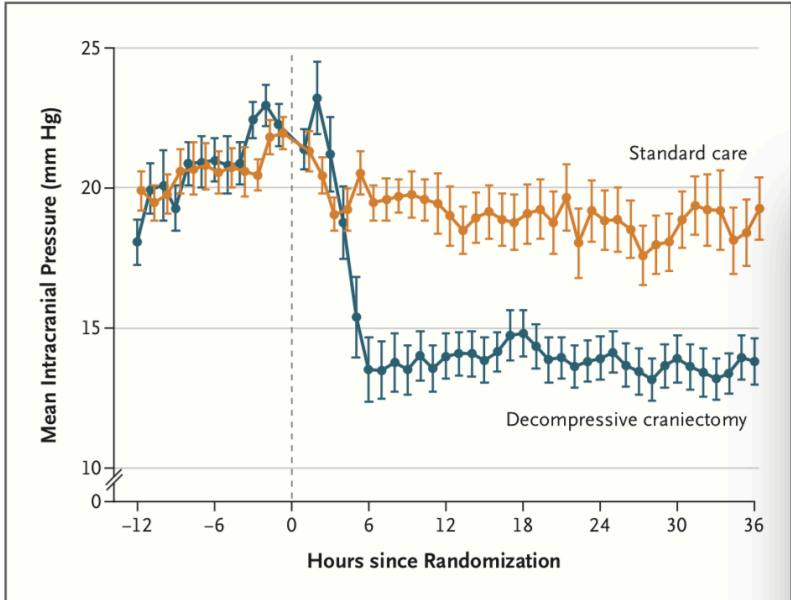


Discuss methods for reducing intracranial hypertension in traumatic brain injury

## Decompressive Craniectomy in Diffuse Traumatic Brain Injury – NEJM 2011, DECRA Trial - seminal article

- METHODS
  - Severe, non-penetrating TBI (GCS 3-8) or moderate diffuse injury on CT
  - Refractory hypertension = increase in ICP for more than 15mins within 1hr despite optimized first tier interventions including external ventricular drainage
  - Randomized to either standard care or standard care + craniectomy
  - Surgery = large bifrontotemporoparietall craniectomy with bilaterally opening of dura (bone frozen or stored SQ to replace in 2-3months!)
  - Additional tier 2 measures = mild hypothermia &/or barbituates
  - Unfavorable outcome = death, vegetative state or severe disability at 6months
- RESULTS
  - 155 enrolled
  - Similar baseline characteristics except **less reactive pupils in craniectomy group**
  - 15 patients in standard care group had delayed craniectomy at 72hrs, another 4 had craniectomy prior to 72hrs against protocol
  - Craniectomy had lower ICP
  - Craniectomy had shorter ICU, shorter ventilation, no difference in hospitalization
  - 37% had complications with treatment vs 17%
  - Functional outcome worse in craniectomy (OR 1.84, 2.31 after adjusting for other variables)
  - **After adjusting for the difference in pupil reactivity at baseline there was no significant difference** (OR 1.9, CI 0.95-3.79)
  - No difference in death at 6months
- Limitations
  - Patients had craniectomy as rescue – these were clearly more effected – what group were they included in?
  - Cannot apply to other methods of surgery eg unilateral
  - Specific for diffuse TBI
  - Eg hematomas should be surgically evacuated
- DISCUSSION
  - Decreased function due to axonal stretch with swelling outside skull?

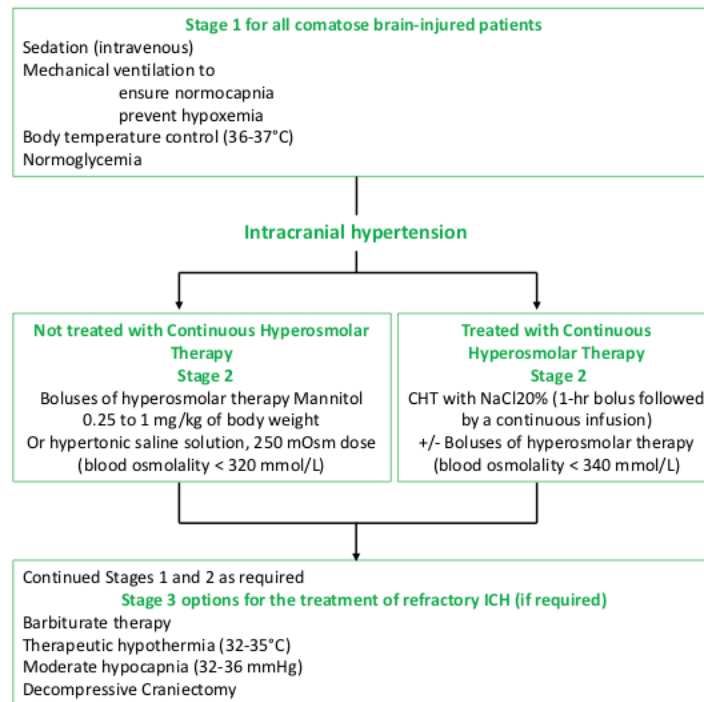


**Figure 1. Intracranial Pressure before and after Randomization.**

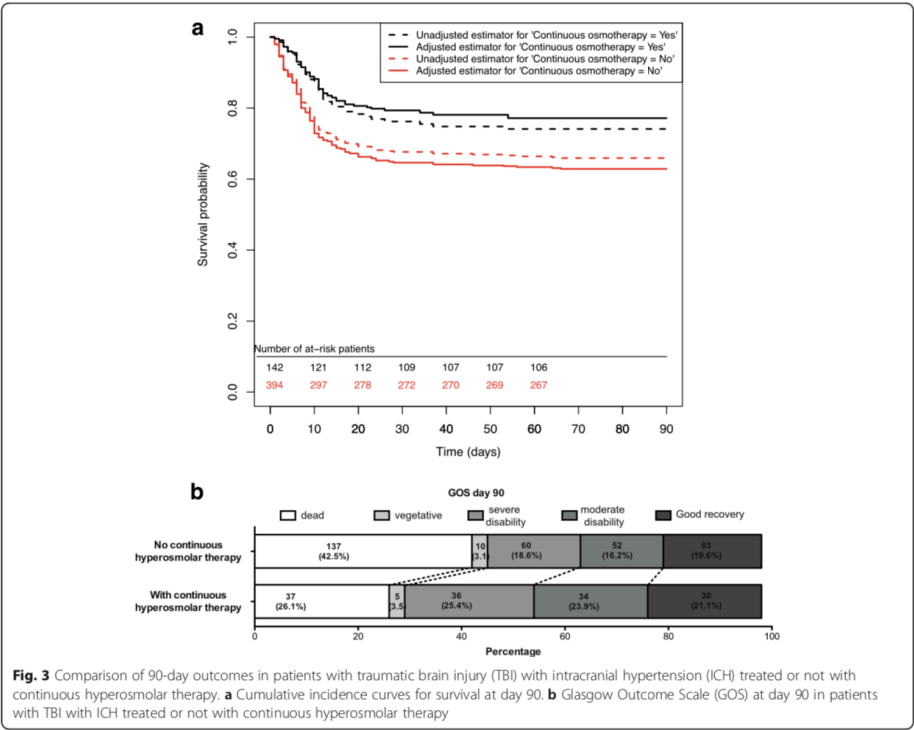
Shown are the mean measurements of intracranial pressure in the two study groups during the 12 hours before and the 36 hours after randomization. The I bars indicate standard errors.

**Association between continuous hyperosmolar therapy and survival in patients with traumatic brain injury – a multicentre prospective cohort study and systematic review – Critical Care Medicine 2017**

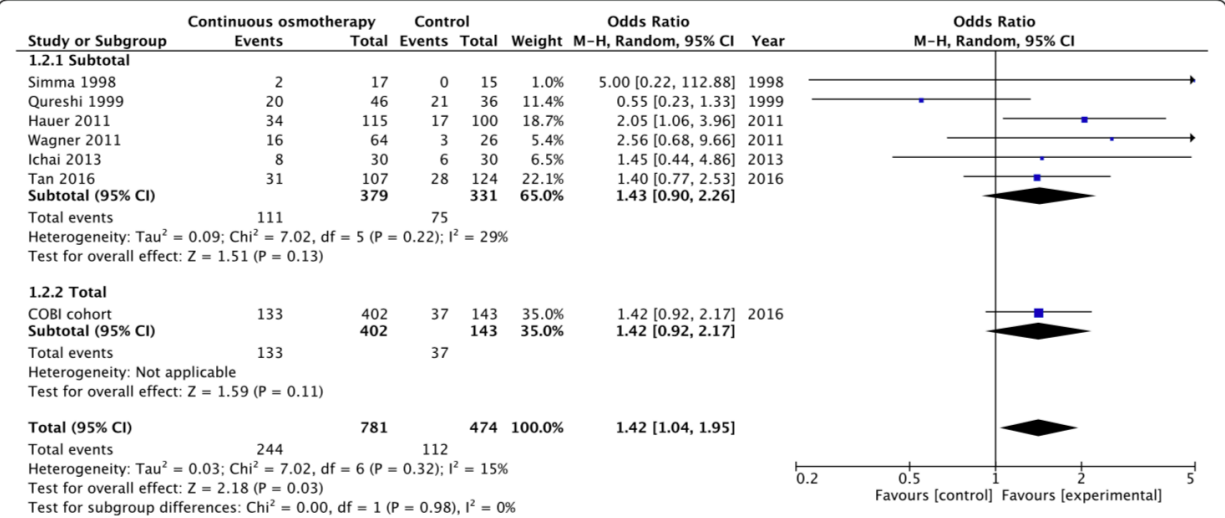
- 33% mortality rate for TBI, 33% poor neurologic outcomes
- Uncontrolled intra-cranial hypertension most common cause of death in severe TBI
- Use of bolus therapy to treat ICH results in only transient improvement
- METHODS
  - o Observational trial and systematic review using patients from other trials
  - o All patients mechanically ventilated with moderate to severe TBI (GCS 9-12 and 3-8 respectively) with CT changes and ICP monitoring
  - o For patients that received continuous hyperosmolar therapy CRI of hypertonic saline administered as 1hr bolus then extended CRI with rate adjusted to increase sodium at increments of 5mmol/L as needed to max of 155. When discontinued slowly decreased to 145.



- RESULTS
  - o 143/545 received CHT
  - o ICP lower in CHT patients, less frequently needed hypocapnea or decompressive craniectomy
  - o Survival improved at 90days (not significant for ICU survival)
  - o More hypernatremia but no other complications



**Fig. 3** Comparison of 90-day outcomes in patients with traumatic brain injury (TBI) with intracranial hypertension (ICH) treated or not with continuous hyperosmolar therapy. **a** Cumulative incidence curves for survival at day 90. **b** Glasgow Outcome Scale (GOS) at day 90 in patients with TBI with ICH treated or not with continuous hyperosmolar therapy



**Fig. 4** Number of patients deceased on day 28 or hospital discharge in the review of literature. *M-H* Mantel-Haenszel

**Major limitations**

- Observational
- All patients with CHT were at one hospital

Explain one theory by which hyperglycemia may worsen outcome in traumatic brain injury

### **Hyperglycemia in dogs and cats with head trauma: 122 cases (1997–1999) – JAVMA 2001**

- Prior experimental and humane evidence that hyperglycemia associated with worse outcome in TBI
- Occurs from sympathoadrenal response to injury so degree of hyperglycemia may reflect injury severity
- May also potentiate injury – increased free radical production, release of excitatory aminoacids, cerebral edema, **cerebral acidosis (more substrate for anaerobic metabolism)**, altered cerebral vasculature
- METHODS:
  - o Retrospective
  - o Included if evaluated in ER within 12hrs of incident, prior to interventions, and BG within 1hr
  - o Excluded if hypoglycemic, diabetic, glucose altering drugs
    - Hypoglycemia defined as <80 with clinical signs (seizures...) or <60 with or without signs
  - o Mild, moderate or severe based on gait, mentation, pupils
  - o Age matched controls, traumatic and non traumatic
- RESULTS:
  - o 52 dogs 70 cats
  - o Significant association with severity in dogs and cats

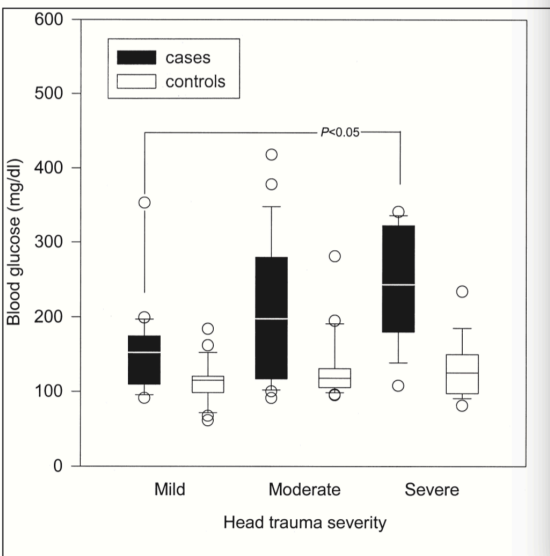


Figure 1—Box-and-whisker plots of blood glucose concentrations at the time of admission in 52 dogs with head trauma, grouped on the basis of severity of injury (cases), and of 52 age-matched control dogs (controls). The horizontal line in each box represents the median value. The boxes themselves represent the 25th to 75th percentile (ie, the middle 50% of the data). The whiskers represent the 10th to 90th percentile (ie, the middle 80% of the data). Circles represent outliers.

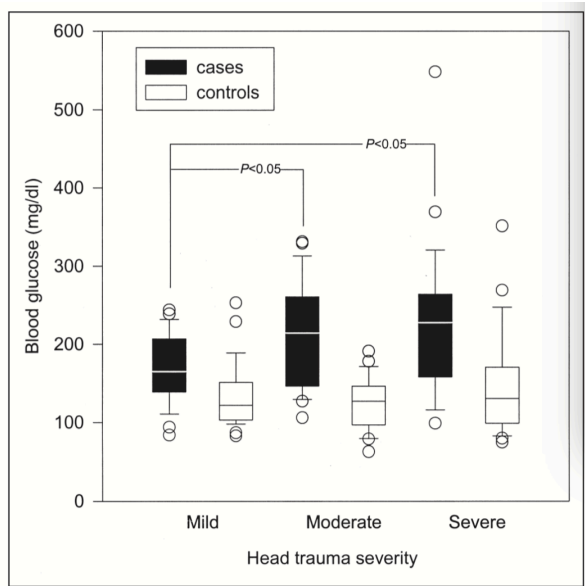


Figure 2—Box-and-whisker plots of blood glucose concentrations at the time of admission in 70 cats with head trauma (cases) and of 70 age-matched control cats (controls). See Figure 1 for key.

- In dogs with severe head trauma, and cats with moderate head trauma, also significantly different from controls with trauma
- Admission BG in dog survivors 151, died 271, euth 205 – not statistically significant
- In cats 192, 209, 212 with no statistical significance
- May have found significant results with more patients, or if serial monitoring over 24hrs (those that fail to improve have worse prognosis)

## The Prognostic Value of the Modified Glasgow Coma Scale in Head Trauma in Dogs –

### JVIM 2001

- MGCS proposed by Shores in Kirk 1983 but association with prognosis not previously investigated
- METHODS
  - o Retrospective
  - o Patients admitted to ICU after head trauma, that had neuro exam recorded, plus skull radiographs and follow up for 48hrs
  - o Excluded if outcome influenced by finances or ‘emotional concerns’ of owners, or if death was from systemic injuries
  - o Single MGCS given retrospectively from neuro exam records prior to treatments

**Table 2.** Modified Glasgow Coma Scale score category and suggested prognosis.

Score Category	Actual MGCS score	Suggested Prognosis
I	3–8	Grave
II	9–14	Guarded
III	15–18	Good

MGCS, Modified Glasgow Coma Scale.

#### - RESULTS

- 38 dogs
- MGCS 5-18
- 7 dogs died within 48hrs
- Almost linear association with survival at 48hrs; 50% survival >8
- Score above not as useful

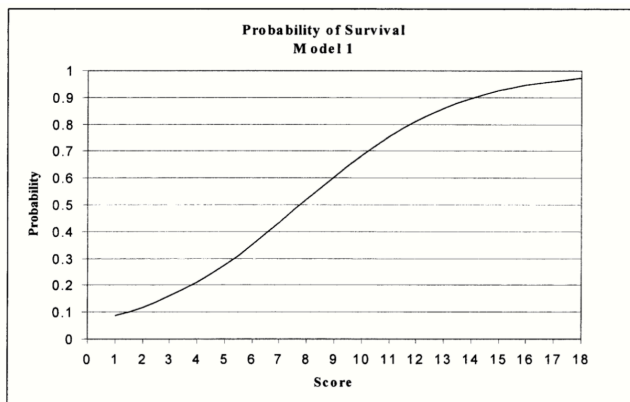


Fig 1. Graph of the probability of survival of a head trauma patient as it relates to the modified Glasgow Coma Scale score assigned to the patient upon admission.

## Retrospective evaluation of prognostic indicators in dogs with head trauma: 72 cases (January–March 2011) – JVECC 2015

#### - METHODS

- Patients admitted for head trauma
- Evaluated first recorded exams and variables, calculated MGCS, mentation score (0-4) and ATT score
- Outcome = survival vs nonsurvival

#### - RESULTS

- 72 dogs
- 15% mortality (1 died, 10 euthanized)
- Blunt vs penetrating not associated with prognosis



- 89% had TBI (MGCS <18)

**Table 2:** Clinical and laboratory variables recorded at hospital admission that predict nonsurvival in dogs with head trauma

Variables	Unit of measure*	OR	95% CL	P value
SpO <sub>2</sub> (%)	↓ 1	1.45	1.03–2.43	0.029
pH	↓ 0.1	1.30	1.11–1.61	<0.001
HCO <sub>3</sub> (mmol/L)	↓ 1	1.27	1.06–1.54	0.007
BE (mmol/L)	↓ 1	1.35	1.12–1.66	<0.001
K (mmol/L)	↑ 1	3.22	1.13–10.20	0.028
Lactate (mmol/L)	↑ 1	1.59	1.18–2.21	0.002
TPP (g/L)	↓ 1	2.13	1.12 – 4.34	0.018
(g/dL)	↓ 0.1	2.13	1.12–4.34	0.018
BUN category	↑ 1	2.86	1.38–6.54	0.003
Albumin (g/L)	↓ 1	15.8	11.4–>10.0	0.001
(g/dL)	↓ 0.1	1.58	1.14–>100	0.001
MGCS score	↓ 1	1.49	1.17–2.00	<0.001
Mentation score	↑ 1	3.28	1.42–10.31	0.002
ATT score	↑ 1	1.45	1.12–1.94	0.003

CL, confidence limit; SpO<sub>2</sub>, pulse oximetry value; BE, base excess; K, potassium concentration; TPP, total plasma protein concentration; ATT, animal trauma triage; MGCS, Modified Glasgow Coma Scale.

\*“Unit of measure” refers to the incremental change of each variable unit that resulted in the associated OR and increased risk of nonsurvival; an arrow pointing up indicates an increase and an arrow pointing down indicates a decrease in that variable that resulted in an increased risk of nonsurvival.

- MGCS <11 84% sensitive, 73% specific for nonsurvival
- 100% survival >15
- 43% non survival ≤8, 54% ≤7
- ATT ≥7 85% sensitive and 64% specific for non-survival, 51% non-survival at 9
- Treatment with hypertonic saline or intubation also associated with non-survival
- BG and BP not significant

### **Computed tomographic findings in dogs with head trauma and development of a novel prognostic computed tomography–based scoring system. AJVR 2017**

- Head trauma identified in 25% of dogs with severe blunt trauma, mortality 15-24%
- CT imaging modality of choice in humans and scoring system is used routinely to determine prognosis
- METHODS
  - Retrospective, dog that had traumatic brain injury + CT

- Short term survival = 10d, long term = >6months, phone survey >6months asked to score QOL 1-5
- No contrast administered, images retrospectively reviewed by one radiologist for study
- RESULTS
  - 27 dogs
  - MGCS median in hospital was 14 and 14.5 for short and long term survivors, and 7 and 9 for non-survivors
  - 30% had seizures, not associated with outcome
  - 56% had cranial vault fractures, 85% had parenchymal abnormalities (most commonly hypodensity of the brain in cerebrum or cerebellum), only 11% had only facial bone fractures
  - 59% had intracranial hemorrhage
  - 70% survival to 10 days (6 euth, 2 died), 1 lost to follow up, 2 were euthanized after discharge due to no improvement
  - QOL excellent 13/16, good in 3
  - **KCTS System**
    - intra or extra axial hemorrhage significantly associated with short term survival (OR for ST survival without hemorrhage 23 (CI 1.2 to 456...))
    - ventricular asymmetry significantly associated with long term survival (OR for LT survival without asymmetry 7.0 (1.2-41))
    - therefore 1 point in scoring system to hemorrhage, 1 to asymmetry or to midline shift
    - other factors were included despite lack of statistical significance:
      - detection of cranial vault fractures also 1 point (present in 6/8 non survivors, 9/19 survivors), 1 point for depressed fractures
      - infratentorial lesions present in half of non-survivors and no survivors, and have been associated with adverse outcomes in MRI studies so received 3 points
    - So score is from 0-7 with 7 having poorest prognosis
  - The system was then not validated in any way...

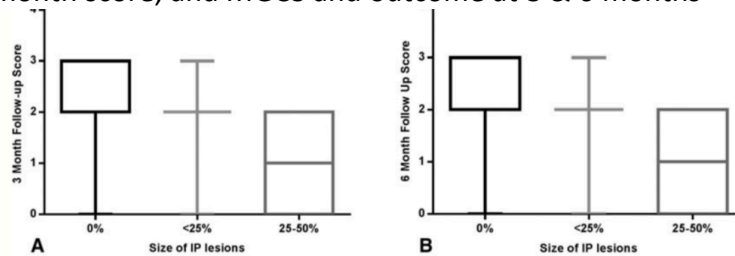
### **Prognostic Value of Early Magnetic Resonance Imaging in Dogs after Traumatic Brain Injury: 50 Cases – JVIM 2014**

- GCS is being recognized as having limited utility
- Onset of seizures after TBI categorized as immediate (<24hr), early (within 1wk) and late (>1wk)
- In humans CT modality of choice for acute TBI
- MRI has superior sensitivity for small focal lesions, and more severe contusion on imaging associated with poorer outcome
- METHODS
  - Retrospective

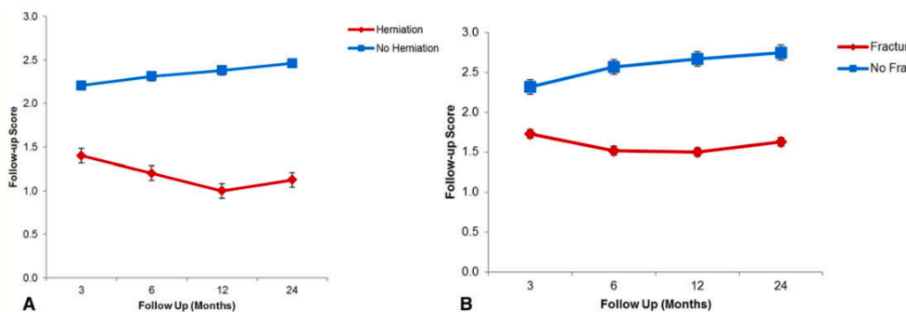
- TBI, neuro exam, MGCS, follow up for minimum 48hrs, MRI within 14 days
- MRI lesions graded as (1) normal, (2) only cerebral/cerebellar hemisphere effected **without** midline shift (3) only cerebral/cerebellar hemisphere effected **with** midline shift (4) lesions of corpus callosum, thalamus, or basal nuclei (5) unilateral brainstem lesions (6) bilateral brainstem lesions
- Outcome short term (48hrs), and long term at 3, 6, 12 and 24months
- Scored as 0 (dead/euthanized), 1 (persistent severe neuro deficits), 2 (good recover with mild neuro deficits and/or seizure meds), 3 (full recovery)

- RESULTS

- 50 dogs included, median presentation MGCS 16 (8-18)
- 66% had abnormal MRI, median severity grade 3
- Brain herniation present in 10 dogs (20%)
- Association between MRI grade and MGCS, as well as lesion size and MGCS
- Seizures significantly associated with >25% brain lesion size as well as herniation through fracture site, caudotranstentorial herniation and skull fractures
- MGCS at presentation significantly lower in dogs with herniation than those without, and lower in herniation through fracture site than other types of herniation
- 36% had seizures during hospitalization or follow up period (8 immediate, 6 early, 4 late). 10% were recurrent, 1 was euthanized for clustering 3 months later
- 5 had surgery, 80% of these had seizures
- 6% dead at 28hrs – associated with herniation, depressed skull fractures, and had a higher size of lesion (>25%) than those alive at 48hrs
- 
- Significant association between MRI grade and outcome scores at 3 & 6 months as well as % midline shift and outcome 6months, size of lesions and 3, 6, 12, and 24month score, and MGCS and outcome at 3 & 6 months



- Lower scores with fractures or herniation, and surgical decompression



**Results of magnetic resonance imaging performed within 48 hours after head trauma in dogs and association with outcome: 18 cases (2007–2012) – JAVMA 2015**

- METHODS:
  - o Retrospective, dogs that had MRI within 48hrs of known head trauma
  - o Reviewed images by blinded radiologist for study
  - o Outcome classified as complete recovery, partial recovery with mild deficits, partial recovery with deficits that effect QOL, or death
- RESULTS
  - o 18 dogs included
  - o Surgery for 4 dogs (only one for brain – decompression)
  - o 1 died on anesthetic recovery, 1 euthanized for lack of improvement, 1 euthanized for severity of head and spinal injury post imaging
  - o 1 had partial recovery with major deficits
  - o 14 had good outcome – 5 of these had mild deficits
  - o Location of parenchymal changes seemed less important than extent of affected parenchyma, dogs with both gray and white affected had poorer prognosis
    - Best seen on T2, hypereintense
  - o Extraaxial hemorrhage best identified on FLAIR images
  - o Fractures was NOT associated with outcome

Table 1—Imaging findings in 18 dogs that underwent MRI within 48 hours after known head trauma.

Intracranial change	Outcome	
	Poor	Good
Gray matter changes only (n = 7)	0	7
White matter changes only (n = 1)	0	1
White matter and gray matter changes (n = 5)	3	2
Extra-axial changes (n = 13)	2	11
Midline shift (n = 6)	1	5
Transtentorial herniation (rostral or caudal; n = 3)	2	1
Transcranial herniation (n = 2)	0	2
Changes affecting the rostral fossa only (n = 12)	0	12
Changes affecting the caudal fossa only (n = 1)	1	0
Changes affecting both the rostral and caudal fossae (n = 4)	3	1

Outcome was classified as good (complete recovery or partial recovery with minor persistent deficits) or poor (partial recovery with major persistent deficits, died, or euthanized).

## Hypothermia for traumatic brain injury.

Lewis SR<sup>1</sup>, Evans DJ, Butler AR, Schofield-Robinson OJ, Alderson P.

### Author information

#### Abstract

**BACKGROUND:** Hypothermia has been used in the treatment of brain injury for many years. Encouraging results from small trials and laboratory studies led to renewed interest in the area and some larger trials.

**OBJECTIVES:** To determine the effect of mild hypothermia for traumatic brain injury (TBI) on mortality, long-term functional outcomes and complications.

**SEARCH METHODS:** We ran and incorporated studies from database searches to 21 March 2016. We searched the Cochrane Injuries Group's Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library), MEDLINE (OvidSP), Embase Classic+Embase (OvidSP), PubMed, ISI Web of science (SCI-EXPANDED, SSCI, CPCI-S & CPSI-SSH), clinical trials registers, and screened reference lists. We also re-ran these searches pre-publication in June 2017; the result from this search is presented in 'Studies awaiting classification'.

**SELECTION CRITERIA:** We included randomised controlled trials of participants with closed TBI requiring hospitalisation who were treated with hypothermia to a maximum of 35 °C for at least 12 consecutive hours. Treatment with hypothermia was compared to maintenance with normothermia (36.5 to 38 °C).

**DATA COLLECTION AND ANALYSIS:** Two review authors assessed data on mortality, unfavourable outcomes according to the Glasgow Outcome Scale, and pneumonia.

**MAIN RESULTS:** We included 37 eligible trials with a total of 3110 randomised participants; nine of these were new studies since the last update (2009) and five studies had been previously excluded but were re-assessed and included during the 2017 update. We identified two ongoing studies from searches of clinical trials registers and database searches and two studies await classification. Studies included both adults and children with TBI. Most studies commenced treatment immediately on admission to hospital or after craniotomies and all treatment was maintained for at least 24 hours. Thirty-three studies reported data for mortality, 31 studies reported data for unfavourable outcomes (death, vegetative state or severe disability), and 14 studies reported pneumonia. Visual inspection of the results for these outcomes showed inconsistencies among studies, with differences in the direction of effect, and we did not pool these data for meta-analysis. We considered duration of hypothermia therapy and the length of follow-up in collected data for these subgroups; differences in study data remained such that we did not perform meta-analysis. Studies were generally poorly reported and we were unable to assess risk of bias adequately. Heterogeneity was evident both in the trial designs and participant inclusion. Inconsistencies in results may be explained by heterogeneity among study participants or bias introduced by individual study methodology but we did not explore this in detail in subgroup or sensitivity analyses. We used the GRADE approach to judge the quality of the evidence for each outcome and downgraded the evidence for mortality and unfavourable outcome to very low. We downgraded the evidence for the pneumonia outcome to low.

**AUTHORS' CONCLUSIONS:** Despite a large number studies, there remains no high-quality evidence that hypothermia is beneficial in the treatment of people with TBI. Further research, which is methodologically robust, is required in this field to establish the effect of hypothermia for people with TBI.

## Severe seizures associated with traumatic brain injury managed by controlled hypothermia, pharmacologic coma, and mechanical ventilation in a dog

Galina M. Hayes, BVSc, Cert SAS, MRCVS