ICU Management of Acute Ischemic Stroke

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Disclosures / Objectives

- Disclosures: Grants / Research
  - NIH, DoD, UCB Pharma
- Objectives
  - Review ICU management of AIS
  - Discuss treatment options

Acute Stroke: Optimum Scenario

- Symptoms rapidly identified
- Early presentation to stroke center
- Head CT is negative
- ‘Clot-buster’ drug given
- Resolution of symptoms
- Short stay in ICU

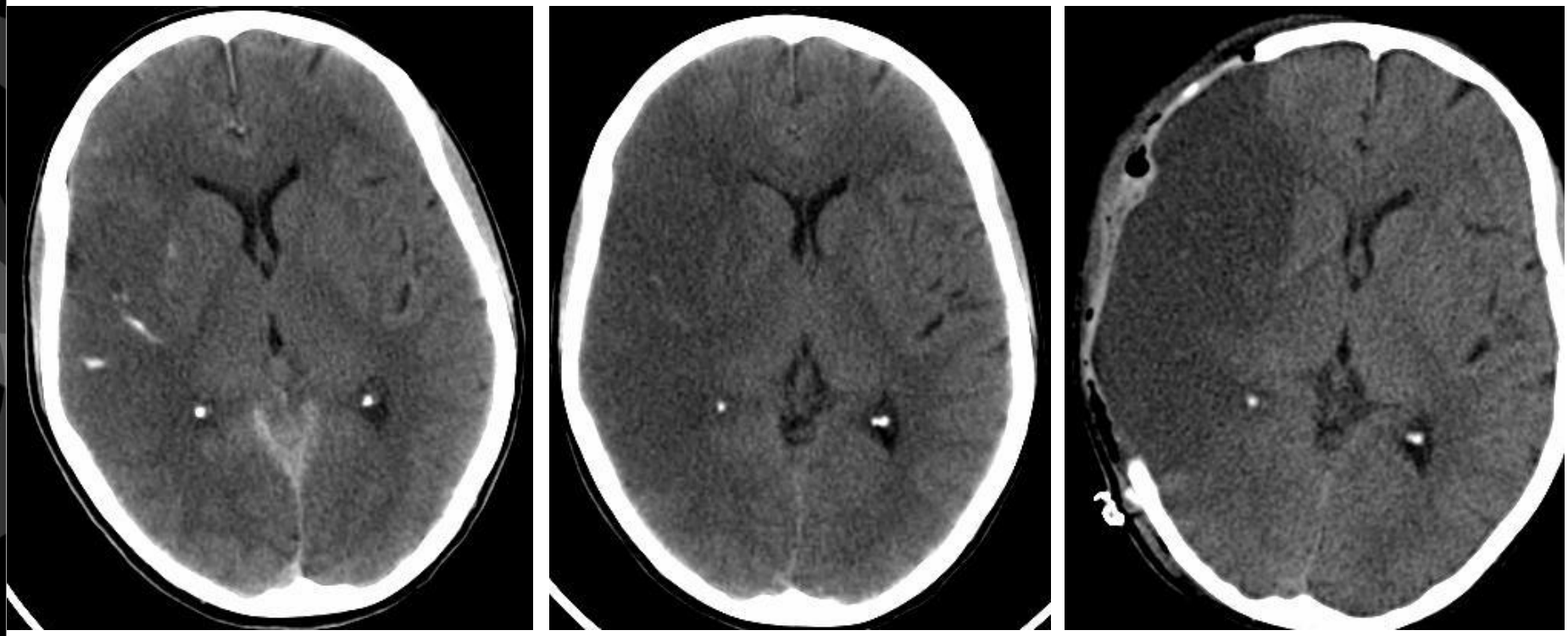
- Unfortunately that is not the typical scenario!

Case Presentation

- 45 yo F presented with acute onset of left sided weakness
  - NIHSS = 22
    - Arousable w/ stimulation, dysarthria, forced right gaze, left hemiparesis, sensory loss, neglect
  - OSH CT read a dense R MCA sign, not confirmed but subtle changes suggestive of hemispheric edema noted
- To angio suite (Day 0)

Case Presentation

- Day 1: lethargic, oriented x 1, following commands with right side. Had emesis x 2 so taken to CT



- Increase mass effect so to OR

Case Presentation

- Day 2 – Stopped following commands, sent to CT

- cEEG, showed epileptiform discharges, started LEV
- Day 6: fully awake, oriented x 4, left hemiplegia, taking po (dysphagia diet)
- Day 8 to rehab

Critical Care Issues

- Blood Pressure Control
- Stroke team, Neurology, or Neurosurgery?
  - How early after onset?
  - What type of stroke
- Medical Co-morbidities
- Mass Effect / Intracranial Hypertension

BP Contributing Factors

- Agitation / Pain
- Vomiting
- Seizures
  - Prophylaxis?
- Increased ICP
  - Avoid hypoxia, fever, hyperglycemia / D5
  - Raise HOB, ventilatory rate
  - Hyperosmotic vs hypertonic therapy

BP after Cerebrovascular Insult

- Data regarding prognostic value of BP is conflicting
- High BP has been associated with increased stroke mortality, impairment of functional outcome and stroke recurrence
- Other studies indicate low BP correlated with poor prognosis
- Problems with studies:
  - variable dx – AIS (embolic, lacunar), ICH
  - Select patients (stroke unit, study group)
  - Timing of BP control

BP Control: AIS

- Acute Ischemic Stroke (no tPA)
  - Generally < 220 / 120
  - Fluctuating symptoms: induced HTN w/ MAP ↑ by 20 – 25%
  - Exceptions
    - aortic dissection; acute MI; heart failure; acute renal failure; hypertensive encephalopathy
- Acute Ischemic Stroke (tPA)
  - < 185 / 110 before; < 180 / 105 after

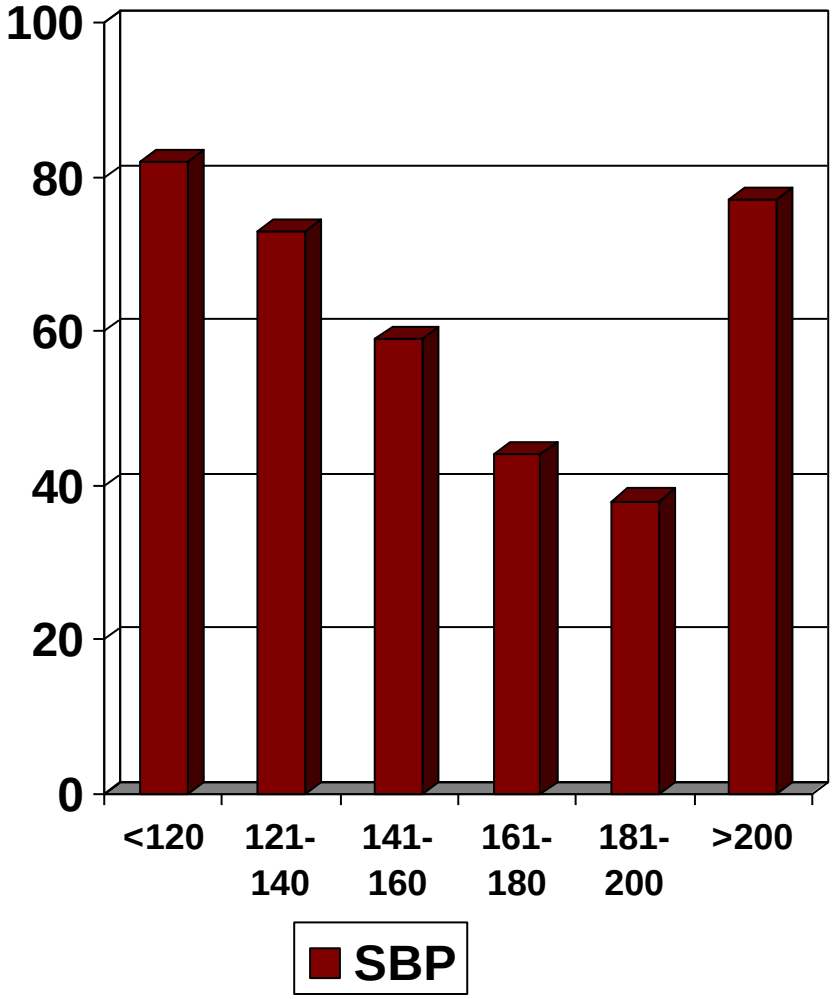
BP Control in AIS

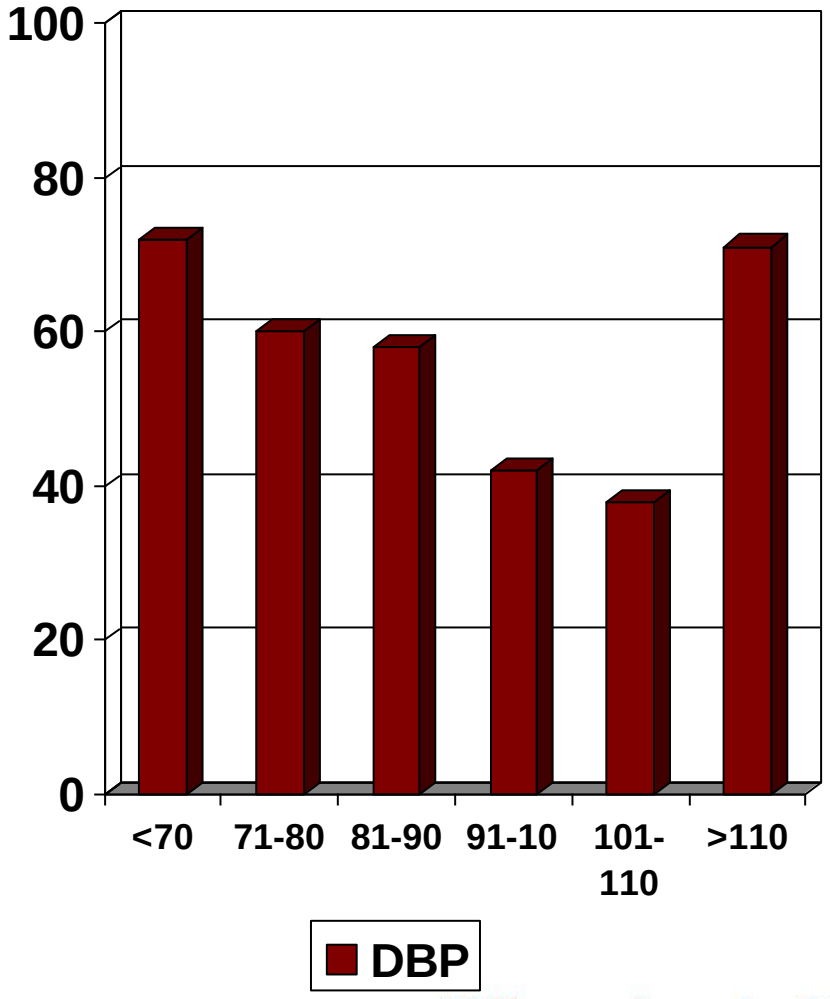
- Admission SBP associated with 1 & 12 month mortality[1]
  - Best mortality 121-140 mm Hg (13% / 25%). Mortality highest in SBP < 101 (35% / 52%); > 220 (29% / 57%)
  - Low SBP associated with heart failure & CAD
  - High SBP associated with hx of HTN, lacunar stroke and death from cerebral edema
- Changes in SBP also associated with mortality, 'END' & functional outcome[2]
  - Best outcome with SBP 180 – 200, DBP 101 – 110
  - SBP changes of 0 – 20 mm Hg had better mortality, lower END / poor outcome, & smaller stroke volumes

1. *Vemmos et al. J Int Med 2004; 255:257-265*
2. *Castillo et al. Stroke, 2004; 35:520-26*

Poor outcome after AIS Relative to Admission BP

Castillo et al. Stroke, 2004; 35:520-26





BP Control Agents

- Optimal agents
  - Short-acting continuous infusions
  - Reliable dose-response relationship
  - Favorable safety profile
- Acute Ischemic Stroke (no tPA)
  - General: labetolol, esmolol or nicardipine IV
  - Fluctuating symptoms / inducing HTN: phenylephrine, dopamine, norepinephrine
- Acute Ischemic Stroke (tPA)
  - Labetolol, esmolol or nicardipine IV

BP Control Agent 'Whys'

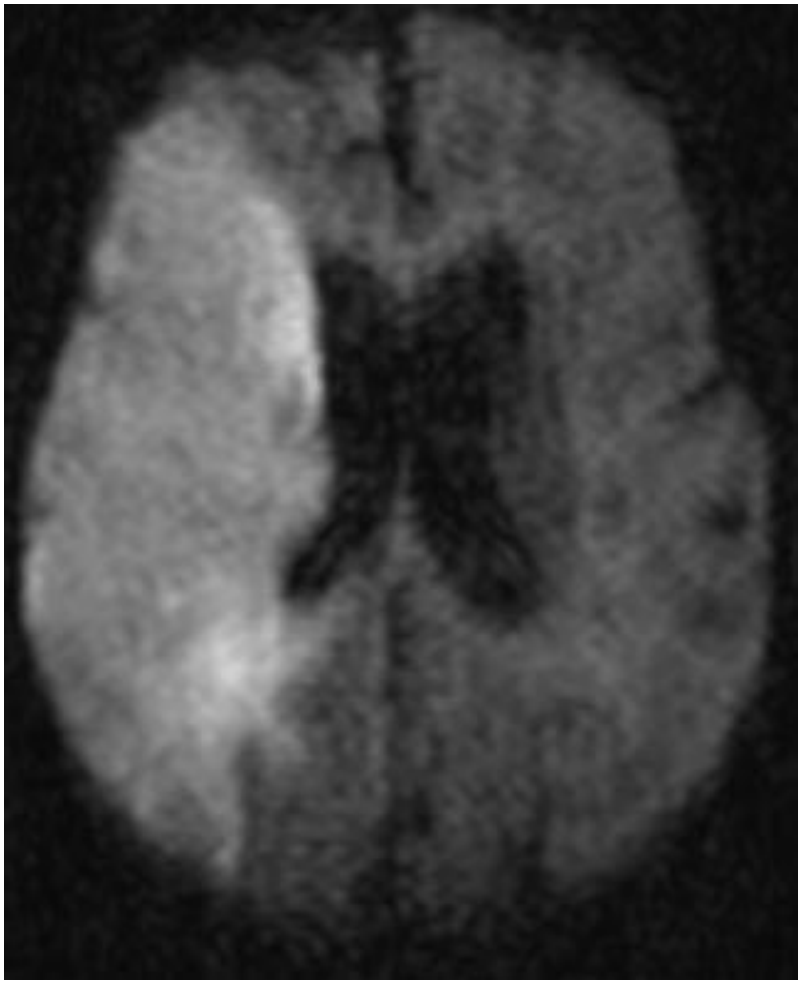
- Lower BP
  - Tachycardia: labetolol, esmolol
  - Bradycardia, CHF, COPD: nicardipine
- Raise BP
  - Tachycardia: phenylephrine
  - Bradycardia: norepinephrine, HD dopamine
- Augment CO when BP up
  - Dobutamine

BP Control Agent 'Whys'

- No Nipride
  - Dilates cerebral vasculature
  - Raises ICP, lowers CPP
  - Impairs autoregulation
  - Lacks smooth dose-response curve
    - Excessive hypotension in elderly or hypovolemic patients
    - Rebound hypertension during withdrawal
  - Cyanide, thiocyanate toxicity

ICP control in CVA

- Predominately cytotoxic
  - Symptoms usually develop 24 – 96 hrs post acute ischemia
- General principles
  - Steroids NOT effective
  - ICP monitoring is controversial
  - Penumbra at risk with traditional ICP therapies
  - Follow AANS guidelines and monitor for GCS ≤ 8



ICP Control in CVA: Treatments

- HOB > 30° to help venous drainage
- Hyperventilation
  - adjust tidal volume & rate to pCO_2 = 25 –30
  - Usually only effective for 6 hrs
  - Rebound ICP elevation if stopped abruptly
- Diuretic/osmotic therapy
  - Lasix or mannitol to ↓intravascular volume and free H_2O, must replace fluids. Limited data
  - ?? Hypertonic saline

Mannitol In Stroke

- 5 RCTs using mannitol for stroke, 4 of these used combination therapy, thus confounding results.
- Remaining study assessed 166 pts, with 3 treatment groups (ergot, dexamethasone, mannitol).
  - 36 patients received mannitol (0.8 – 0.9 gm/kg x 10 days)
- OUTCOME : Change in clinical condition

	Improved	Worsened
Control (N = 41)	14 (34%)	18 (44%)
Treatment (N = 36)	12 (33%)	16 (44%)

Santambrogio, et al. Stroke 1978;9:130-2

Mannitol in AIS

- Mannitol bolus preferentially shrinks non infarcted brain[1]
  - n = 6 MCA infarcts, 1.5gm/kg bolus
  - MRI done 50 – 55 minutes after baseline scan showed a ↓ in brain volume by 8.1 +/- 2.8 ml (0.6%, $p < 0.005$)
    - Non-infarcted hemisphere shrank 0.8 +/- 0.4%
    - Infarcted hemisphere shrank 0 +/- 0.5%.
- Mannitol impact on mortality[2]
  - n = 806, 2/3 treated with mannitol
  - Treated within 24 hrs: 1 yr mortality = 35% (26% plc)
  - Treated within 72 hours: 1mo mortality = 25% (16% plc); 1 yr = 38% (26% plc)

1. *Videen, et al. Neurology 2001; 57:2120-2*
2. *Bereczki, et al. Stroke 2003; 34:1730-5*

ICP Control in CVA: Treatments

- CSF drainage
  - Consider with hydrocephalus or IVH
- Mass evacuation / decompression
  - Cerebral vs. cerebellar lesion
- Barbiturate coma
  - No role do to side effects and no benefit

HTS in CVA

- Extremely limited studies; small numbers
  - Usually as rescue therapy
- ICP control
  - Variable concentrations & solutions
  - Bolus therapy vs continuous infusions
  - Most report Na^+ levels of 145 – 155
  - Results generally show effectiveness
- TUH: 10 AIS patients started on HTS
  - 7 had improved GCS of 1 – 3 points
  - CT done in 8 – worse in 2, stable in 6
  - 1 had decompressive hemicraniectomy 2° worsening
  - Adverse effects: pulmonary edema (1), persistent hypernatremia (1)

Steroids in Stroke

NO BENEFIT!!!

Pop the Top

Decompressive Hemicraniectomy: AIS

- Pooled analysis of 3 RCTs
  - DECIMAL, DESTINY, HAMLET
- Study design
  - 18 – 60 years treated within 48 h after stroke onset
  - Primary outcome measure: dichotomized mRS at 1 year between favorable (0–4) and unfavorable (5 and death)
  - Secondary outcome measures: case fatality rate at 1 year & dichotomized mRS between 0–3 and 4 to death
- Results
  - N = 93 patients
  - NNT = 2 for survival with mRS≤4
  - 4 for survival with mRS≤3;
  - 2 for survival irrespective of functional outcome

Lancet Neurol 2007; 6: 215–22

mRS

Table 1: Modified Rankin Scores		
Score	Classification	Description
1	**No significant disability**	**Able to carry on all usual activities**
2	**Slight disability**	**Some limitations in prior activities, but manages own affairs**
3	**Moderate disability**	**Requires help, but able to walk without assistance**
4	**Mod – severe disability**	**Requires assistance to walk & carry out bodily needs**
5	**Severe disability**	**Requires constant nursing care, bedridden**
6	**Death**	**Self explanatory**

mRS Results

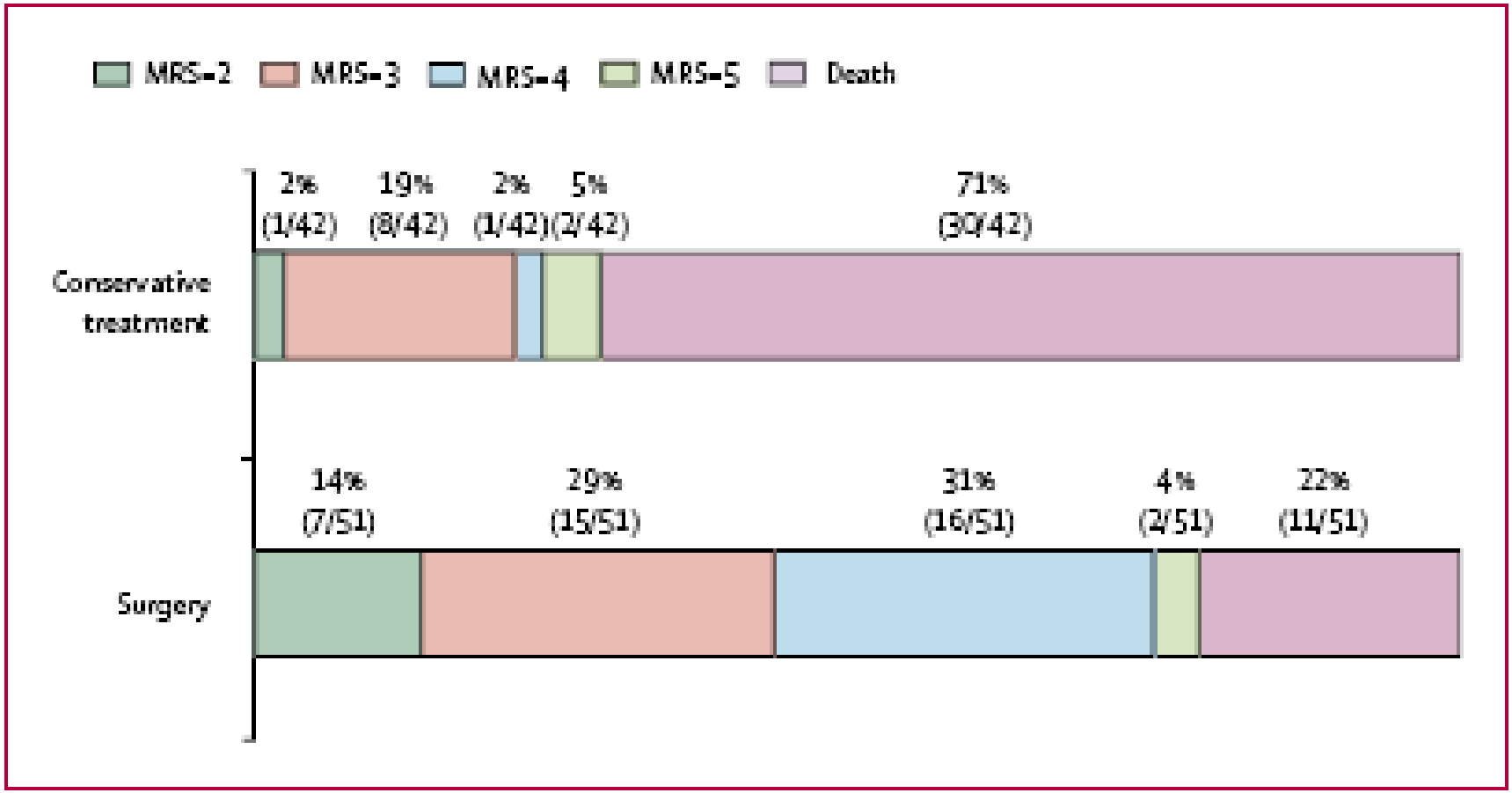


Figure 1: Distributions of the scores on the mRS and death after 12 months for patients treated with or without decompressive surgery

Decompressive Hemicraniectomy: TUH AIS Protocol

- Eligibility criteria
  - Age 18–60 years
  - Clinical deficits suggest MCA infarction with a NIHSS score >12 for dominant, > 10 for non-dominant.
  - Decrease in LOC to a score of 1 (ie, not alert, but arousable with minimal stimulation) or greater on item 1a of the NIHSS.
  - Infarct on CT/MRI involving at least 50% of MCA
- Triggers for decompression
  - Above + either clinical deterioration not explained by meds/other medical conditions; or CT with $\geq$ 4 mm ↑ MLS
  - Family discussion
  - 6 hrs since thrombolytic therapy

Decompressive Hemicraniectomy: TUH AIS Protocol

Exclusion criteria

- Absolute contraindications
  - Pre-stroke score on the mRS ≥ 3
  - Two fixed dilated pupils
  - GCS ≤ 4 without improvement in the first 24 hours.
  - Space-occupying hemorrhagic transformation
  - Life expectancy <3 years
  - Irreversible coagulopathy or systemic bleeding disorder
- Relative contraindications
  - Complete ICA distribution ischemia on affected side
  - Contralateral ischemia or other brain lesion
  - Other serious illness that could affect outcome

view: STICH
mparison: 01 Early surgery v initial conservative
tcome: 16 Prognosis based GOS

Favours surgery Favours control

udy sub-category	Early surgery n/N	Initial conservative n/N	OR (fixed) 95% CI	OR (fixed) 95% CI
age				
5	182/262	204/284		0.89 [0.62, 1.29]
65	164/206	174/212		0.85 [0.52, 1.39]
GCS				
CS 5-8	80/88	83/99		1.93 [0.78, 4.75]
CS 9-12	140/187	158/196		0.72 [0.44, 1.16]
CS 13-15	126/193	137/201		0.88 [0.58, 1.34]
side				
ft hemisphere	186/246	208/265		0.85 [0.56, 1.28]
ght hemisphere	160/222	170/231		0.93 [0.61, 1.40]
site				
bar	107/181	130/194		0.71 [0.47, 1.08]
sal ganglia/thalam	236/284	247/300		1.05 [0.69, 1.62]
volume				
50ml	211/302	238/323		0.83 [0.58, 1.17]
0 ml	135/166	140/173		1.03 [0.60, 1.77]
depth from cortical surface				
1cm	170/257	192/260		0.69 [0.47, 1.01]
cm	174/208	184/234		1.39 [0.86, 2.25]
intended method of evacuation				
aniotomy	238/324	267/337		0.73 [0.51, 1.04]
hers	108/144	111/159		1.30 [0.78, 2.15]
deficit of affected arm				
rmal/weak	110/182	135/206		0.80 [0.53, 1.21]
ralysed	231/279	238/284		0.93 [0.60, 1.45]
deficit of affected leg				
rmal/weak	150/229	169/248		0.89 [0.61, 1.30]
ralysed	192/232	201/239		0.91 [0.56, 1.48]
deficit of speech				
rmal	72/124	92/136		0.66 [0.40, 1.10]
sphasic/aphasic	216/276	228/289		0.96 [0.64, 1.44]
annot assess	58/68	58/71		1.30 [0.53, 3.20]
any antithrombolytic or anticoagulant thereapy				
nticoagulant thrpy	24/34	38/46		0.51 [0.17, 1.46]
anticoag.	322/434	340/450		0.93 [0.69, 1.26]
country				
K	43/60	49/62		0.67 [0.29, 1.54]
ermany	51/65	66/78		0.66 [0.28, 1.55]
pain	15/19	15/19		1.00 [0.21, 4.76]
land	25/33	33/42		0.85 [0.29, 2.52]
tvia	20/28	20/29		1.13 [0.36, 3.50]
huania	11/20	16/25		0.69 [0.21, 2.29]
ssia	19/26	15/20		0.90 [0.24, 3.43]
zech Republic	39/44	33/43		2.36 [0.73, 7.61]
acedonia	24/36	30/43		0.87 [0.33, 2.24]
outh Africa	29/43	27/34		0.54 [0.19, 1.53]
dia	26/38	35/43		0.50 [0.18, 1.39]
hers with <20 pats	44/56	39/58		1.79 [0.77, 4.14]

Depth

0.1 0.2 0.5 1 2 5 10

Favors early surgery Favors initial cons

Other Management Issues

- Fluids
  - Start with NS (no dextrose), aggressively treat low Na^+
  - Use ½ NS cautiously for high Na^+, can ↑ ICP
  - Avoid hypovolemia (associated w/ worse outcomes)
- Glucose control
  - Early hyperglycemia associated with poor outcomes
  - Recent study found patients w/ intensive glucose control had improved ICP & CPP control, fewer seizures, similar mortality (w/ lower GCS), and better 6 & 12 month outcomes

Other Management Issues

- Nutrition
  - Start tube feeds early, TPN if necessary
- DVT Prophylaxis
  - Start 24 hr after injury unless known hemorrhagic lesions or post-op. If so, start when CT stable.
  - SQ heparin and mechanical prophylaxis.
  - Surveillance: day 3 after admission, then q week
- Early rehabilitation
  - PM&R, PT, OT, Speech
  - positioning, splints, monitor for HO

Questions?

http://www.ucneurocriticalcare.com/physicians