SNO-SIN
MEETING DELLE NEUROSCIENZE TOSCANE
DALLA EPIDEMIOLOGIA AI PERCORSI INTERDISCIPLINARI
Grosseto, 6-8 aprile 2017

Diagnosi e management dell'emorragia cerebrale intraparenchimale

UNIVERSITÀ DI SIENA
1240

Vitaliano Francesco Muzii
Neurochirurgia
Dipartimento di Scienze Mediche, Chirurgiche e Neuorscienze

- 10-15/100.000 per year
- 10-30% of all stroke admissions
- Race and socio-economic factors
- Doubling incidence every 10 yrs after age 35
- 22-62% mortality (half within 2 days after onset)
- Independent factors for mortality:
  - Large ICH volume, IVH, infratentorial location
  - Coma
  - Older age
- 20% independence at 6months
- US$ 125,000 per year

- Definition
  - Primary: “spontaneous rupture of small arteries or arterioles damaged by chronic hypertension or amyloid angiopathy” *(Mayer& Rincon, Lancet Neurol, 2005)*
  - Secondary: trauma, aneurysm, vascular malformation, coagulopathy, tumor, etc.
- Location:
  - Deep (basal ganglia) 50%
  - Cerebral hemispheres (lobar) 35%
  - Cerebellum 10%, brainstem 5%
- IVH 40-45% → 50% hydrocephalus
  - raised risk of death from 20 to 51%

Background

- “Despite extensive study, no medical or surgical intervention has ever been demonstrated to reduce mortality or improve outcomes in patients with ICH” *(Zuckerman, World Neurosurgery 2017).*

- “…most patients present with small ICHs that are readily survivable with good medical care. This suggests that excellent medical care likely has a potent, direct impact on ICH morbidity and mortality” *(Hemphill, Stroke 2015).*

Risk factors

- Hypertension
  - 60-70% of primary ICH
  - Degeneration, fragmentation, fibrinoid necrosis (penetrating vessels)
  - *Charcot-Bouchard* aneurysms (distal arterioles 100-600 μm)
  - "Typical" location (BG, pons, cerebellum, deep white matter)
- Amyloid angiopathy:
  - 15% of primary ICH
  - Cerebral hemispheres
  - Less severe
  - Recurrence in 5-15%
- Alcohol abuse
- Hypercholesterolaemia
- Scarce evidence for smoking and antiplatelet agent
  (Stroke, 2001 and 2003)

AHA/ASA Guideline

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons, the Congress of Neurological Surgeons, and the Neurocritical Care Society

J. Claude Hemphill III, MD, MAS, FAHA, Chair; Steven M. Greenberg, MD, PhD, Vice-Chair; Craig S. Anderson, MD, PhD; Kyra Becker, MD, FAHA; Bernard R. Bendok, MD, MS, FAHA; Mary Cushman, MD, MSc, FAHA; Gordon L. Fung, MD, MPH, PhD, FAHA; Joshua N. Goldstein, MD, PhD, FAHA; R. Loch Macdonald, MD, PhD, FRCS; Pamela H. Mitchell, RN, PhD, FAHA; Phillip A. Scott, MD, FAHA; Magdy H. Selim, MD, PhD; Daniel Woo, MD, MS; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, and Council on Clinical Cardiology

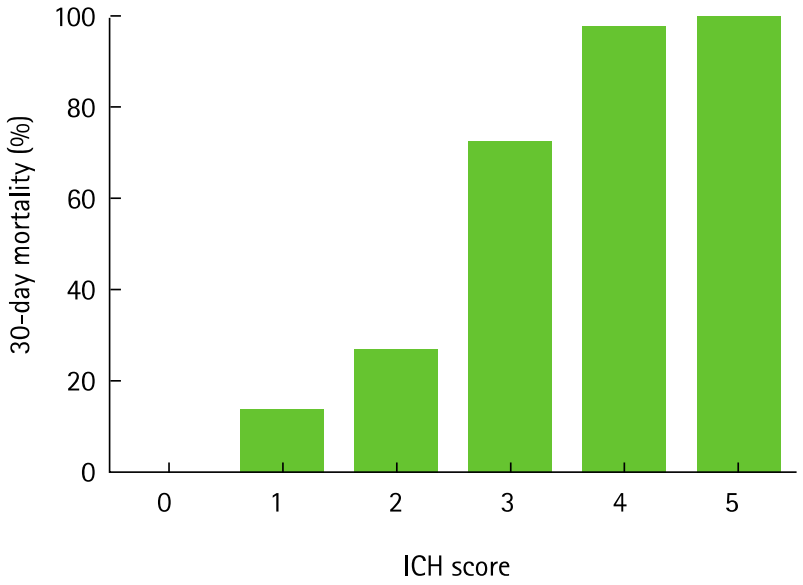
Stroke 2015

Emergency Diagnosis and Assessment

- Prehospital
  - 20% ↓ 2pts GCS from prehospital to hospital
  - Rapid diagnosis and management is crucial
  - ABC (preventing secondary injury, ICP raise, ICH expansion)
- Emergency Department
  - 15-23% continue deteriorating in the first hours after hospital admission
  - Severity score *(Class I, Level B)*
  - CT, MRI *(Class I, Level A)*

ICH severity score

Component	ICH Score Points
GCS score	
3–4	2
5–12	1
13–15	0
ICH volume (cm^3)	
≥ 30	1
< 30	0
IVH	
Yes	1
No	0
Infratentorial origin of ICH	
Yes	1
No	0
Age (year)	
≥ 80	1
< 80	0
Total ICH Score	0–6

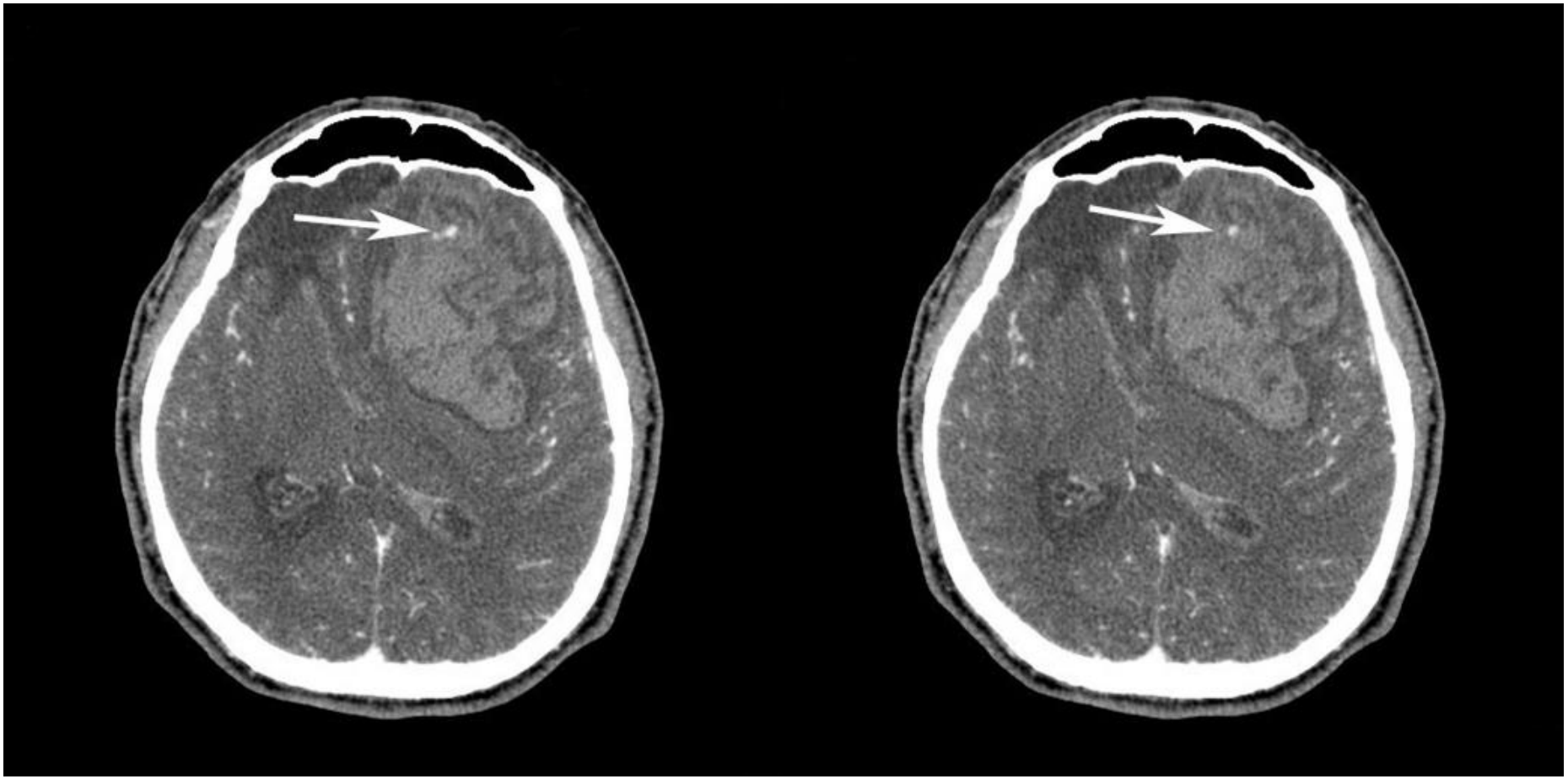


Hemphill et al. The ICH score: a simple, reliable grading scale for intracerebral hemorrhage. ***Stroke 2001.***

Neuroradiological assessment

- Early haematoma growth
  - 28-38% have >1/3 expansion within 3 hours
  - 2/3 of them within 1h
  - only 5% grow after 6h
  - Timing for repeated CT
- Risk factor for ICH expansion
  - High blood pressure
  - Anticoagulation
  - Spot sign CTA *(Class IIb, Level B)*

Spot sign



Rincon & Mayer. Clinical review: Critical care management of spontaneous intracerebral hemorrhage. ***Critical Care 2008.***

Neuroradiological assessment

- Secondary ICH
  - AVM, aneurysm, cavernoma, Dural AV fistula, venous angioma
  - Tumor
  - Trauma
  - Cerebral infarction
  - Dural sinus thrombosis
  - Vasculitis
  - Coagulopathy (iatrogenic)
  - Cocaine, sympathomimetic drugs

Neuroradiological assessment

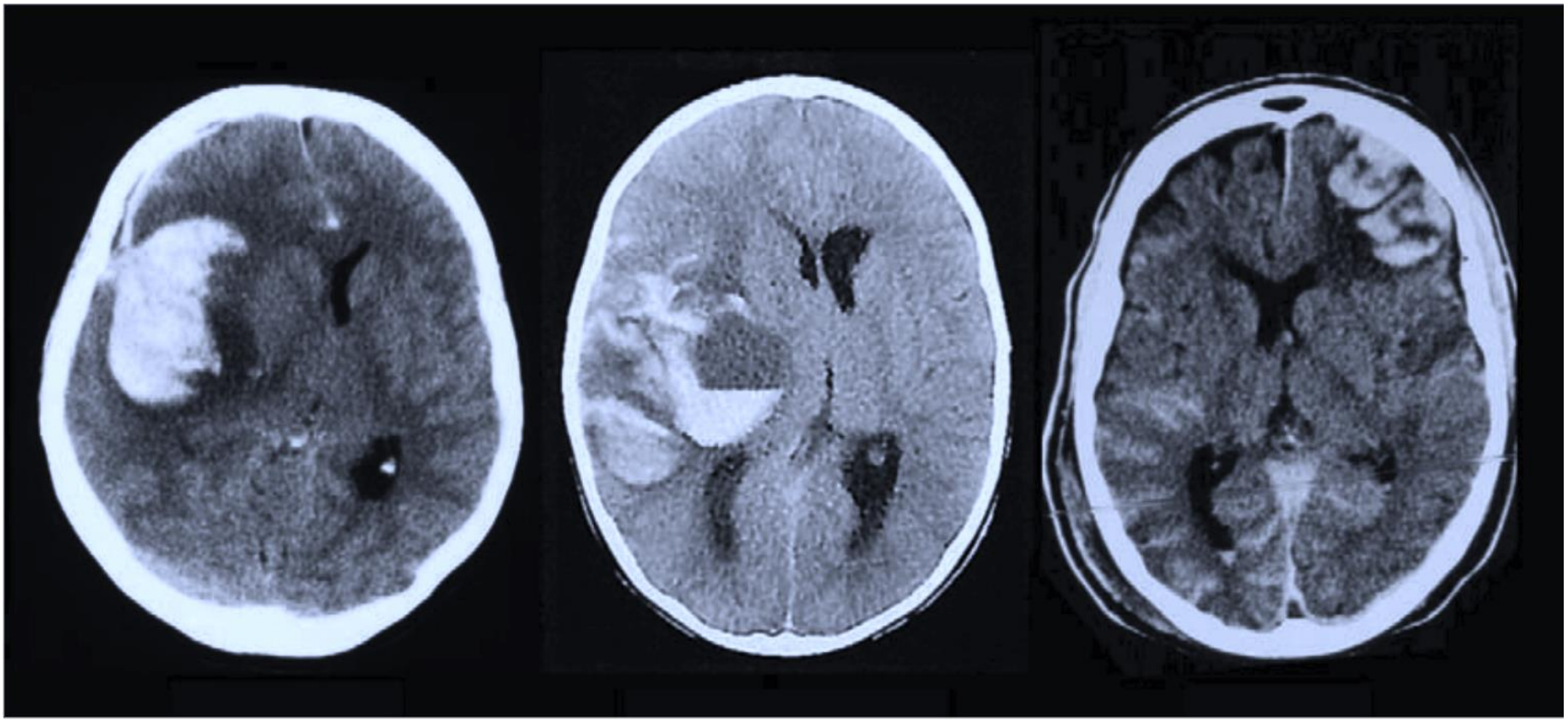
- Risk factors for underlying lesion
  - Lobar location
  - Age<55 yrs
  - No history of hypertension

No vascular malformation found with DSA in people over 45 with history of hypertension and “typical” location…

- Clinical/radiological suspicion *(Class IIa, Level B)*
  - CTA-CT contrast
  - MRI
  - DSA

…but vascular malformation found in 65% non-hypertensive people with IVH and lobar ICH (JAMA 2004)

Clues for secondary ICH



Rincon & Mayer. Clinical review: Critical care management of spontaneous intracerebral hemorrhage. ***Critical Care 2008.***

Medical treatment

- Haemostasis and Coagulopathy
- Blood pressure
- Glycaemia
- Body temperature
- Seizure
- ICP
- Medical complications

Haemostasis and Coagulopathy

- Oral anticoagulation therapy (OAC)
  - 5 to 10-fold risk of ICH
  - 12-20% of patients with ICH
  - Increasing with aging and anticoagulant therapy
  - ⬆ risk of expansion, two-fold risk of mortality after ICH
  - Vit. K antagonists (VKAs)
  - dabigatran, rivaroxaban, apixaban (lower risk than VKAs)

Vitamin K antagonist-related ICH

- Vitamin K needed but insufficient alone
  - 2-24h action time
- Fresh frozen plasma (FFP)
  - 17% with INR>1.4 at 24h *(Goldstein, Stroke 2006)*
  - Infection, allergy, large volume infusion
- Prothrombin complex concentrates (PCCs)
  - Rapid reversal (INR<1.3 after 30' in 69% vs 9% with FFP. *Sarode, Circulation 2013*)
  - Low volume, low risks
- rFVIIa
  - Does not replace all vit K dependent factors, clotting may not be restored
  - Not as effective as PCCs

AHA-ASA Guidelines 2015

VKAs related ICH

- vitamin K–dependent factors + i.v. vitamin K *(Class I, Level C)*.
- PCCs might be considered over FFP *(Class IIb, Level B)*.
- rFVIIa is not recommended for VKAs reversal in ICH *(Class III, Level C)*.

AHA-ASA Guidelines 2015

Antiplatelet agent-related ICH

- Conflicting results among studies for heamatoma growth and outcome
- The usefulness of platelet transfusions is uncertain *(Class IIb; Level of Evidence C)*

"Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial". *Lancet 2016*

- 190 randomized patients.
- Higher mortality and dependency rate with platelet transfusion

AHA-ASA Guidelines 2015

rFVIIa in not OAC-related ICH

- N Engl J Med 2005, Phase II trial: Limited hematoma growth and better outcome
- N Engl J Med 2008, Phase III trial: No benefit with an increased frequency of thromboembolic events compared with placebo
- rFVIIa is not recommended *(Class III, Level A)*

AHA-ASA Guidelines 2015

Blood pressure treatment

- Elevated BP is very common after ICH
  - Raised risk of expansion, neurological deterioration, death and dependency
- INTERACT2, N Engl J Med 2013:
  - Target SBP <140 vs <180 mmHg
  - Intensive treatment safe with better outcome but no difference in ICH growth
- With SBP between 150 and 220 mmHg acute lowering of SBP to 140 mm Hg is safe *(Class I, Level A)* and can be effective for improving functional outcome *(Class IIa, Level B)*
- With SBP >220 mmHg, aggressive reduction of BP with a continuous intravenous infusion is reasonable *(Class IIb; Level C)*

Surgical treatment

- Goals of surgery (clot removal)
  - Reducing ICP
  - Preventing herniation
  - Relieving mass effect and toxicity of blood products
- No clear benefit of surgery in RCT

STICH (Surgical treatment for ICH)

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

Lancet 2005; 365: 387–97

- 1033 pts, extended GOS at 6 months
- Favourable outcome:
  - 26% of surgery group
  - 24% of conservative group (n.s)
- Conclusion: "no overall benefit from early surgery when compared with initial conservative treatment"

STICH II

Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial

Lancet 2013; 382: 397–408

- 601 conscious pts, superficial lobar ICH, no IVH, within 48h
- extended GOS at 6 months
- Favourable outcome:
  - 41% of surgery group
  - 38% of conservative group (n.s)
- Reduced mortality: 18 vs 24% for surgery (n.s.)
- Benefit in poor prognosis pts (GCS, age, volume)
- Conclusion: " surgery might have a small but clinically relevant survival advantage for patients with spontaneous superficial intracerebral haemorrhage without intraventricular haemorrhage"

AHA-ASA Guidelines 2015

- Patients with cerebellar hemorrhage and:
  - neurological deterioration
  - or brainstem compression
  - and/or hydrocephalus from ventricular obstruction

  Surgical removal of hemorrhage as soon as possible *(Class I, Level B)*

  Initial treatment with ventricular drainage rather than surgical evacuation is not recommended *(Class III, Level C).*

- Decompressive craniectomy in patients with:
  - large hematomas with significant midline shift
  - or high ICP refractory to medical management

  Might reduce mortality for patients with supratentorial ICH in a coma *(Class IIb, Level C)*.

- Minimally invasive clot evacuation with stereotactic or endoscopic aspiration with or without thrombolytic usage:

  Effectiveness is uncertain *(Class IIb, Level B)*

- “For most patients with supratentorial ICH, the usefulness of surgery is not well established” *(Class IIb, Level A)*
- “A policy of early hematoma evacuation is not clearly beneficial compared with hematoma evacuation when patients deteriorate” *(Class IIb, Level A)*
- “Supratentorial hematoma evacuation in deteriorating patients might be considered as a life-saving measure” *(Class IIb, Level C)*

Conclusioni

- Il trattamento dell'emorragia cerebrale intraprenchimale è ancora oggi di efficacia limitata, poiché il danno primario è spesso determinante e non reversibile.
- La terapia medica massimale in ambito multidisciplinare resta il caposaldo per la cura dei pazienti con emorragia cerebrale, con l'obiettivo principale di prevenire l'espansione dell'ematoma, lo sviluppo di danno cerebrale secondario e le complicazioni sistemiche
- Il ruolo della chirurgia è limitato, anche i più recenti RCT e le linee guida sembrano confermare ciò che la pratica clinica e il buon senso hanno sempre suggerito al neurochirurgo: l'intervento è utile in quei pazienti non troppo gravi, che mostrano un deterioramento neurologico e che tuttavia hanno delle ragionevoli possibilità di recupero con un tempestivo svuotamento dell'ematoma