Spontaneous intracerebral and intracerebellar hematomas

Andras Buki M.D., Ph.D.
Department of Neurosurgery
Medical Faculty, Pecs University, Pecs, Hungary
Chair: Prof. Dr. Tamas Doczi M.D., Ph.D., D.Sc.
• Epidemiology, pathogenesis, pathology
• Symptoms and signs
• Clinical - diagnostic evaluation
• Management of ICH
• Haematoma growth
• Medical management
• Surgical treatment
Causes of ICH

- Trauma
- Non-traumatic

50% is associated with arterial hypertension
  - chronic
  - acute
  - cold related
  - trigeminal nerve stimulation
  - posterior fossa surgery
  - cardiac surgery
  - scorpion bite
  - electroconvulsive therapy
  - carotid endarterectomy
  - migraine attack
Other causes

Coagulopathy
anticoagulants
antiplatelet agents
fibrinolytics
blood dyscrasias

• Coagulopathy
  anticoagulants
  antiplatelet agents
  fibrinolytics
  blood dyscrasias

• Structural vascular lesions
  aneurysms
  arteriovenous malformations
  cavernous angiomas
  vasculopathy
  collagen vascular disease
  vasculitis

• Drug related
  sympathomimetics
  substance abuse

• Tumours

• Postoperative cerebrovascular accident

• Miscellaneous
  neonatal
  secondary brainstem
  cerebral endometriosis
Independent predictors of outcome:

- age
- ICH-size
- **haematoma growth**
- IVH
- hydrocephalus
- anticoagulant, antiplatelet therapy, GCS on admission, blood glucose levels
Epidemiology-ICH

• 12-15/100.000
• mortality: 10-50%
• 60-day survival-rate around 50%
• 20% independent after 6 months

(Broderick, Stroke, 1993, Flaherty, Neurology, 2006)
Epidemiology-ICH+OAC

• 10x more frequent:
  – 1.7% X treatment year on warfarine

• expansion over 33% of initial ICH volume:
  – 56% with OAC
  – 26% in normal hemostasis

• mortality: over 65%

Conditions behind OAC-ICH

- age
- hypertension
- previous stroke
- cerebral amyloid angiopathy
- concomitant use of antiplatelet drugs

OAC is rather an exacerbating agent than a real cause of ICH!
Fibrinolytic agents

• intra-arterial urokinase an alteplase (tPA) in acute ischemic stroke resulted in a 55% reperfusion rate while leading to ICH in 11% (Pessin et al. 1990)

• ECASS and NINDS study with iv tPA: 10x higher risk of ICH is the cost for the significantly better functional outcome (JAMA, N Engl J Med 1995)
Antiplatelet therapy

- poor short-term outcomes, increased mortality, (rapid enlargement of ICH?), in patients taking regularly moderate doses of aspirin (250 mg)
  
  (Saloheimo et al., Stroke, 2006)

- antiplatelet therapy (197 mg) proved to be an independent predictor of 30D mortality
  
  (Roquer et al., J Neurol 2005)
Antiplatelet therapy - Update

- No association between antiplatelet therapy and:
  
  • initial ICH-volume
  • expansion of ICH
  • 90 D outcome

CHANT-investigators, Neurology, 2009
Broderick JP, Neurology, 2009
Hanger C, J Neurol 2008
OAC - indications

- atrial fibrillation
- cardiac valve replacement
- deep venous thrombosis
OAC – drugs

- **warfarin and coumarin**
- inhibit the formation of the reduced form of vitamin K in the liver that would activate prothrombin and factor (F)VII, IX and X.
- half life:
  - warfarin: 2d
  - coumarin: 7d

*From: Steiner T, Stroke 2006*
Monitoring of OAC

- INR - international normalized ratio
- does not reflect the level of FIX
- thrombelastography would be the “state of the art” approach
Monitoring of OAC

- 85% of OAC+ICH occurs in therapeutic (2-4) or subtherapeutic (under 2) INR-level

(Rosand C, Arch Int Med 2004, Steiner T, Stroke 2006)
Analysis of the Pécs Severe TBI Database

- 06/2002-12/2008 305 severe TBI

- Analysis of the effect of primary and secondary coagulopathy on mortality
ROC: on admission INR
Management of ICH

- independent predictors of outcome:
  - age
  - ICH-size
  - haematoma growth
    - IVH
    - hydrocephalus
  - anticoagulant, antiplatelet therapy, GCS on admission, blood glucose levels
Management of ICH

• Halt further hematoma expansion by: conservative and/or surgical treatment
Management of ICH

- conservative treatment:
- „hypertension appears to be a modifiable risk factor for morbidity and mortality from intracerebral hemorrhage” (Fric-Shamji E, Can Fam Physician 2008)

-Reversal of OAC
<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism of action</th>
<th>Dose required</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin K</td>
<td>activates prothrombin, FVII,IX,X</td>
<td>5-20mg, iv. is preferred over sc.</td>
<td>Cheep, delayed action, can be used for days</td>
<td>Delayed action: inadequate for acute reversal of OAC</td>
</tr>
<tr>
<td>PCC</td>
<td>Contains prothrombin, FVII,IX,X, protein C,S,Z in concentrated form</td>
<td>1 IU of F IX/kg body weight increases the level of plasma F IX by 1 IU/dL</td>
<td>Prompt action, all F in small volume, rapid reversal of OAC</td>
<td>Risk of thrombosis and DIC</td>
</tr>
<tr>
<td>FFP</td>
<td>All F in non-concentrated form</td>
<td>1 mL of FFP/kg body weight increases the levels of coagulation factors by 1 to 2 IU/dL.</td>
<td>Contains all F</td>
<td>Delay due to thawing, F-level is not reliable, circulatory overload</td>
</tr>
<tr>
<td>Activated FVII</td>
<td>Activated FVII</td>
<td>5 to 30, max. 320 ug/kg</td>
<td>Prompt action, documented reduction in haematoma growth</td>
<td>No documented change in outcome Increased arterial thromboembolism</td>
</tr>
<tr>
<td>Surgery</td>
<td>Halt haematoma growth, provide surgical haemostasis</td>
<td>Within 2-24 hrs to reduce haematoma growth</td>
<td>Prompt reduction of ICP, prevention of haematoma growth</td>
<td>No benefit except a subset of patients</td>
</tr>
</tbody>
</table>
Recombinant activated factor VII.

- phase IIB randomized, double-blind, placebo-controlled, dose-ranging "proof-of-concept" trial, 399 ICH patients
- 50% relative reduction in haematoma growth (40, 80, and 160 µg/kg),
- an average reduction in absolute ICH growth of 5 mls.
- 38% relative reduction in mortality and significantly improved functional outcome
- 5% frequency of arterial thromboembolic events (primarily ischemic stroke and myocardial infarction).
- FAST trial [Factor Seven for Acute Haemorrhagic Stroke Treatment]

Factor Seven for Acute Hemorrhagic Stroke (FAST) study

- 16th European Stroke Conference, Glasgow, May 2007
- „Shock and Disappointment.“ (Stephan Mayer, Columbia University, NY)
- 20 µg/kg or 80 µg/kg of rFVIIa with placebo in 821 patients with ICH at 180 sites
- Patients > 18y, diagnosed within 3 hours of symptom onset by CT scan, treatment administered within 1 hour of baseline scan.
- Main outcome was the proportion of patients who died or had severe disability graded as 5 or 6 on the mRS at 90 days.
- the drug effectively stopped intracerebral bleeding
- Proportion of patients who died or were severely disabled at 90 days:
  - Placebo 24%
  - rFVIIa 20 µg/kg 26%
  - rFVIIa 80 µg/kg 29%
- a subgroup of younger ICH patients (less than 75 years) who, if treated within 3 hours of symptom onset, may benefit from rFVIIa treatment...
Reversal and resumption of anticoagulant therapy

- **Reversal:**
  - prothrombin complex concentrates
  - +/- fresh frozen plasma
  - or: recombinant activated factor VII.
  - discontinuing anticoagulant therapy with administration of vitamin K does not reverse the hemostatic defect for many hours and is inadequate

- **Resumption:**
  - *primary prevention* of ischemic stroke in elderly patients with nonvalvular atrial fibrillation: risk of recurrent ICH may outweigh its benefit
  - in patients with prosthetic cardiac valves or for *secondary prevention* in atrial fibrillation the risk-benefit assessment favors reinitiation of anticoagulation.

Reversal and resumption of anticoagulant therapy

- *in the absence of anticoagulants the chance for thromboembolic complication is 22/100 patient year that is 0.06%/day*

  Cannegieter SC, Circulation 1994
Surgical treatment

• **Goal:**
  - inhibit haematoma growth
  - inhibit early oedema formation
  - improve local CBF
  - prevent IVH
  - treat or prevent raised ICP

• **Contraindications:**
  - age
  - volume
  - location
  - miscellaneous
Age

- 60y or older had a poor prognosis in several studies
- 65y, rapidly progressive haematoma: 100% mortality
- particularly close association in thalamic haemorrhages
Volume/Location

- largest diameter (A), diameter orthogonal to it (B) and the number of 1-cm slices (C):
  \[ V = \frac{4}{3} \pi \times ABC \div 8 \]
- \[ ABC \div 2 \]
- volume over 30cc, GCS under 9 is associated with poor outcome
- thalamic haemorrhages d>3cm may have poor prognosis
- cerebellar haematomas over 4cm have poor prognosis
  (brainstem compression/propagation, occlusive hydrocephalus)
Volume/Location

• largest diameter ($A$), diameter orthogonal to it ($B$) and the number of 1-cm slices ($C$):
  \[ V = \frac{4 \div 3 \times \pi \times ABC}{8} \]

• $ABC / 2$

• volume over 30cc, GCS under 9 is associated with poor outcome
• thalamic haemorrhages d>3cm may have poor prognosis
• cerebellar haematomas over 4cm have poor prognosis
  (brainstem compression/propagation, occlusive hydrocephalus)
Timing

- radiographic progression/rebleeding: 3-4 hours
- deterioration: 4-6 hours
- oedema formation: 7-8 hours
- further haematoma growth: up to 24 hours

- EARLY INTERVENTION IS SUGGESTED, PARTICULARLY IN P-FOSSA ICH!
Indications for surgery

- **1961 McKissock:**
  51% mortality for 244 operated cases
  with 100% mortality in comatose patients

- Lack of evidence for the beneficial role of surgical intervention

- **2006 Teernstra:**
  meta-analysis of surgery versus conservative treatment
  failed to show a statistically significant reduction in the odds of death (OR: 0.84, 95% CI: 0.67–1.07) in surgically treated patients

- Underpowered studies

  *(Acta Neurochir)*
Indications for surgery

Patients randomised to early surgery had their haematoma evacuated within 24h of randomisation by the method of choice of the responsible neurosurgeon, combined with the appropriate and best medical treatment.

- Primary outcome: death or disability (GOSe) 6 months after ictus
- Secondary outcomes: mortality, BI, mRS
## Indications for surgery

Table 4: Outcomes at 6 months

<table>
<thead>
<tr>
<th></th>
<th>Early surgery (n=468)</th>
<th>Initial conservative treatment (n=497)</th>
<th>Absolute benefit (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favourable</td>
<td>122 (26%)</td>
<td>118 (24%)</td>
<td>2.3 (-3.2 to 7.7)</td>
</tr>
<tr>
<td>Unfavourable</td>
<td>346 (74%)</td>
<td>378 (76%)</td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alive*</td>
<td>304 (64%)</td>
<td>316 (63%)</td>
<td>1.2 (-4.9 to 7.2)</td>
</tr>
<tr>
<td>Dead</td>
<td>173 (36%)</td>
<td>189 (37%)</td>
<td></td>
</tr>
<tr>
<td>Prognosis-based modified Rankin index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favourable</td>
<td>152 (33%)</td>
<td>137 (28%)</td>
<td>4.7 (-1.2 to 10.5)</td>
</tr>
<tr>
<td>Unfavourable</td>
<td>312 (67%)</td>
<td>351 (72%)</td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>4</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Prognosis-based Barthel index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favourable</td>
<td>124 (27%)</td>
<td>110 (23%)</td>
<td>4.1 (-1.4 to 9.5)</td>
</tr>
<tr>
<td>Unfavourable</td>
<td>341 (73%)</td>
<td>377 (77%)</td>
<td></td>
</tr>
<tr>
<td>Not recorded</td>
<td>3</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

Data are number (%). *Includes 17 patients who were alive at 6 months but status was unknown.
Indications for surgery

Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial

A David Mendelow, Barbara A Gregson, Helen M Fernandes, Gordon D Murray, Graham M Tsaftalis, D Terence Hope, Abbas Karimi, M Donald M Shaw, and David H Barer for the STICH Investigators


Interpretation Patients with spontaneous supratentorial intracerebral haemorrhage in neurosurgical units show no overall benefit from early surgery when compared with initial conservative treatment.
Indications for surgery

Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial

SUBGROUP ANALYSIS

• Patients with haematomas 1 cm or less from the cortical surface were more likely to have a favourable outcome from early surgery than those with deep haematomas.

• For patients in coma, surgery is probably harmful, and even at the most optimistic estimate, about 40 operations would be needed to achieve one more favourable outcome (probably upper severe disability) in such patients.
Surgical techniques, approaches

CRANIOTOMY

- minimally invasive – maximal access:
- operating microscope, microsurgical techniques
- small cortical incision
- *putaminal*: transcisternal-trans-Sylvian-transinsular approach with 2cm insular corticotomy
- use of self-retaining retractors (?)
- haemostasis is of crucial importance:
  - raise BP to assess rest-bleeding
- *other*: stay in the epicenter, while avoiding eloquent areas, minimize corticotomies
- apply ventriculostomy when necessary
Surgical techniques, approaches

BUR HOLE ASPIRATION

- minimally invasive – minimal access:
- control of the operative field is limited
- low efficacy, high rate of recurrence
Surgical techniques, approaches

STEREOTACTIC ASPIRATION

- 1965 Benes et al. (Acta Neurochir)
- deeply seated lesions
- with the aid of fibrinolytics, mechanically assisted devices, CT-, MR-guidance
- lack of direct visualisation
- risk of rebleeding
- from the medico-economical point it may have advantages in putaminal haematomas in moderately disabled patients

(Hattori et al., Surg Neurol, 2006)
Surgical techniques, approaches

FIBRINOLYTIC THERAPY

- Simple needle aspiration from a bur hole, followed by urokinase or tPA via a catheter
- the former also inhibits further clot-formation
- the latter is more effective
- risk of rebleeding: 6 hours delay suggested
- stereotactic guidance can improve accuracy
Surgical techniques, approaches

MECHANICALLY ASSISTED ASPIRATION

- suction of hard clot in conjunction with twist-drill maneuver
- complicated with limited or no advantage over other techniques
Surgical techniques, approaches

NEUROENDOSCOPIC TECHNIQUES

• stereotaxy or ultrasonography guided
• haematomas with ventricular expansion
• haematoma evacuation, third ventriculostomy, ventricular drainage
• Longatti et al., Stroke, 2004: 13 cases in 7y…
Summary-I.

- the treatment of spontaneous ICH is still controversial
- early aggressive medical management including BP control, neuro-ICU-treatment
- prompt reversal of anticoagulant therapy
Summary-II.

• despite the results of the STICH-trial one could speculate that early intervention to remove clot and provide haemostasis might improve outcome (inhibition of oedema formation and haematoma growth)

• failure of the FAST-study despite of significant inhibition of haematoma-growth speaks against these assumptions...
Summary-III.

SURGERY COULD STILL BE INDICATED:

1. in large lobar lesions situated not further than 1cm from the cortical surface
2. in cerebellar ICH with rapid deterioration and/or ICH d>3cm
3. moderate sized deeply seated haematomas with moderate neurologic deficit (GCS over 8) where an ultra-early intervention (within 4-8hrs of haemorrhage) is feasible
4. in cases where the age (young patient), praemorbid status, lack of comorbidity and rapid progression of symptoms, signs and ICH-size calls for surgery
Summary-IV.

SURGERY IS NOT INDICATED:
1. in large putaminal/thalamic lesions (d>3cm, GCS>9)
2. volume over 30cc, GCS under 9
3. age over 60, GCS under 9
4. rapid ICH-growth with IVH and coma on the basis of coagulopathy
5. brainstem haemorrhages
Dilemmas of p-fossa hematomas

• relatively older population
• rapid deterioration:
  – hydrocephalus
  – brainstem compression
  – coning
• shorter therapeutic window
factors associated with outcome

(Dammann et al., Neurosurg Rev 2011 34:77-86)

• GOOD OUTCOME:
  – GCS ≥ 13
  – Hess-Bassetti consciousness score ≤ 2

• POOR OUTCOME:
  – tight p-fossa
  – brainstem compression
  – hematoma size is not necessarily a player!
Summary - I

• Close observation of all cases with a neurosurgeon nearby is mandatory
• deterioration and secondary surgery do not necessarily preclude good outcome
• evd should not necessarily been followed by hematoma evacuation
• poor clinical condition is a bad predictor, yet early intervention can be lifesaving in these cases
Summary - II

• Surgery is indicated:
  - GCS 6-12, hematoma diameter is 4cm
  - bleeding and edema compressing 4th ventricle regardless the size of the hematoma

• Surgery is contraindicated:
  - GCS under 6 for more than an hour and the patient is over 70
  - brainstem propagation
  - life expectancy is under 1y due to other condition

• Ventriculostomy (stand alone) can be done:
  - the bleeding is under 4cm, GCS is over 12
Summary - III

• Method of choice:
  - Ventriculostomy and ICP monitoring either contemporarily, before or after surgery
  - decompressive -fossa craniectomy
  - w/o CI-II laminectomy
  - w/o duraplasty
• INDIVIDUAL JUDGEMENT

• COMMONSENSE APPROACH
Aknowledgement

• Prof. Dr. Tamas Doczi, M.D., Ph.D., D.Sc., Head of the Department of Neurosurgery,
• Ferenc Kover, M.D., Ph.D.
• Ferenc Veto, M.D., Ph.D.
• Laszlo Szapary M.D., Ph.D. (Dept. Neurology),
• Monika Szots, M.D. (Dept. Neurology),
Medical Faculty, University of Pecs, Hungary