Neuroprotective Effects for TBI

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Neuroprotection in Traumatic Brain Injury

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Disclosures

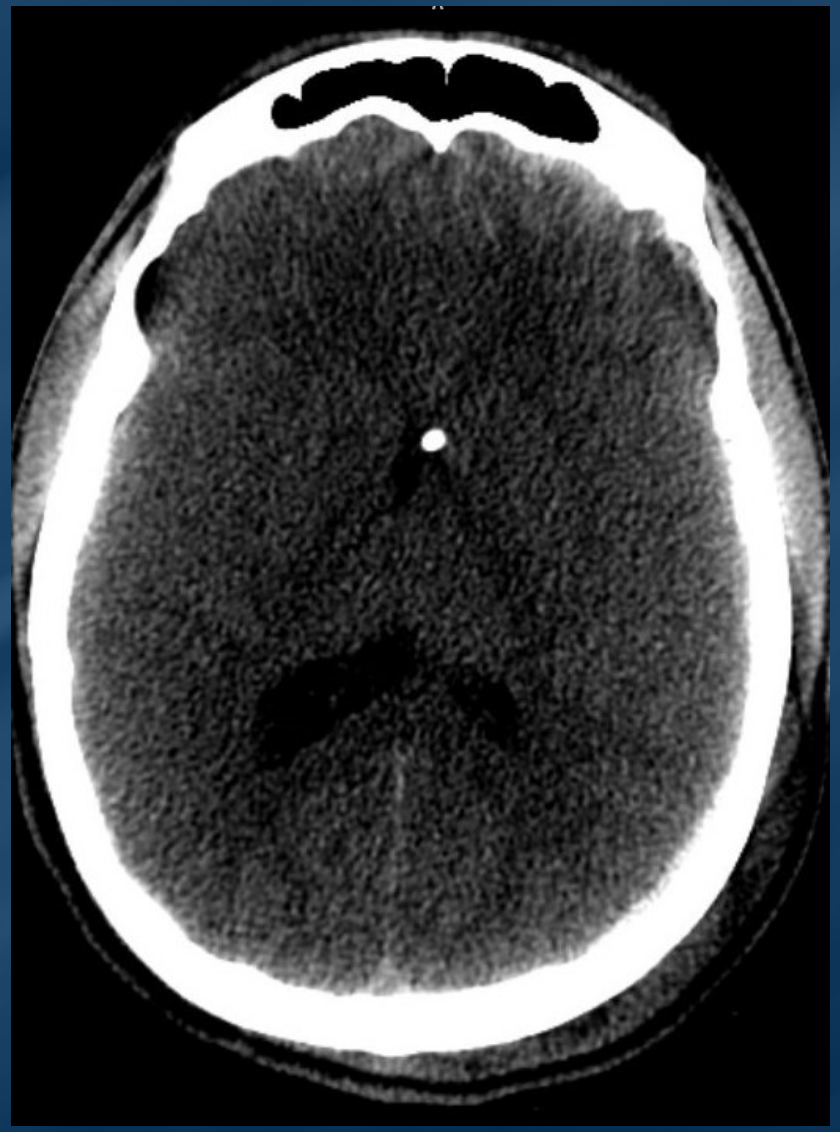
- I will discuss off-label use of medications
- Otherwise, nothing to disclose

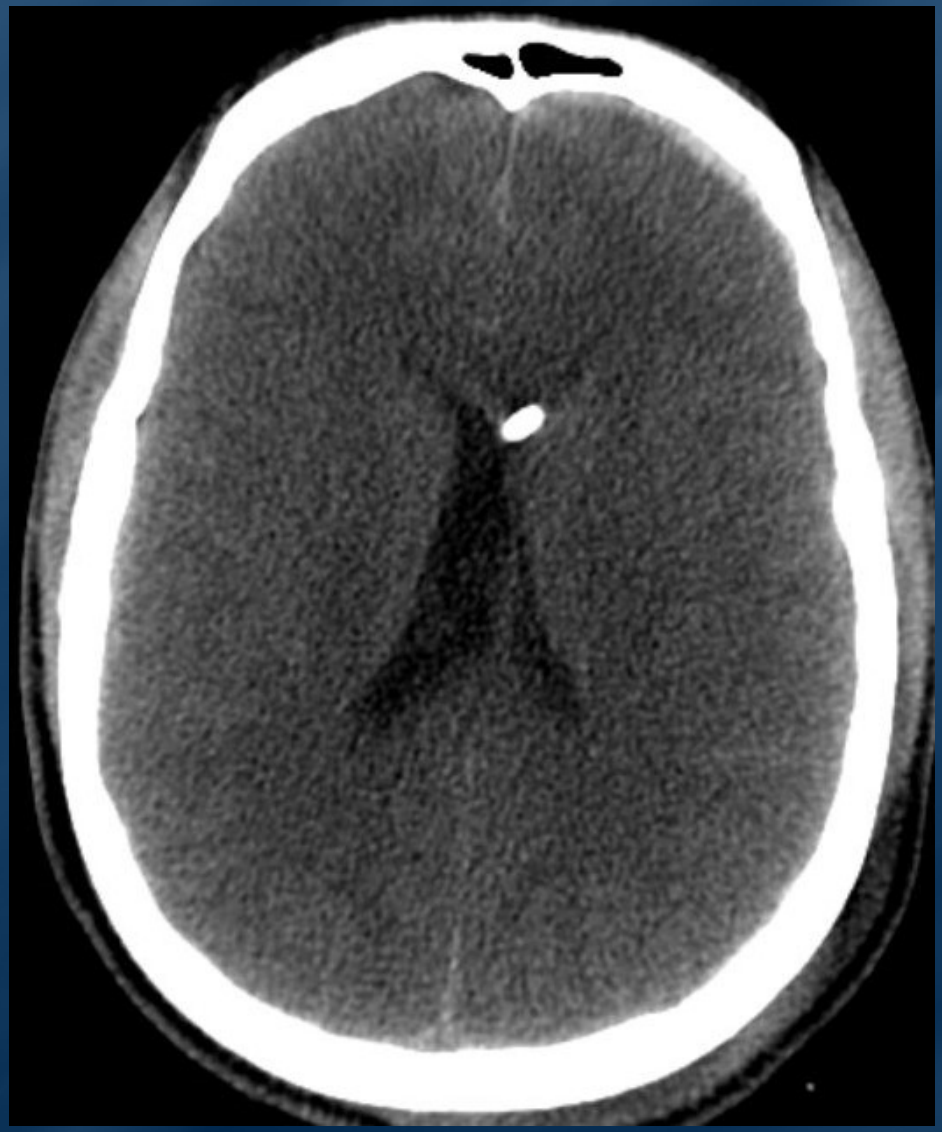
Talk Overview

- Clinical Case
- Sedation and analgesia strategies
- ICP and CPP optimization

Clinical Case

- XX yo male unhelmeted cyclist is struck by an automobile
- GCS 6 in field and on ED arrival. Intubated.
- CT head showed L frontal SDH, small bifrontal contusions and temporal bone fracture
- Briskly localizing upon arrival to neuro ICU. GCS E1V1TM5. EVD is placed





First-line neuroprotective measures

- Elevate head of bed
- Control pain and agitation
- Target normothermia
- Avoid hypotension
- Avoid hypercarbia and hypoxia
  - End-tidal CO_2 helpful for monitoring

Sedation goals in critical illness

Sedation Intensity in the First 48 Hours of Mechanical Ventilation and 180-Day Mortality: A Multinational Prospective Longitudinal Cohort Study*

Yahya Shehabi, PhD, FCICM, FANZCA, EMBA[1,2]; Rinaldo Bellomo, MD (Hons), FRACP, FCICM[3,4,5]; Suhaini Kadiman, MD, M.MED[6]; Lian Kah Ti, MBBS, Mmed[7]; Belinda Howe, RN, BN[8]; Michael C. Reade, MBBS, MPH, Dphil, FCICM[9]; Tien Meng Khoo, MBBS, MRCP, EDIC[10]; Anita Alias, MD, MMed(Anaesth)[11]; Yu-Lin Wong, FANZCA, MMed (ICM)[12]; Amartya Mukhopadhyay, FRCP, MPH[7]; Colin McArthur, MBChB, FANZCA, FCICM[13]; Ian Seppelt, MBBS, BSc (Med), FANZCA, FCICM[14]; Steven A. Webb, MPH, PhD, FCICM[8,15]; Maja Green, PhD, MSc, BSc (Hons)[1]; Michael J. Bailey, PhD, MSc (statistics), BSc (Hons)[1,8]; for the Sedation Practice in Intensive Care Evaluation (SPICE) Study Investig
New Zealand Intensive Care Society Clinical Trials Group

Balzer *et al. Critical Care* (2015) 19:197
DOI 10.1186/s13054-015-0929-2

CRITICAL CARE

RESEARCH Open Access

Early deep sedation is associated with decreased in-hospital and two-year follow-up survival

Felix Balzer[1], Björn Weiß[1], Oliver Kumpf[1], Sascha Treskatsch[1], Claudia Spies[1], Klaus-Dieter Wernecke[2], Alexander Krannich[3] and Marc Kastrup[1*]

TBI-specific analgesia and sedation?

Sedation for critically ill adults with severe traumatic brain injury: A systematic review of randomized controlled trials*

Derek J. Roberts, MD; Richard I. Hall, MD, FRCPC, FCCP; Andreas H. Kramer, MD, MSc, FRCPC; Helen Lee Robertson, MLIS; Clare N. Gallagher, MD, PhD, FRCSC; David A. Zygun, MD, MSc, FRCPC

Objectives: To summarize randomized controlled trials on the effects of sedative agents on neurologic outcome, mortality, intracranial pressure, cerebral perfusion pressure, and adverse drug events in critically ill adults with severe traumatic brain

cealed allocation and six were blinded. Insufficient data exist regarding the effects of sedative agents on neurologic outcome or mortality. Although their effects are likely transient, bolus doses of opioids may increase intracranial pressure and decrease ce-

neurocritical care society Neurocrit Care (2011) 15:175–181
DOI 10.1007/s12028-009-9315-8

PRACTICAL PEARL

Dexmedetomidine Controls Agitation and Facilitates Reliable, Serial Neurological Examinations in a Non-Intubated Patient with Traumatic Brain Injury

Julin F. Tang · Po-Liang Chen · Eric J. Tang · Todd A. May · Shirley I. Stiver

Clinical Case

- ~12 hrs after admission ICP sustains between 20 and 25 mm Hg
- ABG on 30% FiO2: 7.47/34/137
- Head CT shows no interval change in SDH or bifrontal contusions

- Next management step?

Anaesthesia, 1988, Volume 43 (Supplement), pages 42–43

Effect of propofol on cerebral blood flow and metabolism in man

A. VANDESTEENE, V. TREMPONT, E. ENGELMAN,
T. DELOOF, M. FOCROUL, A. SCHOUTENS
AND M. DE ROOD

Summary

Cerebral blood flow, cerebral oxygen consumption, lactate and glucose metabolism were measured in 13 patients during anaesthesia with nitrous oxide, oxygen and enflurane 0.5% and after 30 minutes infusion of propofol. The mean blood concentration

Clinical Case

- Sedation transitioned to propofol → ICP transiently decreased as did systolic blood pressure
  - Started on norepinephrine to maintain CPP > 60

- ICP abruptly increases to 36 mmHg during tracheal suctioning
  - Normalizes with administration of 30 cc 23.4% saline

Anesthesiology
57:242–244, 1982

A Randomized Study of Drugs for Preventing Increases in Intracranial Pressure during Endotracheal Suctioning

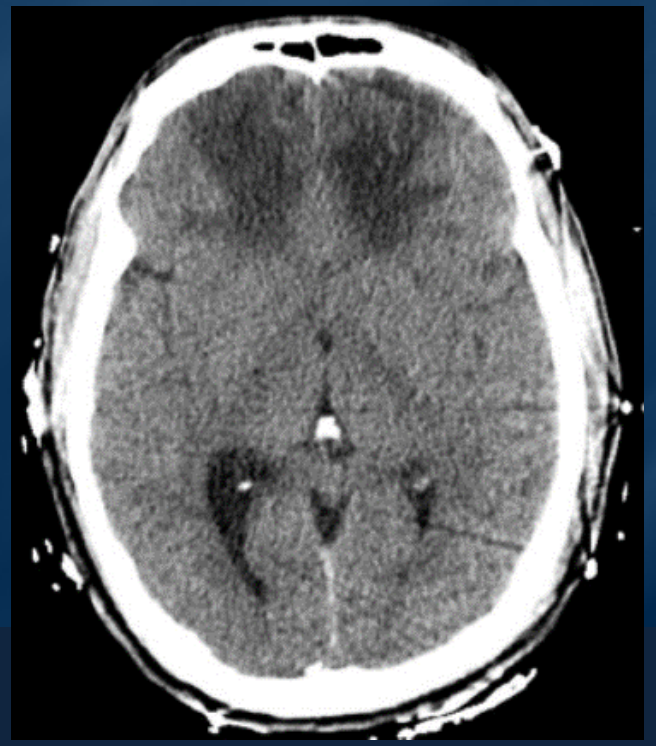
PAUL F. WHITE, M.D., PH.D.,* RICHARD M. SCHLOBOHM, M.D.,† LAWRENCE H. PITTS, M.D.,‡
JAMES M. LINDAUER, M.D.§

Prevention of cerebral ischemia and acute intracranial hypertension are the primary goals in managing patients

ants. However, the efficacy of thiopental or lidocaine in controlling ICP in nonparalyzed patients has not been

Clinical case contd.

- A few hours later ICP again spikes to 36 mmHg
  - Normalizes with mannitol administration
- Portable head CT obtained after bolusing propofol and fentanyl



Clinical Contd.

- Patient continued on propofol 80 mcg/kg/min and fentanyl infusion is uptitrated to 200 mcg/hr.
- Bolused 23.4% alternating with mannitol during ICP spikes. Na increases to 155 and serum osms to 330
- ICPs consistently sustaining > 25 with transient spikes into 30s and even low 40s anytime pt is stimulated
- CPP maintained > 60 mmHg except very brief periods during ICP spikes.

- Remaining management options?

Decompressive Craniectomy?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 21, 2011 VOL. 364 NO. 16

Decompressive Craniectomy in Diffuse Traumatic Brain Injury

D. James Cooper, M.D., Jeffrey V. Rosenfeld, M.D., Lynnette Murray, B.App.Sci., Yaseen M. Arabi, M.D., Andrew R. Davies, M.B., B.S., Paul D'Urso, Ph.D., Thomas Kossmann, M.D., Jennie Ponsford, Ph.D., Ian Seppelt, M.B., B.S., Peter Reilly, M.D., and Rory Wolfe, Ph.D., for the DECRA Trial Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

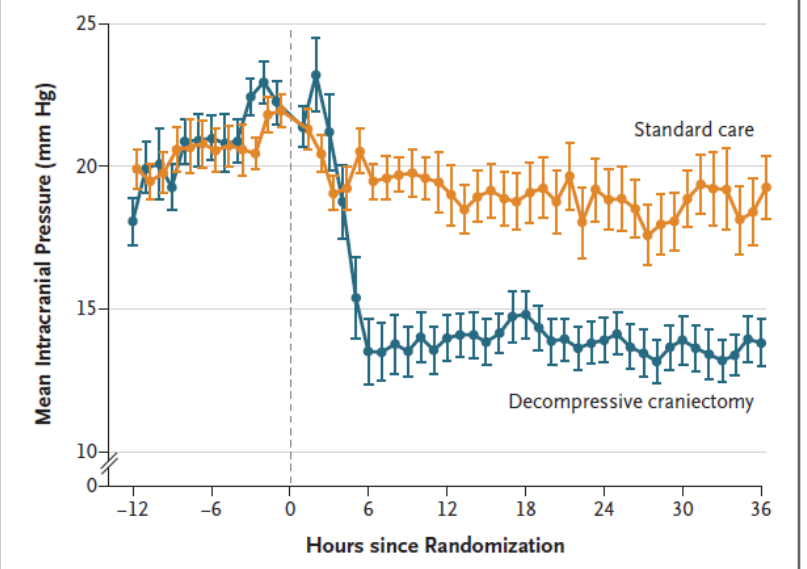
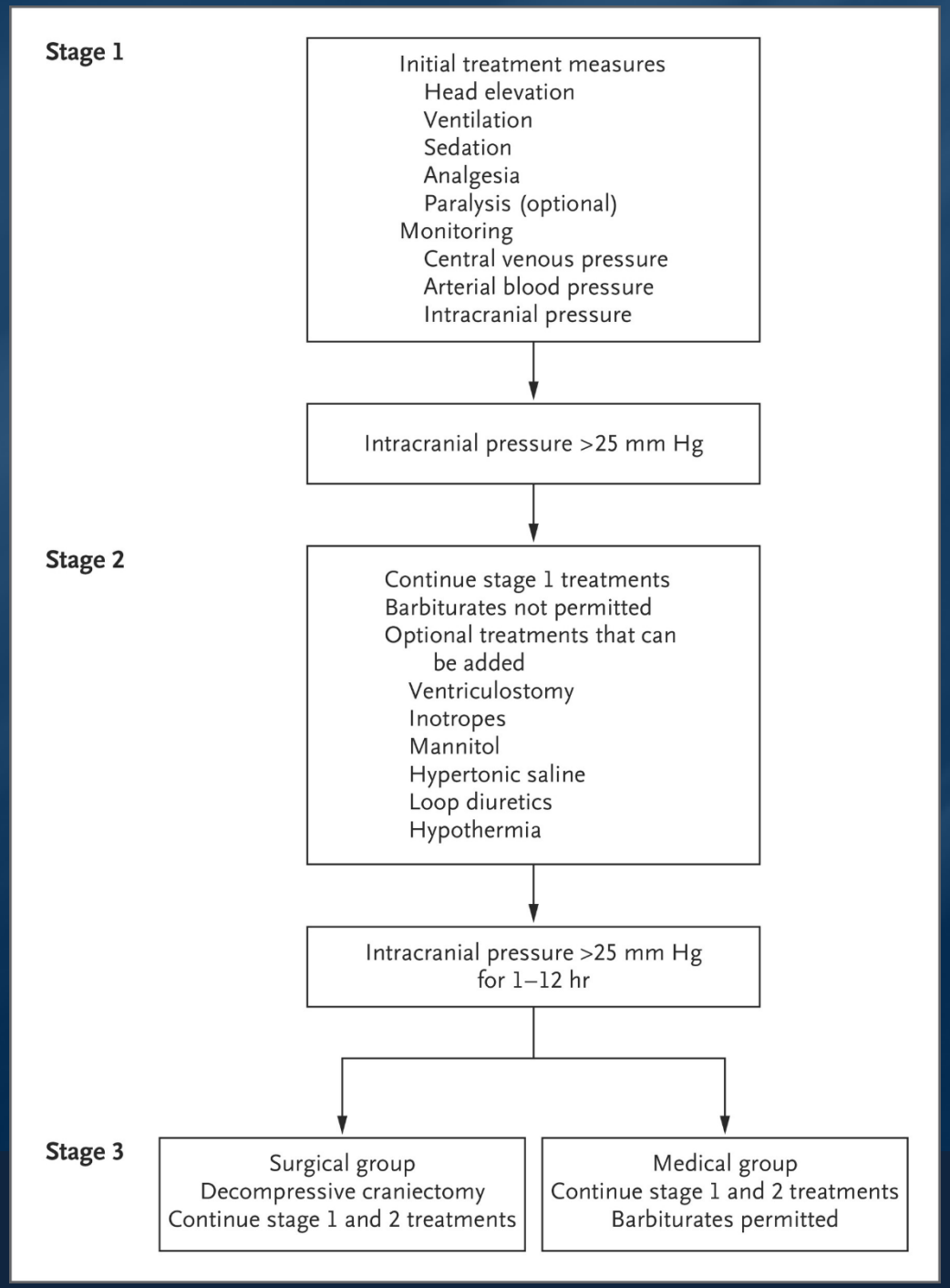
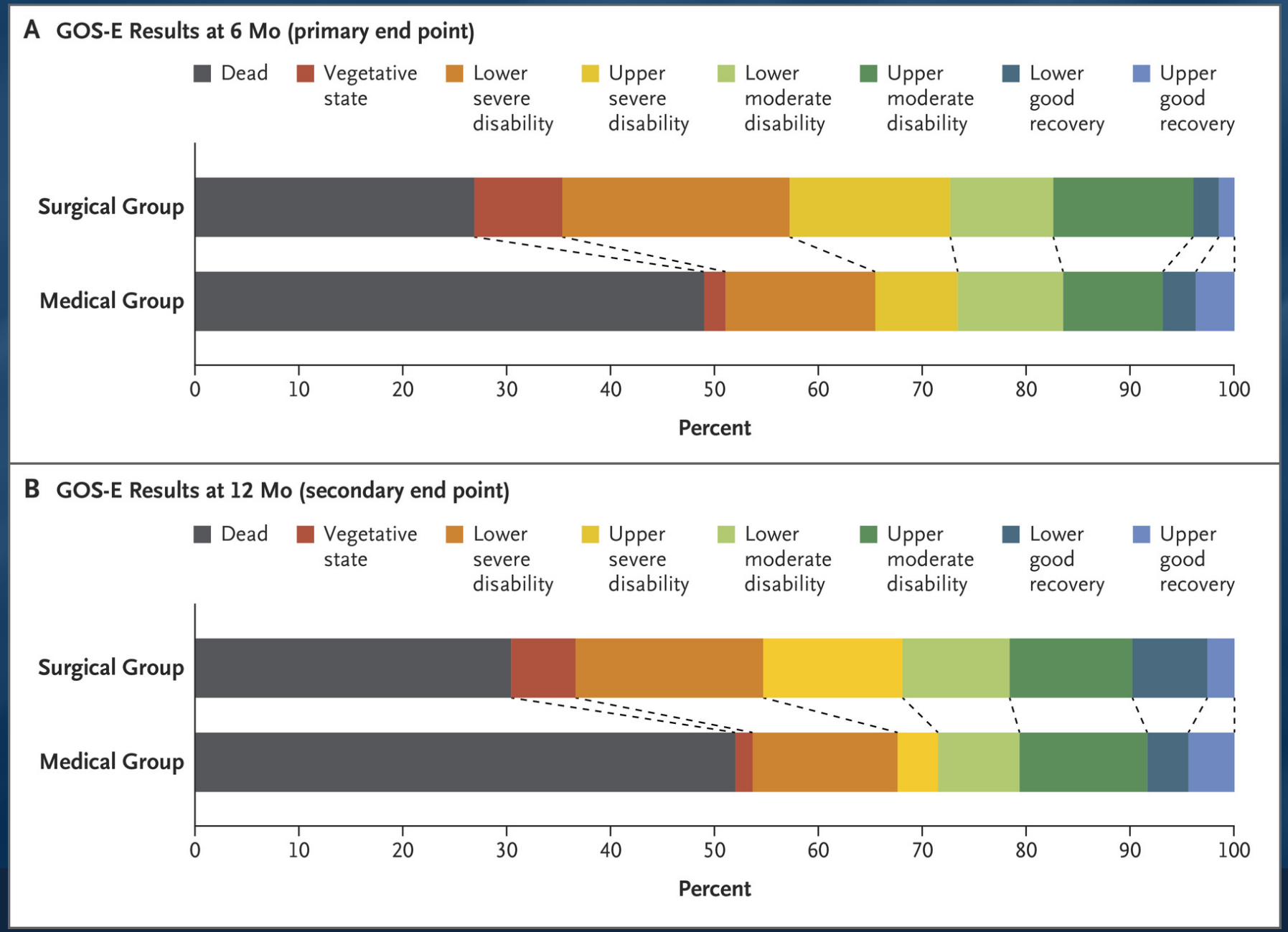


Figure 1. Intracranial Pressure before and after Randomization.
Shown are the mean measurements of intracranial pressure in the two study groups during the 12 hours before and the 36 hours after randomization. The I bars indicate standard errors.

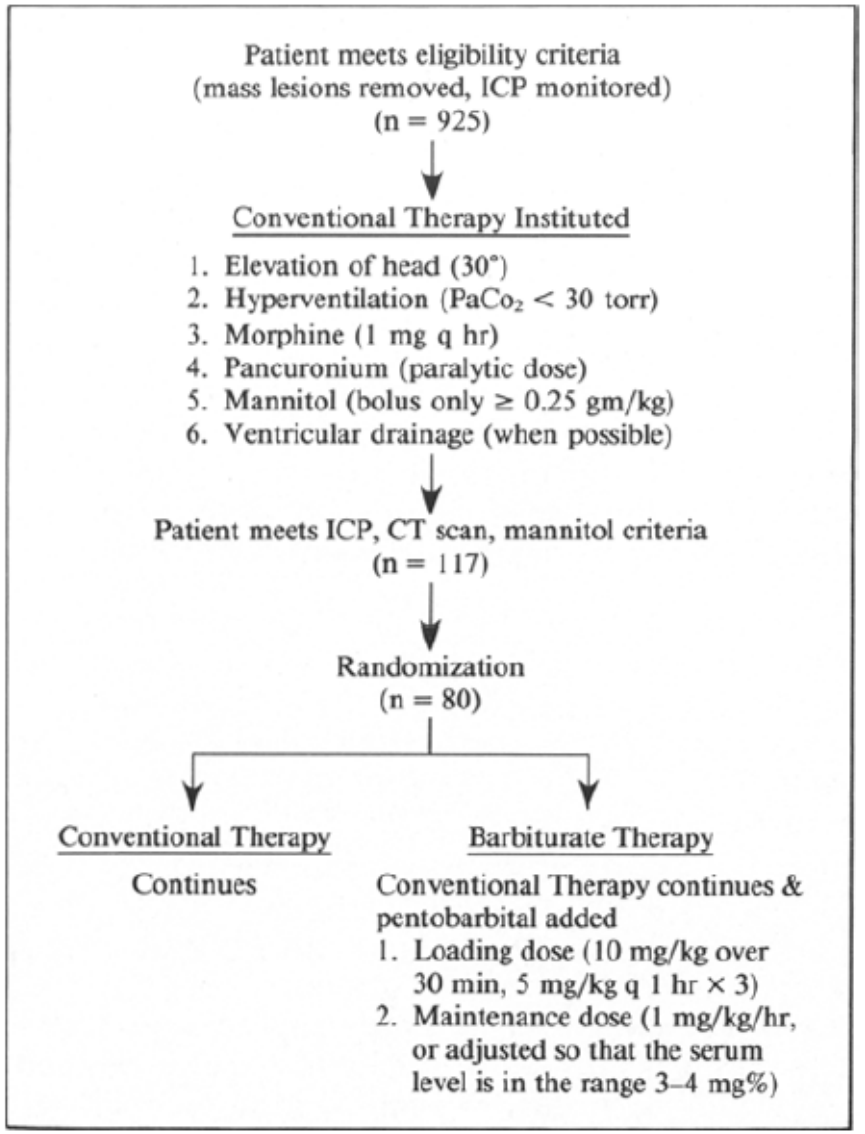

Stage 1
Initial treatment measures
Head elevation
Ventilation
Sedation
Analgesia
Paralysis (optional)
Monitoring
Central venous pressure
Arterial blood pressure
Intracranial pressure
Intracranial pressure >25 mm Hg
Stage 2
Continue stage 1 treatments
Barbiturates not permitted
Optional treatments that can be added
Ventriculostomy
Inotropes
Mannitol
Hypertonic saline
Loop diuretics
Hypothermia
Intracranial pressure >25 mm Hg for 1–12 hr
Stage 3
Surgical group
Decompressive craniectomy
Continue stage 1 and 2 treatments
Medical group
Continue stage 1 and 2 treatments
Barbiturates permitted


A GOS-E Results at 6 Mo (primary end point)
Dead
Vegetative state
Lower severe disability
Upper severe disability
Lower moderate disability
Upper moderate disability
Lower good recovery
Upper good recovery
Surgical Group
Medical Group
0
10
20
30
40
50
60
70
80
90
100
Percent
B GOS-E Results at 12 Mo (secondary end point)
Dead
Vegetative state
Lower severe disability
Upper severe disability
Lower moderate disability
Upper moderate disability
Lower good recovery
Upper good recovery
Surgical Group
Medical Group
0
10
20
30
40
50
60
70
80
90
100
Percent

Pentobarbital?

J Neurosurg 69:15–23, 1988

High-dose barbiturate control of elevated intracranial pressure in patients with severe head injury



Using pentobarbital in TBI

- Place continuous EEG and titrate to deep burst suppression (~1 burst/10s page)

- Load 10 mg/kg over 30 minutes
- Continue 5 mg/kg for 1-3 hrs until adequate sedation achieved on EEG

- Maintenance dose 1 mg/kg titrated to EEG burst suppression

Pentobarbital adverse effects

- Hypotension → increased pressor requirements
- Respiratory depression
- Ileus
  - Gut ischemia
- Venous thromboembolism
- Impaired cough and ciliary clearance → pneumonia and mucus plugging

Clinical case contd.

- ICPs ~ 20-30 with continued brief spikes with nursing care
- Cool to 34 C
- Continue to treat ICP spikes with hyperosmolar therapy
- Develops pneumonia, atelectasis, abrupt mucus plugging leading to severe desaturation
- Tracheostomy placed on post-trauma day 15 when first able to tolerate reverse Trendelenberg
- ICPs normalize by ~ day 18 and pentobarbital weaned
- Subsequently develops recurrent pneumonia → severe ARDS requiring paralysis and prone positioning

Clinical case contd.

- Pt developed stage 2 pressure ulcers
- Severe agitation and withdrawal → methadone and benzodiazepine taper necessary to wean off of high-dose sedation
- Discharged to acute rehab after 34 days
- Improves rapidly → initial neurocognitive performance in the average to above average range. Decannulated
- Neurocognitive scores all above average at the time of discharge from rehab 24 days later
- Patient discharged home and cleared to return to work without restrictions

Clinical case takeaways

- Be cautious in prognostication for young patients with severe intracranial hypertension
- Sustained ICP > 20 can be tolerated provided there is adequate cerebral blood flow and oxygenation
- Patients on prolonged barbiturate infusion *will* develop pneumonia, hypoxic respiratory failure and, usually, sepsis
  - Patient selection is important
  - Closely discuss risks/benefits of craniectomy with neurosurgery and patient's family
- Sedation and analgesia important factors in TBI
  - Avoid unnecessary oversedation, but sometimes it's necessary

Future Directions

ponding editorial in this issue, pp 891–892.

J Neurosurg 120:893–900, 2014

Patient-specific thresholds of intracranial pressure in severe traumatic brain injury

Clinical article

Christos Lazaridis, M.D.,[1,2] Stacia M. DeSantis, Ph.D.,[3] Peter Smielewski, Ph.D.,[1] David K. Menon, M.D., Ph.D., F.Med.Sci.,[4] Peter Hutchinson, F.R.C.S.(SN), Ph.D.,[1] John D. Pickard, F.R.C.S., M.Chir., F.Med.Sci.,[1] and Marek Czosnyka, Ph.D.[1]

Future Directions

- Improved methods to personalize ICP and CPP goals
- New monitoring methods may be helpful … or just provide additional data
  - Brain tissue oxygen monitoring
  - Cerebral blood flow monitoring
  - Autoregulatory assessment
- Better data to guide early prognostication and patient selection for 3rd line ICP therapies
- Clear guidelines for sedation and analgesia
- **High quality collaborative trauma care, not magic bullets, will improve patient outcomes**

Thank you!