



Management of Elevated Intracranial Pressure: a Review

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Abstract

Purpose of Review Principles of intracranial pressure (ICP) management continue to be an essential part of the neurointensivist's skillset as appropriate treatment decisions can prevent secondary injury to the central nervous system. This review of the literature aims to: discuss commonly encountered pathologies associated with increased ICP, summarize diagnostic approaches used in evaluating ICP, and present evidence-based treatment paradigms that drive clinical care in intensive care units.

Recent Findings Recent topics of discussion include invasive and non-invasive modalities of diagnosis and monitoring, recent developments in hypothermia, hyperosmolar therapy, pharmacological interventions, and surgical therapies. The authors also present an example of an algorithm used within our system of hospitals for managing patients with elevated ICP.

Summary Recent advances have shown the mortality benefits in appropriately recognizing and treating increased ICP. Multiple modalities of treatment have been explored, and evidence has shown benefit in some. Further work continues to provide clarity in the appropriate management of intracranial hypertension.

Keywords Intracranial pressure · Intracranial hypertension · Pupillometry · Optic nerve sheath diameter · Hypothermia · Hyperosmolar therapy

Introduction

Management of intracranial pressure (ICP) is at the core of neurocritical care. Monitoring and normalizing the ICP reduces secondary neurological injury and its associated morbidity and mortality. This review of the literature aims to do the following: introduce rudimentary principles in the anatomy and physiology of ICP management, discuss commonly encountered pathologies that lead to increased ICP, summarize diagnostic approaches being used in the evaluation of ICP, and present evidence-based treatment paradigms that drive clinical care in intensive care units today. Lastly, the authors present an example of an algorithm that is used within our system of hospitals for managing patients with changes in ICP.

Detection of Elevated Intracranial Pressure

Invasive ICP Monitoring

Invasive ICP monitoring with external ventricular drains (EVD) and intraparenchymal monitors (IPM) continue to be the gold standards for measurement. While invasive ICP monitoring is commonplace in the management of traumatic brain injury (TBI), the recent “Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure” (BEST:TRIP) [1] trial caused some to re-evaluate its use. BEST:TRIP [1], a randomized control trial published in 2012, showed that aggressive ICP monitoring using IPMs in patients with severe TBI did not improve long-term outcomes compared to management based on clinical signs and neuroimaging [1]. The study setting of Bolivia and Ecuador in which pre-hospital resuscitation is not as robust as other countries is a point of contention against its generalizability [1, 2]. Post-ICU-stay care is also different from other countries, which likely played a part in the relatively high 14-day mortality rate of 35% [1]. Despite being a well-designed, robust trial, these limitations diminish its results in countries with well-established ICP monitoring protocols.

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Additionally, those in the ICP monitoring had lower therapeutic intensity, so ICP management may be a cost-effective and less labor-intensive means to manage patients. Neurocritical care in North America and Europe has not moved away from invasive ICP monitoring as a standard and the authors themselves have argued for continued monitoring of these patients.

EVDs are considered the gold standard and provide the clinician a therapeutic modality of cerebrospinal fluid (CSF) drainage if needed. Recently, Bales showed that the choice of ICP monitoring may not be frivolous, highlighting that severe TBI patients may benefit more from IPM rather than EVD placement [3]. This is contradictory to previous studies showing no benefit [4] or EVD superiority [5]. Regardless of which invasive ICP monitor is used, the complications of placement must be considered. Complications include ventriculostomy-associated infections, procedural hemorrhage, and monitor misplacement [6].

Non-invasive Ultrasonography of Optic Nerve Sheath

With the increasing use of ultrasound (US) in hospital settings, bedside point-of-care diagnostics such as optic nerve sheath diameter (ONSD) measurements have become more commonplace. The space between the optic nerve and its sheath is contiguous with the subarachnoid space, allowing for changes in ICP to be transmitted to the retrobulbar sheath quickly, causing its expansion [7, 8]. Recent meta-analyses have confirmed the utility of ONSD to detect elevated ICP in patients presenting with TBI, with the areas under the curve (AUC) of 0.981 [9] and 0.932 [10]. Each meta-analysis included between 320 and 350 patients and most studies were single-center, prospective studies of TBI patients in emergency departments with known high rates of intracranial hypertension (13.6–83%). Note, some studies did have concerns for bias including improper blinding. Most studies defined hypertension as an ICP > 20 mmHg, although two defined it higher at > 25 mmHg. All studies measured the ONSD 3 mm behind the globe with 2–3 measurements taken in each eye; however, the threshold ONSD measurement for denoting elevated ICP ranged from 0.48 cm [7] to 0.63 cm [11]. Recent studies have tried to overcome variability by different means. Agrawal et al. have shown that coronal axis insonation of the ONSD had less variability amongst measurements, however, was not able to replicate the ICP estimation efficacy of axial insonation [12]. Du et al. built on ONSD by using eyeball transverse diameter (ETD) to form a ratio: ONSD/ETD, which was more predictive of increased ICP than ONSD alone [13]. Similarly, they also found that a predecessor study [14] had different ONSD/ETD ratio thresholds for optimal diagnosis of increased ICP (0.25 [13] vs. 0.29 [14]).

While the utility in TBI looks promising, ONSD had poor performance in predicting intracranial hypertension in the largest series to date of patients presenting with acute liver failure [15]. The AUC was only 0.59 (85% CI 0.37–0.79) for ONSD, however, ICP calculated from transcranial Doppler (TCD) flow velocities using the estimated cerebral perfusion pressure (CPP) technique showed good correlation and excellent negative predictive value [16]. The ability to perform non-invasive assessments in these patients is paramount given high rates of cerebral edema and intracranial hypertension with concurrent severe coagulopathy limiting safety of invasive ICP monitoring. In general, however, the accuracy of non-invasive ICP measurements using TCDs has been variable across studies, with none reaching the accuracy necessary to replace invasive monitoring [17].

Although ONSD-US has shortcomings, Rajajee suggested internal standardization to find an institutional-specific ONSD value correlating with ICP above 20 mmHg to overcome technique and operator variability [7]. After standardization, ONSD-US in TBI can be very powerful in clinical practice due to its accessibility at bedside, speed of obtaining information, and accuracy in diagnosing intracranial hypertension.

While ONSD is most often studied with respect to its correlating with instantaneously measured ICP, it can also be used to predict which patients may have ICP elevations during their admission. In a group of severe TBI patients, Robba found that an initial admission ONSD measurement significantly correlated to the following: mean ICP while in the intensive care unit (ICU), time of ICP above 20 mmHg while in the ICU, and ICU mortality [18]. However, further confirmatory work needs to be done in order to employ ONSD as a prognosticating index.

Pupillometry

The diagnostic value of pupil size and reactivity have been discussed as qualitative neurological exam findings, however, a more quantitative approach through the use of a pupillometer also is effective in providing evidence of increased ICP. Chen et al. introduced the Neurological Pupil index (NPI) as a measure that incorporated pupil size, latency, constriction velocity, and dilation velocity to successfully determine, and even predict by an average of about 16 h before, the presence of intracranial hypertension [19]. NPI was able to separate the study cohort into 3 groups: normal NPI (3–5) which had a mean peak ICP of 19.6 mmHg, abnormal NPI (< 3) with a peak mean of 30.5 mmHg, and unreactive NPI with peak mean of 33.8 mmHg. These differences in mean peak ICP were statistically significant when considering ICP and NPI trends although the study did not address the notion of single-point abnormal NPI values that were associated with normal ICP values [19]. Although the temporal relationship of isolated NPI values is still being investigated, recent studies

have provided encouraging evidence showing NP_i improvement as early as 2 h after administration of hyperosmolar therapy, highlighting pupillometry as a non-invasive method to validate response of hyperosmolar intervention [20, 21].

Electroencephalography

The advent of multimodality monitoring in neurocritical care has put forth avenues of utilizing continuous electroencephalography (cEEG) to analyze patient data. Newey et al. demonstrated a case in which the presence of cerebral edema had been tipped off by cEEG asymmetries that evolved into burst suppression before any clinical signs manifested in the patient [22]. Also, pathologies that increase ICP can also cause seizures, which in itself can lead to cerebral hypermetabolism, in turn, increasing cerebral blood flow (CBF) and increasing ICP. Therefore, proactively identifying and halting epileptic activity should be a goal with patients that have intracranial pathologies with associated tenuous ICP. Isolated cEEG recordings may not be sensitive in determining increases in ICP until it is significantly elevated to the point of significantly limiting CBF [23], however, utilizing quantitative cEEG parameters may be beneficial to detect smaller changes in CBF, and thus, subclinical increases in ICP. Hartings et al. was able to show that timing of cortical spreading depression (CSD) was loosely tied to blood pressure instability and increased ICP; however, the study was unable to state whether CSDs were causing the increased ICP or if they were resulting from increased ICP [24]. Today, cEEG is not strictly used as a non-invasive ICP monitor due to its lack of sensitivity, however, it can provide valuable clues to signal increased ICP when used in the right context.

Treatment of Elevated ICP

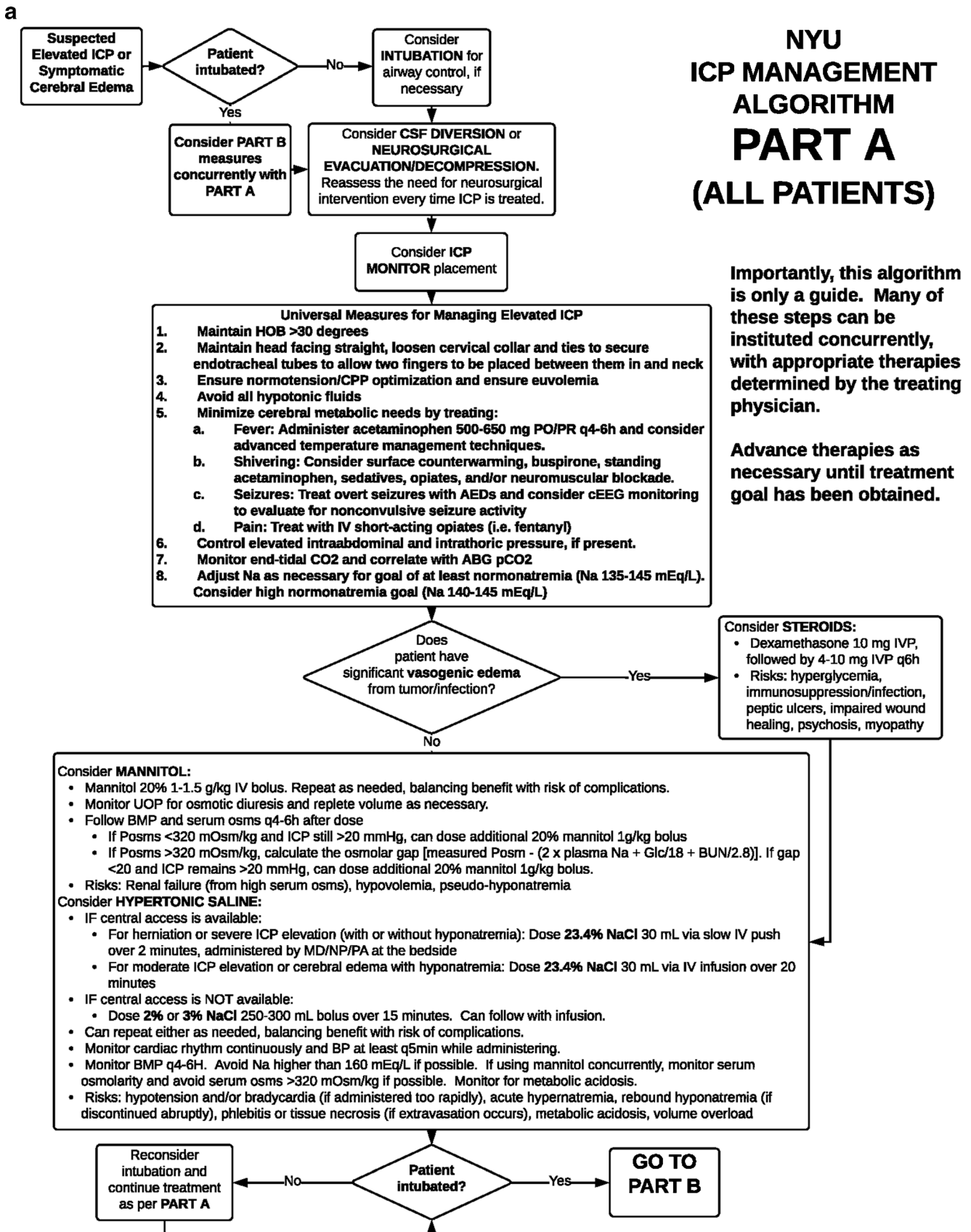
Hyperosmolar and Pharmacological Therapies

When faced with focal edema from intracranial pathology, hyperosmolar therapy (HOT) is used principally to draw interstitial fluid intravascularly for clearance, decreasing cerebral edema, and intracranial ICP. HOT has shown benefit in TBI-related edema, stroke-related edema, and perihematomal edema in intracranial hemorrhage (ICH) [25–27]. Mainstays of hyperosmolar therapy are mannitol and hypertonic saline (HTS). Agent choice depends on patient comorbidities and characteristics, e.g., volume status and serum tonicity [27, 28], with an aim to minimize the consequent side effects of HOT. Gu et al. published a meta-analysis of 12 randomized controlled trials (RCT) comparing HTS and mannitol. Overall, the meta-analysis did not show superiority of either HTS or mannitol in magnitude of ICP reduction ($p = 0.149$; 11 of 12 studies); however, control of ICP reduction, or time of

treatment effect, was significantly ($p = 0.044$; 8 of 12 studies) longer with HTS than mannitol. There was no significant difference between mortality (relative risk of 0.78, $p = 0.216$; 6 of 12 studies) or neurological function using the Glasgow Outcome Scale (relative risk of 1.17, $p = 0.258$; 5 of 12 studies). The included studies were heterogeneous in terms of sample size, sample criteria (e.g., TBI and non-TBI neurosurgical patients), study design (e.g., crossover-control trials), and definitional thresholds. The authors tried to limit this by selectively comparing proportions of the 12 RCTs based on the studied variable and the provided data, however, there were still noted differences [29]. Mangat et al. used a small sample of 25 case-control matched pairs of HTS and mannitol (note 1 patient from HTS cohort received 23.4% HTS boluses) to show that HTS had a statistically significant ($p = 0.0003$) shorter period of cumulative intracranial hypertension (15.5% of monitoring period) when compared to mannitol (36.5% of monitoring period) [30]. A subsequent 2019 study using the same matched patient data further showed HTS usage led to significantly less days with low CPP compared to mannitol with a cumulative burden trending towards HTS superiority. The study also looked at cumulative burden of high ICP/low CPP concomitance; this was found to be significantly less in the HTS group than the mannitol group [31••].

Intravenous (IV) glyburide is being investigated as a method of preventing post-large hemispheric stroke edema by inhibiting SUR1 receptors, whose upregulation and activation in ischemia leads to microvascular instability and subsequent edema [32, 33]. The “Glyburide Advantage in Malignant Edema and Stroke” (GAMES-RP) trial [34] showed that intravenous glyburide administration within 10 h of symptoms onset in anterior circulation strokes with large infarct volumes (lower limit of 82 cm³) that were not considered to be futile (upper limit of 300 cm³) showed benefit in reducing the rate of cerebral edema-related deaths [34, 35••]. IV Glyburide administration did not decrease the rate of malignant edema between placebo and intervention cohorts; however, in the subgroup of patients that developed malignant edema, glyburide administration decreased the rate of midline shift and degree of worsening seen on the NIH stroke scale. However, IV glyburide was associated with a higher rate of decompressive craniectomies although the difference amongst the arms was not significant [35••]. Post hoc subgroup analysis of GAMES-RP participants that were ≤ 70 years old showed a significant functional benefit on the Barthel Index and a non-significant benefit on the modified Rankin scale [36].

Corticosteroids are mainstays in treating mass effect and increased ICP from intracranial neoplastic tumors [37]. Tumors increase intracranial tissue and also evoke inflammatory cascades to produce peritumoral edema, increasing interstitial fluid. Steroids limit the interstitial vasogenic edema and decrease mass effect until definitive surgical intervention, if possible, is performed [38–40].



◀ **Fig. 1** **a** New York University-Langone ICP Management Algorithm that is used within our system that describes the steps taken to initially assess patients suspected of having increased intracranial pressure in addition to therapies used to treat non-intubated patients. **b** New York University-Langone ICP Management Algorithm describing the steps taken to manage intubated patients with suspected increased intracranial pressure, of note, therapies can be used concurrently with therapies used in **a**

Corticosteroids were also tested in acute head injury in the “Corticosteroids Randomisation after Significant Head injury” (MRC-CRASH) trial, in which intravenous methylprednisolone was given within 8 h of head injury in patients with resulting GCS < 14. The results at 2 weeks showed that mortality was greater in the corticosteroid cohort compared to the placebo cohort [41]. At 6 months, the corticosteroid group again had greater mortality compared to placebo [42]. Given these results, steroids are not recommended in the setting of traumatic brain injury.

Hypothermia for Intracranial Hypertension After Traumatic Brain Injury

Hypothermia aims to reduce cerebral metabolism and CBF, subsequently reducing ICP. While prophylactic hypothermia after TBI has been extensively studied in the “National Acute Brain Injury Study: Hypothermia” (NABISH) [43] trials and the recently published “Prophylactic Hypothermia Trial to Lessen Traumatic Brain Injury” (POLAR) RCT with little success, the specific use of “late-rescue” hypothermia to treat intracranial hypertension after TBI has garnered less attention [44••]. EuroTherm3235, an open-label RCT compared use versus non-use of hypothermia prior to administration of hypertonic solutions as part of a staged treatment of intracranial hypertension after TBI [45]. All subjects were closed-TBI patients with ICP of >20 mmHg for at least 5 min that was refractory to stage 1 treatments (defined as mechanical ventilation, sedation, head of bed to 30°, analgesia, CPP optimization, +/- ventriculostomy, or +/- surgical removal of space-occupying lesions). Those randomized to the hypothermia group received therapeutic temperature modulation (TTM) with initial target of 35 °C but lowered incrementally down to as low as 32 °C until ICP was below 20 mmHg; hypertonic solutions were then administered if hypothermia was ineffective. Patients in the control group received hypertonic solutions once stage-1 therapies had failed to bring the ICP to ≤ 20 mmHg. Once hypothermia was started, it was maintained for at least 48 h and then re-warmed using a standardized protocol if ICPs were under control. The primary outcome was scored using the Extended Glasgow Outcome Scale (GOS-E) at 6 months.

The trial was designed to enroll 600 patients but was stopped early after enrolling and randomizing 387 subjects due to worse outcomes in the hypothermia group. Note, the

groups were well matched in baseline characteristics. The common odds ratio for the GOS-E score was 1.53 (95% CI 1.02–2.3), indicating a worse outcome in the hypothermia group. A favorable GOS-E (5–8) was seen in 26% of the hypothermia group and 37% in the control group. Notably, patients in the hypothermia group received less stage-3 treatments (stage-3 treatments included barbiturate therapy, decompressive craniectomy, or further surgical intervention), mainly barbiturates, than those in the control group (44% vs 54%). Measured ICPs, however, were similar between groups throughout the study.

This trial gave fairly convincing evidence that application of hypothermia to 32–35 °C likely has more risks than benefits for treatment of intracranial hypertension in TBI. However, many practitioners still use hypothermia in the following contexts, which were not studied in Eurotherm3235-Trial:

- a) Use only after hypertonic solutions have failed,
- b) For more severe ICP elevations (> 25–30 mmHg), or
- c) Only after barbiturate coma has failed.

The use of hypothermia in these clinical situations remains unclear, especially for utilization in patients with severe, refractory elevations in ICP. At our center, we continue to utilize TTM management to 33 °C for those patients with ICP > 25 mmHg who have failed hypertonic solutions in order to reduce the use of barbiturate-induced coma. However, there is no data to support the use of hypothermia prior to barbiturate use, vice versa, or at all. Figure 1 demonstrates how we integrate hypothermia into the step-wise management of ICP elevation at our institution (Fig. 1a, b).

Eurotherm3235-Trial lends evidence that early use of therapeutic hypothermia in the staged management of ICP elevation is not beneficial. Furthermore, there is mounting evidence that prophylactic hypothermia does not benefit patient outcomes and does not meaningfully impact levels of intracranial hypertension. Combined with the earlier NABISH trials, the question of prophylactic hypothermia for TBI has been answered: as currently practiced, it does not help patients.

Surgical Decompression for Intracranial Hypertension After Traumatic Brain Injury

The “Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP” (RESCUEicp) Trial was designed to answer whether TBI patients benefited from decompressive craniectomy in the setting of refractory intracranial hypertension [46]. RESCUEicp was designed to overcome the study design criticisms of its predecessor, “Decompressive Craniectomy” (DECRA) trial, which enrolled patients with diffuse, bilateral injury and defined intracranial hypertension as ICP > 20 mmHg for at least 15 min in a 1-h period [47]. Please see Table 1 for a comparison of the DECRA and RESCUEicp trials. RESCUEicp included TBI patients with more commonly encountered mass lesions and

b

NYU ICP MANAGEMENT ALGORITHM PART B (INTUBATED PATIENTS)

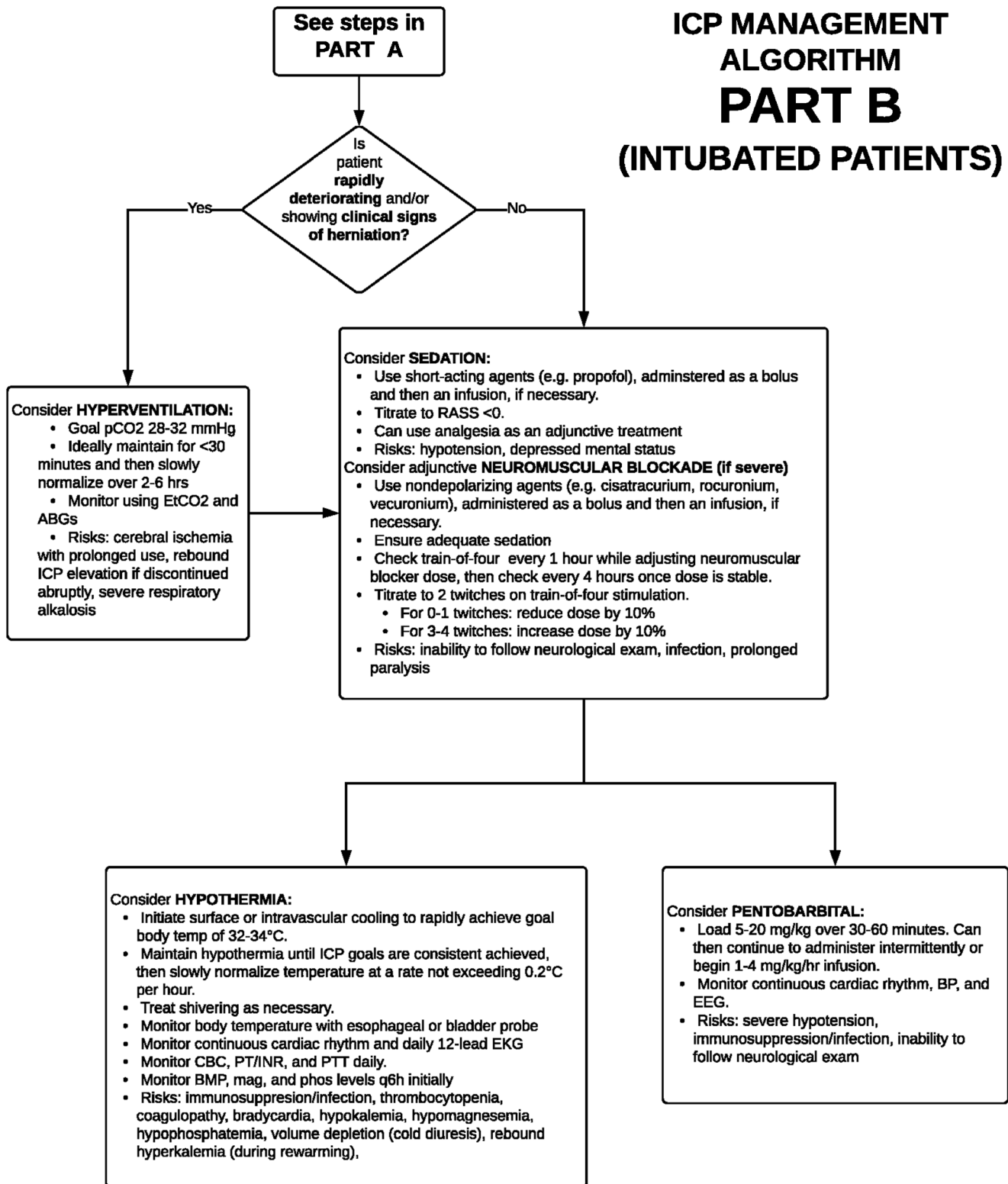


Fig. 1 (continued)

had a sample size of 398 patients with well-balanced baseline demographics in both groups. RESCUEicp defined refractory intracranial hypertension as ICP elevation > 25 mmHg for 1 to

12 h [48]. Patients randomized into the surgical intervention arm underwent a decompressive craniectomy no later than 4 to 6 h after randomization, with the decision on craniectomy

Table 1 Comparison of two recent trials in decompressive craniectomy for ICP elevation after TBI

		DECRA		RESCUEicp	
Study design	Study type	Open-label, blinded outcome RCT		Open-label, blinded outcome RCT	
	Patient population	<ul style="list-style-type: none"> • Severe, non-penetrating TBI • Age 15–59 • GCS 3–8 or Marshall III (mod diffuse injury) • Failed all medical therapies except hypothermia and barbiturate coma 		<ul style="list-style-type: none"> • Severe, non-penetrating TBI • Age 10–65 • No GCS criteria, CT must be “abnormal” • Excluded patients with bilateral fixed, dilated pupils • Failed all medical therapies (including hypothermia) except barbiturate coma 	
	Timing	Randomization within 72 h of injury		No requirement, but surgery 4–6 h s/p randomization	
	Surgical arm	Bilateral frontotemporoparietal decompressive craniectomy + dural opening		Unilateral or bilateral frontotemporoparietal decompressive hemicraniectomy at discretion of study surgeon	
	Medical arm	TTM to 35C, barbiturates		Barbiturates	
	Definition of ICP failure	> 20 mmHg for > 15 min in a 1-h period despite optimized 1st-tier interventions		> 25 mmHg for 1–12 h despite optimized 1st- and 2nd-tier therapies (excluding barbiturates, including TTM to no less than 34C)	
	Primary outcome	6-month eGOS (proportional odd-analysis)		6-month eGOS (proportional odd-analysis)	
Study results	GCS	Surgical (<i>n</i> = 73)	Medical (<i>n</i> = 82)	Surgical (<i>n</i> = 202)	Medical (<i>n</i> = 196)
	Neither pupil reactive	Median 5 IQR (3-7)	Median 6 IQR (4-7)	3–8 in 69%	3–8 in 72%
	Injury to randomization	27%	12%	14%	18%
	Delayed craniectomy	Median 35.2 h	Median 34.8 h	< 72 h 57%	< 72 h 55%
	Median eGOS 6-month (IQR)	n/a	18%	n/a	37%
	6-month eGOS (%)	3 (2–5)	4 (3–5)	Not reported, but statistical between group difference	
	Death	19%	18%	27%	49%
	Vegetative state	12	2	9	2
	Lower severe disability	25	21	22	14
	Upper severe disability	14	10	15	8
	Lower moderate disability	18	24	10	10
	Upper moderate disability	8	16	13	10
	Lower good recovery	3	5	3	3
	Upper good recovery	1	4	1	4
	Unfavorable outcome (eGOS 1–4)	70%	51%	73%	73%
Mortality	19%	18%	27%	49%	

laterality left to the discretion of the surgeon. The primary outcome was measured using an ordinal analysis of the GOS-E at 6 months with a pre-specified sensitivity analysis for “favorable outcome” on the GOS-E at 6 months.

The ordinal analysis demonstrated a difference in GOS-E scores at 6 months and the pre-specified sensitivity analysis showed good outcomes in 45.4% in the surgical group as compared with 32.4% in the medical group (*p* = 0.01). Mortality was considerably lower in the surgical group but this was counterbalanced by an increased number of vegetative patients in this group. Interestingly, the European majority of enrolling centers led to almost 2/3 of the total craniectomies being bilateral, reflecting European practice patterns. Barbiturates were

utilized in 87% of the medical group and in 9% of those in the surgical group. Importantly, over 1/3 of patients in the medical group ended up needing a surgical decompression thereby diluting the treatment effect seen in the study.

Given these results, the practitioner is faced with a dilemma very similar to that for patients presenting with malignant MCA infarct: will this patient “benefit” from surgery? Surgery is often life-saving but comes at the expense of increased levels of severe neurological impairment. Therefore, in-depth conversations with the family to ascertain the patient’s known wishes, as well as an open dialog about the expected functional outcomes, are essential to guide proper management based on individual patient preference.

Determining Optimal Cerebral Perfusion Pressure Thresholds

Ziai [49•] analyzed patient outcomes and ICP and CPP readings of 499 patients from the “Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase-III” (CLEAR-III) trial [50] to determine optimal ICP and CPP targets for patients presenting with hypertensive intraventricular hemorrhage. ICP elevations were not infrequent, with around 10% of q4 hour ICP readings above 20 mmHg and almost 2% above 30 mmHg. Given that ICP targets are mainly derived from the TBI literature, this important observational study found that sustained, unmitigated ICP elevations even as low as 18 mm Hg are associated with early mortality. The authors noted different ICP thresholds based on age, with those over 55 having lower ICP thresholds than younger patients (18 vs 22 mmHg). Low CPPs were correlated with both mortality and poor functional outcomes with a clear “dose” response for the amount of time spent at low CPPs.

Conclusion

Since the advent of the neurocritical care unit, elevated ICP management has been a central and essential point of goal-directed therapy. Significant progress has been made in evolving from invasive ICP monitoring to more non-invasive methods, however, gold standard continues to be invasive monitors such as EVDs which can also therapeutically drain CSF, if needed. Multiple avenues of treatment have also come forth in the care of these critical patients, and evidence has shown benefit and efficacy. Further work continues to provide clarity in the appropriate therapeutic treatment of intracranial hypertension.

Compliance with Ethics Guidelines

Conflict of Interest Abhinav R. Changa, Barry M. Czeisler, and Aaron Sylvan Lord each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Abbreviations ICP, intracranial pressure; EVD, external ventricular drain; IPM, intraparenchymal monitors; TBI, traumatic brain injury; BEST:TRIP, Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure; CSF, cerebrospinal fluid; US, ultrasound, ultrasonography; ONSD-, optic nerve sheath diameter; AUC, area under the curve; ETD, eyeball transverse diameter; TCD, transcranial Doppler; CPP, cerebral perfusion pressure; ICU, Intensive care unit; NPi, neurological pupil index; cEEG, continuous electroencephalography; CBF, cerebral blood flow; CSD, cortical spreading depression; HOT, hyperosmolar therapy; ICH, intracranial hemorrhage; HTS, hypertonic saline; IV, intravenous; GAMES-RP, glyburide advantage in

malignant edema and stroke; MRC-CRASH, Corticosteroids Randomisation after Significant Head injury; NABISH, National Acute Brain Injury Study: Hypothermia; POLAR, Prophylactic Hypothermia Trial to Lessen Traumatic Brain Injury; TTM, therapeutic temperature modulation; GOS-E, extended Glasgow outcome scale; RESCUEicp, Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of ICP; DECRA, Decompressive Craniectomy trial; CLEAR-III, Clot Lysis: Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase-III

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Chesnut RM, Temkin N, Carney N, et al. A trial of intracranial pressure monitoring in traumatic brain injury. *N Engl J Med*. 2012;367:2471–81. <https://doi.org/10.1056/NEJMoA1207363>.
2. Ropper AH. Brain in a box. *N Engl J Med*. 2012;367:2539–41. <https://doi.org/10.1056/NEJMe1212289>.
3. Bales JW, Bonow RH, Buckley RT, Barber J, Temkin N, Chesnut RM. Primary external ventricular drainage catheter versus intraparenchymal icp monitoring: outcome analysis. *Neurocrit Care*. 2019;31:11–21. <https://doi.org/10.1007/s12028-019-00712-9>.
4. Aiolfi A, Khor D, Cho J, Benjamin E, Inaba K, Demetriades D. Intracranial pressure monitoring in severe blunt head trauma: does the type of monitoring device matter? *J Neurosurg*. 2018;128:828–33. <https://doi.org/10.3171/2016.11.JNS162198>.
5. Liu H, Wang W, Cheng F, Yuan Q, Yang J, Hu J, et al. External ventricular drains versus intraparenchymal intracranial pressure monitors in traumatic brain injury: a prospective observational study. *World Neurosurg*. 2015;83:794–800. <https://doi.org/10.1016/j.wneu.2014.12.040>.
6. Tavakoli S, Peitz G, Ares W, et al. Complications of invasive intracranial pressure monitoring devices in neurocritical care. *Neurosurg Focus*. 2017;43:E6. <https://doi.org/10.3171/2017.8.FOCUS17450>.
7. Rajajee V, Vanaman M, Fletcher JJ, Jacobs TL. Optic nerve ultrasound for the detection of raised intracranial pressure. *Neurocrit Care*. 2011;15:506–15. <https://doi.org/10.1007/s12028-011-9606-8>.
8. Rosenberg JB, Shiloh AL, Savel RH, Eisen LA. Non-invasive methods of estimating intracranial pressure. *Neurocrit Care*. 2011;15:599–608. <https://doi.org/10.1007/s12028-011-9545-4>.
9. Kim SE, Hong EP, Kim HC, et al. Ultrasonographic optic nerve sheath diameter to detect increased intracranial pressure in adults: a meta-analysis. *Acta Radiol*. 2019;60:221–9. <https://doi.org/10.1177/0284185118776501>.
10. Robba C, Santori G, Czosnyka M, et al. Optic nerve sheath diameter measured sonographically as non-invasive estimator of intracranial pressure: a systematic review and meta-analysis. *Intensive Care Med*. 2018;44:1284–94. <https://doi.org/10.1007/s00134-018-5305-7> **This study was a meta-analysis looking at multiple studies, and they showed that there is utility in using ONSD as a means of detecting increased ICP in a present versus absent fashion.**
11. del Saz-Saucedo P, Redondo-Gonzalez O, Mateu-Mateu A, et al. Sonographic assessment of the optic nerve sheath diameter in the diagnosis of idiopathic intracranial hypertension. *J Neurol Sci*. 2016;361:122–7. <https://doi.org/10.1016/j.jns.2015.12.032>.

12. Agrawal A, Cheng R, Tang J, Madhok DY. Comparison of two techniques to measure optic nerve sheath diameter in patients at risk for increased intracranial pressure. *Crit Care Med*. 2019;47: e495–501. <https://doi.org/10.1097/CCM.0000000000003742>.
13. Du J, Deng Y, Li H, et al. Ratio of optic nerve sheath diameter to eyeball transverse diameter by ultrasound can predict intracranial hypertension in traumatic brain injury patients: a prospective study. *Neurocrit Care*. 2019. <https://doi.org/10.1007/s12028-019-00762-z>.
14. Vaiman M, Sigal T, Kimiagar I, et al. Noninvasive assessment of the intracranial pressure in non-traumatic intracranial hemorrhage. *J Clin Neurosci*. 2016;34:177–81. <https://doi.org/10.1016/j.jocn.2016.06.008>.
15. Rajajee V, Williamson CA, Fontana RJ, Courey AJ, Patil PG. Noninvasive intracranial pressure assessment in acute liver failure. *Neurocrit Care*. 2018;29:280–90. <https://doi.org/10.1007/s12028-018-0540-x>.
16. Czosnyka M, Matta BF, Smielewski P, et al. Cerebral perfusion pressure in head-injured patients: a noninvasive assessment using transcranial Doppler ultrasonography. *J Neurosurg*. 1998;88:802–8. <https://doi.org/10.3171/jns.1998.88.5.0802>.
17. Robba C, Cardim D, Sekhon M, Budohoski K, Czosnyka M. Transcranial Doppler: a stethoscope for the brain-neurocritical care use. *J Neurosci Res*. 2018;96:720–30. <https://doi.org/10.1002/jnr.24148>.
18. Robba C, Donnelly J, Cardim D, Tajsic T, Cabeleira M, Citerio G, et al. Optic nerve sheath diameter ultrasonography at admission as a predictor of intracranial hypertension in traumatic brain injured patients: a prospective observational study. *J Neurosurg*. 2019;1–7. <https://doi.org/10.3171/2018.11.JNS182077>.
19. Chen JW, Gombart ZJ, Rogers S, Gardiner SK, Cecil S, Bullock RM. Pupillary reactivity as an early indicator of increased intracranial pressure: The introduction of the Neurological Pupil index. *Surg Neurol Int*. 2011;2:82. <https://doi.org/10.4103/2152-7806.82248>.
20. Ong C, Hutch M, Barra M, Kim A, Zafar S, Smirnakis S. Effects of osmotic therapy on pupil reactivity: quantification using pupillometry in critically ill neurologic patients. *Neurocrit Care*. 2019;30:307–15. <https://doi.org/10.1007/s12028-018-0620-y>.
21. Jahns FP, Miroz JP, Messerer M, Daniel RT, Taccone FS, Eckert P, et al. Quantitative pupillometry for the monitoring of intracranial hypertension in patients with severe traumatic brain injury. *Crit Care*. 2019;23:155. <https://doi.org/10.1186/s13054-019-2436-3>.
22. Newey CR, Sarwal A, Hantus S. Continuous electroencephalography (cEEG) changes precede clinical changes in a case of progressive cerebral edema. *Neurocrit Care*. 2013;18:261–5. <https://doi.org/10.1007/s12028-011-9650-4>.
23. Kurtz P, Hanafy KA, Claassen J. Continuous EEG monitoring: is it ready for prime time? *Curr Opin Crit Care*. 2009;15:99–109. <https://doi.org/10.1097/MCC.0b013e3283294947>.
24. Hartings JA, Strong AJ, Fabricius M, Manning A, Bhatia R, Dreier JP, et al. Spreading depolarizations and late secondary insults after traumatic brain injury. *J Neurotrauma*. 2009;26:1857–66. <https://doi.org/10.1089/neu.2009.0961>.
25. Brain Trauma F, American Association of Neurological S, Congress of Neurological S, et al. Guidelines for the management of severe traumatic brain injury. II. Hyperosmolar therapy. *J Neurotrauma*. 2007;24(Suppl 1):S14–20. <https://doi.org/10.1089/neu.2007.9994>.
26. Farrokh S, Cho SM, Suarez JJ. Fluids and hyperosmolar agents in neurocritical care: an update. *Curr Opin Crit Care*. 2019;25:105–9. <https://doi.org/10.1097/MCC.0000000000000585>.
27. Diringer MN. New trends in hyperosmolar therapy? *Curr Opin Crit Care*. 2013;19:77–82. <https://doi.org/10.1097/MCC.0b013e32835eba30>.
28. Rangel-Castilla L, Gopinath S, Robertson CS. Management of intracranial hypertension. *Neurol Clin*. 2008;26:521–41, x. <https://doi.org/10.1016/j.ncl.2008.02.003>.
29. Gu J, Huang H, Huang Y, Sun H, Xu H. Hypertonic saline or mannitol for treating elevated intracranial pressure in traumatic brain injury: a meta-analysis of randomized controlled trials. *Neurosurg Rev*. 2019;42:499–509. <https://doi.org/10.1007/s10143-018-0991-8>.
30. Mangat HS, Chiu YL, Gerber LM, Alimi M, Ghajar J, Härtl R. Hypertonic saline reduces cumulative and daily intracranial pressure burdens after severe traumatic brain injury. *J Neurosurg*. 2015;122:202–10. <https://doi.org/10.3171/2014.10.JNS132545>.
31. Mangat HS, Wu X, Gerber LM, et al. Hypertonic saline is superior to mannitol for the combined effect on intracranial pressure and cerebral perfusion pressure burdens in patients with severe traumatic brain injury. *Neurosurgery*. 2019. <https://doi.org/10.1093/neuros/nyz046> **This study utilized a TBI cohort to assess for differences in the degree of increased ICP, decreased CPP, and the degree of their concomitance when administered either hypertonic saline or mannitol; the study showed hypertonic saline superiority in decreasing the cumulative burden of concomitant increased ICP with decreased CPP.**
32. King ZA, Sheth KN, Kimberly WT, Simard JM. Profile of intravenous glyburide for the prevention of cerebral edema following large hemispheric infarction: evidence to date. *Drug Des Devel Ther*. 2018;12:2539–52. <https://doi.org/10.2147/DDDT.S150043>.
33. Simard JM, Sheth KN, Kimberly WT, Stern BJ, del Zoppo G, Jacobson S, et al. Glibenclamide in cerebral ischemia and stroke. *Neurocrit Care*. 2014;20:319–33. <https://doi.org/10.1007/s12028-013-9923-1>.
34. Sheth KN, Elm JJ, Molyneaux BJ, et al. Safety and efficacy of intravenous glyburide on brain swelling after large hemispheric infarction (GAMES-RP): a randomised, double-blind, placebo-controlled phase 2 trial. *Lancet Neurol*. 2016;15:1160–9. [https://doi.org/10.1016/S1474-4422\(16\)30196-X](https://doi.org/10.1016/S1474-4422(16)30196-X).
35. Kimberly WT, Bevers MB, von Kummer R, Demchuk AM, Romero JM, Elm JJ, et al. Effect of IV glyburide on adjudicated edema endpoints in the GAMES-RP Trial. *Neurology*. 2018;91: e2163–9. <https://doi.org/10.1212/WNL.0000000000000618> **This study analyzed the GAMES-RP trial results to show that IV glyburide administration within 10 h of symptoms onset in anterior circulation strokes with large infarct volumes showed benefit in reducing the rate of cerebral edema-related deaths.**
36. Sheth KN, Petersen NH, Cheung K, Elm JJ, Hinson HE, Molyneaux BJ, et al. Long-term outcomes in patients aged <=70 years with intravenous glyburide from the phase II GAMES-RP study of large hemispheric infarction: an exploratory analysis. *Stroke*. 2018;49:1457–63. <https://doi.org/10.1161/STROKEAHA.117.020365>.
37. Galicich JH, French LA, Melby JC. Use of dexamethasone in treatment of cerebral edema associated with brain tumors. *J Lancet*. 1961;81:46–53.
38. Kaal EC, Vecht CJ. The management of brain edema in brain tumors. *Curr Opin Oncol*. 2004;16:593–600.
39. Ly KI, Wen PY. Clinical relevance of steroid use in neuro-oncology. *Curr Neurol Neurosci Rep*. 2017;17:5. <https://doi.org/10.1007/s11910-017-0713-6>.
40. Roth P, Happold C, Weller M. Corticosteroid use in neuro-oncology: an update. *Neurooncol Pract*. 2015;2:6–12. <https://doi.org/10.1093/nop/npu029>.
41. Roberts I, Yates D, Sandercock P, Farrell B, Wasserberg J, Lomas G, et al. Effect of intravenous corticosteroids on death within 14 days in 10008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial. *Lancet*. 2004;364:1321–8. [https://doi.org/10.1016/S0140-6736\(04\)17188-2](https://doi.org/10.1016/S0140-6736(04)17188-2).

42. Edwards P, Arango M, Balica L, Cottingham R, el-Sayed H, Farrell B, et al. Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury-outcomes at 6 months. *Lancet*. 2005;365:1957–9. [https://doi.org/10.1016/S0140-6736\(05\)66552-X](https://doi.org/10.1016/S0140-6736(05)66552-X).
43. Clifton GL, Valadka A, Zygun D, Coffey CS, Drever P, Fourwinds S, et al. Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial. *Lancet Neurol*. 2011;10:131–9. [https://doi.org/10.1016/S1474-4422\(10\)70300-8](https://doi.org/10.1016/S1474-4422(10)70300-8).
44. Cooper DJ, Nichol AD, Bailey M, Bernard S, Cameron PA, Pili-Floury S, et al. Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury: the POLAR randomized clinical trial. *JAMA*. 2018;320:2211–20. <https://doi.org/10.1001/jama.2018.17075> **The POLAR study was a randomized controlled trial that tested the efficacy of prophylactic hypothermia in the setting of TBI; the study showed that there was no significant difference in favorable outcome rates at 6 months when comparing patients that underwent normothermia protocol versus patients that underwent prophylactic hypothermia.**
45. Andrews PJ, Sinclair HL, Rodriguez A, Harris BA, Battison CG, Rhodes JK, et al. Hypothermia for intracranial hypertension after traumatic brain injury. *N Engl J Med*. 2015;373:2403–12. <https://doi.org/10.1056/NEJMoal507581>.
46. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J, et al. Trial of decompressive craniectomy for traumatic intracranial hypertension. *N Engl J Med*. 2016;375:1119–30. <https://doi.org/10.1056/NEJMoal605215>.
47. Cooper DJ, Rosenfeld JV, Murray L, et al. Decompressive craniectomy in diffuse traumatic brain injury. *N Engl J Med*. 2011;364:1493–502. <https://doi.org/10.1056/NEJMoal102077>.
48. Shutter LA, Timmons SD. Intracranial pressure rescued by decompressive surgery after traumatic brain injury. *N Engl J Med*. 2016;375:1183–4. <https://doi.org/10.1056/NEJMe1609722>.
49. Ziai WC, Thompson CB, Mayo S, McBee N, Freeman WD, Dlugash R, et al. Intracranial hypertension and cerebral perfusion pressure insults in adult hypertensive intraventricular hemorrhage: occurrence and associations with outcome. *Crit Care Med*. 2019;47:1125–34. <https://doi.org/10.1097/CCM.0000000000003848> **This study utilized CLEAR III trial data to show ICP values as low as 18 mmHg can be associated with worsened mortality in older patients and that age may affect ICP thresholds. It also highlighted the relationship between ICP and CPP, calling for investigation in merging the two parameters in management protocols.**
50. Hanley DF, Lane K, McBee N, Ziai W, Tuhim S, Lees KR, et al. Thrombolytic removal of intraventricular haemorrhage in treatment of severe stroke: results of the randomised, multicentre, multiregion, placebo-controlled CLEAR III trial. *Lancet*. 2017;389:603–11. [https://doi.org/10.1016/S0140-6736\(16\)32410-2](https://doi.org/10.1016/S0140-6736(16)32410-2).

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