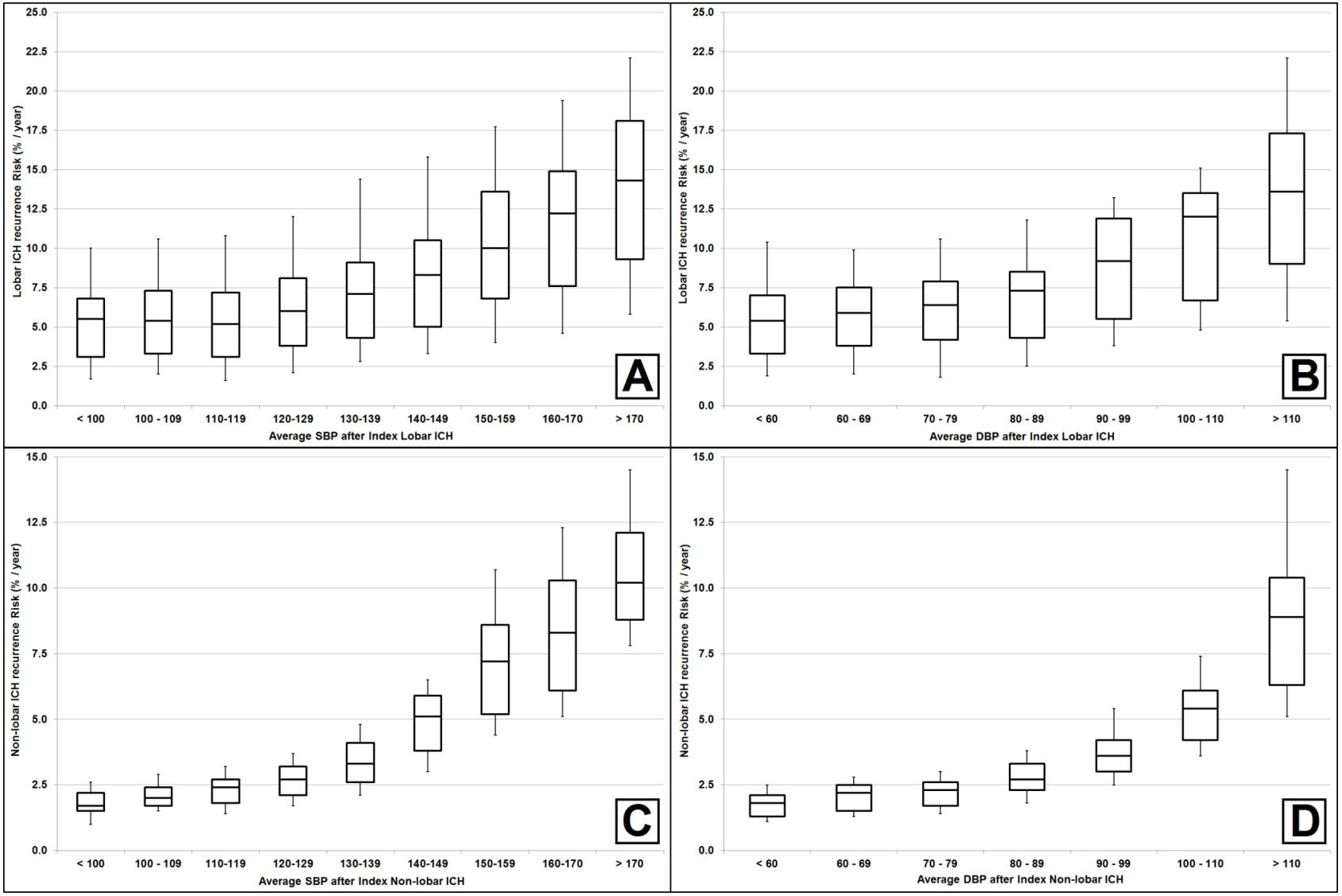
**ICP management**

- Management of ICP in ICH is largely generalized from TBI guidelines
  - ICP<20mmHg and cerebral perfusion pressure (CPP) target of 50-70 (CPP=MAP-ICP).

**INTRAVENTRICULAR FIBRINOLYISIS**

- The role of intraventricular fibrinolysis is still considered investigational. The administration of intraventricular rtPA in conjunction with EVD placement may be beneficial in case of large (>20 mL) IVH (CLEAR III study) [ClinicalTrials.gov NCT00784134]

# Don’t forget about BP at discharge!

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