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Western Trauma Association Critical Decisions in Trauma: Management of Intracranial Hypertension in Patients with Severe Traumatic Brain Injuries

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This manuscript presents a systematic approach for the management of increased intracranial pressures (ICP) in patients with severe traumatic brain injuries (TBI). These recommendations are based upon a detailed review of the literature (including other published guidelines) by the members of the Western Trauma Association (WTA) Critical Decisions in Trauma Committee ("Algorithm Committee"). The final algorithm (Figure 1) is the result of an iterative process including a series of internal reviews and refinements by the committee members, and then a final revision based upon the expert opinions of the WTA members captured during the discussion of the algorithm at the WTA Annual Meeting.

A: Goals

Our goal is to provide an easily understandable and practical protocol that can be used by general surgeons, trauma surgeons, neurosurgeons, and other clinicians to manage intracranial hypertension resulting from severe traumatic brain injuries. This algorithm is not expected to be a substitute for sound clinical judgment, specialized training, or to replace other evidence-based comprehensive recommendations[1]. The goal of this algorithm is not to minimize the valuable input provided by our neurosurgical or neuro-critical care partners, but rather to serve as a guide for the clinicians that often have to manage these patients without easy access to neurosurgical expertise. In addition, this algorithm is not a global guide to the management of the severe TBI patient, but is primarily focused on the evaluation and management of intracranial hypertension.

B: Burden of Disease

TBI is a major cause of death and disability in the United States that can be attributed to approximately 30% of all trauma-related deaths[2]. The Centers for Disease Control reports that

nearly 3 million hospital visits each year in the US are related to TBI, and it results in nearly 50,000 deaths[3]. Moreover, a considerable portion of TBI survivors are left with temporary or permanent disabilities, resulting in an annual total impact of more than $75 billion on the US economy. In the acute phase of TBI, one of the primary management goals is the avoidance of additional brain injury and the optimization of physiology to promote healing and recovery. The cornerstone of this approach is the prevention or treatment of intracranial pressure elevations, which can rapidly result in the progression of brain injury and worse outcomes. Although, operative interventions are rarely needed (e.g. craniectomy rate of 1.6% in the severely injured cohort) for TBI[4], these patients frequently require management of intracranial hypertension and optimization of cerebral perfusion.

C: Existing Guidelines

High quality clinical evidence related to the acute management of TBI is fairly sparse. However, subject matter experts have put together a number of guidelines including the best available information (and expert opinions) over the years. In addition to the well-known Brain Trauma Foundation Guidelines[1], best practice guidelines have also been developed by the American College of Surgeons[5]. These comprehensive documents address almost all aspects of triage, diagnosis, management, prognosis, and rehabilitation for TBI patients, and are therefore excellent source of information. At the same time, it is often difficult for the busy clinicians to distil these complex guidelines into a practical algorithm. Similarly, it is challenging to develop a logical sequence or priority order for the many interventions that can potentially be used to control the ICP. The goal of the WTA Algorithm Committee was to develop a simple and easy

to follow protocol that would comply with the currently available best practice guidelines, while proving a stepwise escalation strategy for the control of intracranial hypertension.

D: Definitions, Concepts and Theoretical Rationales

a. Severity of TBI: For this manuscript, we are using Glasgow Coma Scale (GCS) to stratify the patients as recommended by the American College of Surgeons Committee on Trauma[5], and consistent with the definitions used in the Advanced Trauma Life Support (ATLS) program. A GCS score of 13-15 correlates with mild TBI, 9-12 with moderate injury, and 8 or less with severe injury. To ensure that patients with altered mentation due to non-traumatic reasons are not included, this protocol applies to patients with TBI that is confirmed by a computed tomography (CT) scan. A non-contract CT scan of the head is the imaging modality of choice in patients with acute moderate to severe TBI[6]. Although, mild to moderate TBI is clinically important and more frequent than severe TBI, our algorithm focuses solely on the severe TBI cohort that is more likely to develop intracranial hypertension. Similarly, we have focused our attention on the acute phase (first 3-5 days) when the ICP management is the most challenging, rather than on chronic aspects of increased ICP or delayed complications (e.g. hydrocephalus).

b. Primary and Secondary Brain Injuries: *Primary* injuries to the brain result directly from the initial kinetic energy transfer, which can lead to axonal shearing, parenchymal bleeding, disruption of the meninges and blood vessels, and damage to the various cell types. The only practical method to decrease the incidence of primary brain injury is through prevention (e.g. helmets, avoidance of high risk behavior etc). *Secondary* brain injury, on the other hand, is an indirect consequence of processes initiated by the trauma

as well as other insults that may occur in the hours and days following the primary injury. These play a large role in determining the final extent of the eventual brain damage and its consequences. The area surrounding the primary damage ("penumbra") contains injured cells that can either recover or die, depending upon whether they encounter secondary insults or not. Therefore, avoidance and aggressive treatment of secondary insults is a major focus of post-TBI management. The list of things that can cause secondary brain injury is fairly long, and includes a host of variables, such as: hypotension, hyper/hypo ventilation, hyper/hypo glycemia, cerebral hypoxia, edema, fluid and electrolyte abnormalities especially hypoosmolarity, fever, infections, and seizures.

c. Intracranial Hypertension: Normal ICP in adults is below 15 mmHg (often less than 10 mmHg), with transient increases secondary to coughing, straining, postural changes, and sneezing etc. Sustained ICP values above 20 mmHg are considered to be pathological, and should be treated immediately and aggressively in TBI patients[7]. As the brain is contained within the fixed confines of a rigid bony skull, it is important to understand that its capacity to swell is severely limited. The pressure-volume relationship between ICP, volume of cerebrospinal fluid (CSF) and cerebral blood content is explained by the Monro-Kellie doctrine. Simply stated, the sum of volumes of brain, CSF, and intracranial blood is constant and fixed. An increase in one should cause a resultant decrease in one or both of the remaining two components as compensation[8]. Further increases that exceed this usually limited compensatory ability results in rising intracranial pressure, or "intracranial hypertension". As brain swells after the injury, the ICP increases, which often does not peak until 48-72 hours post injury. With increasing

ICPs, cerebral perfusion pressure (CPP), which is calculated as the mean arterial pressure (MAP) minus the ICP, goes down. Theoretically, an increase in MAP can maintain normal CPP, despite worsening ICPs. In reality, vascular resistance in highly abnormal following TBI, and CPP corelates poorly with the actual cerebral blood flow (CBF). Thus, it is impractical to maintain normal CBF in the setting of markedly increased ICPs by simply pushing the MAPs to supra-physiological levels. Thus, it is imperative to keep the ICPs within an acceptable range to avoid cerebral hypoperfusion and brain herniation. The acceptable upper limits of ICP have ranged from 20 mmHg[9] to 25 mmHg[10] in different randomized controlled trials, and the exact target may have to be tailored to accommodate the unique injury patterns, age and co-morbidities of a given patient[7]. In this algorithm, an ICP target of 22 mmHg or less has been selected, to be consistent with the Brain Trauma Foundation guidelines[1]. It is also important to understand that any restrictions to jugular venous drainage from external compression (e.g. tight c-spine collar) or internal reasons (e.g. increased intra thoracic pressure from positive pressure mechanical ventilation, pneumothorax, dysynchrony with the ventilator, or abdominal compartment syndrome) can manifest as an increase in the ICP. Thus, it is essential to keep the head of bed elevated (or 30-40 degree reverse Trendelenburg position if there is a concern about spinal stability). Similarly, it is important to use appropriate mechanical ventilatory strategies, aggressively treat/prevent fluid overload, and promptly correct any reasons for poor jugular venous drainage (e.g. intra-abdominal or intra-thoracic hypertension). Administration of hyperosmolar agents such as mannitol and hypertonic saline creates an osmotic gradient that can reduce edema by promoting fluid flux across the cell membranes and the blood brain barrier. In addition to promoting fluid shifts into

the vascular system, hypertonic solutions also decrease blood viscosity, which can improve the flow patterns. These agents are widely used to attenuate cerebral edema in the TBI patients[11], and their administration is endorsed by almost all the evidence-based guidelines[1, 5]. A Cochrane systematic review of the data is currently being performed[12], but at this time either mannitol (typically given in doses of 0.25 gm/kg-1.0 kg/kg) or hypertonic saline (reported clinical use from 2% to 23.5% NaCl solutions) can be used based upon the institutional guidelines and the experience of the provider[13]. It is generally accepted that both agents can effectively reduce elevated ICP, but that hypertonic saline is the preferred agent in the polytrauma patient with hemorrhage or severe associated injuries that requires vascular volume expansion in addition to ICP control. This has also made it the preferred fluid for combat related TBI in the U.S. Military Clinical Practice Guidelines[14]. These military guidelines recommend 3% saline bolus (250 ml), followed by an infusion of 50-100 mL/hr (for enroute resuscitation) with a target Na level of 150-160 mmol/L. It is important to remember that these agents can cause rapid fluid shifts with resultant hypotension (more likely with mannitol), and thus maintenance of normovolemia is important. Brisk urine output following mannitol administration should be replaced with isotonic intravenous fluids to prevent volume depletion. Arterial hypocarbia (hyperventilation) also reduces ICP, but does so at the expense of cerebral blood flow (vasoconstriction). This carries a serious risk of secondary brain injury, and guidelines recommend that pCO_2 levels must be monitored and maintained above 35 mmHg[1, 5]. It is critically important to fully understand the numerous variables that regulate CSF dynamics, which in turn influences ICP elevations[15]. pCO_2-driven changes in the pH of the CSF are well known to regulate the

CBF, with elevated and lowered pH causing direct relaxation and contraction of the smooth muscle, respectively[16]. However, newer data also suggest that arterial pCO_2 can directly regulate smooth muscle contractility, and act independently of and/or in conjunction with altered pH through a direct effect of CSF pCO_2 on the smooth muscle, endothelium, nerves, and astrocytes[16]. Plasma pH can also have an impact on brain oxygen delivery. It is logical to maintain pH as close to 7.4 as possible. Theoretically, slightly lower pH (e.g. 7.35) will push the oxygen disassociation curve to the right and offload more oxygen at the tissue level. It would also cause vasodilation of capillary beds that can improve perfusion, but may worsen ICP. Higher pH (e.g. 7.45) can do the opposite.

d. Strategies to Attenuate Brain Metabolism: Another approach that theoretically allows the brain cells to survive hypoperfusion is to decrease their metabolic rate, using either medications (e.g. barbiturates) or mild hypothermia. Sedation is commonly used to treat patient-ventilator dyssynchrony, and in severe cases of uncontrolled intracranial hypertension barbiturate coma may be used as a salvage therapy[17]. However, enthusiasm for barbiturate coma has been tempered by the lack of a proven outcome benefit in adults, and the recognition of serious side effects such as cardiac depression, hypotension, and increased infectious complications[18]. Mild hypothermia (32-34 ^{o}C) is another strategy that decreases cerebral metabolism and ICP. But despite great enthusiasm, and promising early data, it has failed to show benefits in larger controlled trials[19], and the current evidence does not support its general use in TBI patients[20]. There might be some carefully selected sub-populations of TBI patients that could benefit from therapeutic hypothermia, but evidence for this therapy needs to be better defined[21 22]. Currently, it

should only be used as a salvage therapy under an appropriate approved institutional protocol for rare patients that have failed all other standard medical interventions. The practical goal of targeted temperature management (TTM) in TBI patients should be to maintain normothermia and to avoid febrile episodes using external or intravascular cooling devices.

E: Tiers of Interventions

Our algorithm proposes tiered management of intracranial hypertension, similar to the approach taken by the ACS-TQIP[5] (Figure). All patients with TBI should receive supportive care and measures to avoid secondary brain injury, and depending upon the severity of the ICP increase (and its response to treatments), interventions can be escalated in a stepwise fashion.

a. Initial Trauma Evaluation and Management: All trauma patients should receive standard trauma evaluation and management. Secure airway should be obtained, and an oxygen saturation level of at least 90% or a pO_2 greater than 60 mmHg should be targeted. Oxygen values less than these, even transiently, have been shown to increase TBI-associated mortality four-fold[23]. Furthermore, normal ventilation rates, including an end tidal CO_2 ($ETCO_2$) of 35-40 mmHg, should be targeted for patients with severe TBI. Early hemorrhage control and appropriate resuscitation are critically important, especially in TBI patients where each episode of hypotension exaggerates the secondary brain damage and worsens the outcome[24]. Although damage control resuscitation (DCR) with short periods of permissive hypotension is fairly routine for patients with non-compressible bleeding, this is not an appropriate strategy for patients with TBI. A systolic blood pressure greater than 100 mmHg, depending on age, should be targeted for

patients with concurrent severe TBI[1]. For patients between 50 and 69 years old, a SBP of greater than 100mmHg should be targeted[1]. For patients between the ages of 15 and 49 or greater than 70 years old, however, a SBP greater than 110 mmHg should be maintained[1]. Blood products should be administered and massive transfusion protocol initiated, if clinically indicated, and coagulopathy aggressively reversed if detected. Currently, there are no data to support giving any blood products specifically for the TBI. Systemic steroids should be avoided, as their use has been associated with worsened outcomes in multiple studies[25]. Administration of high dose methylprednisolone is clearly associated with increased mortality, and is therefore contraindicated[1].

b. Initial neurological evaluation, imaging, and ICP monitoring: Early neurologic assessment, including GCS, should be performed to help guide severe TBI management. Patients should be frequently monitored for clinical signs of cerebral herniation, which includes dilated, non-reactive, and asymmetric pupils, and a motor exam with extensor posturing or progressive and rapid neurologic deterioration. In patients with concerning signs, it is acceptable to start Tier 1 and/or Tier 2 interventions (e.g. hyperosmolar therapy) prior to obtaining a CT scan.

Once stabilized, computed tomography (CT) of the head should be performed to evaluate the intracranial injuries. In all severe TBI patients, an early neurosurgical consult should be obtained, or a rapid transfer to a higher level of care should be initiated (if no neurosurgical support is immediately available). If the initial CT scan provides evidence to support primary decompressive craniectomy then the patient should be taken to the operating room emergently. These indications typically include space occupying intracranial bleeding or a mass effect on the brain. As this is a complex decision that

must take into account not only the size and location of the lesion but also many other variables, it is essential to develop practical institutional specific guidelines in consultation with neurosurgeons to help in the decision-making process. Placement of an ICP monitor should be strongly considered in patients with: GCS of 8 (or less) who have evidence of structural damage on the CT scan; GCS >8 and structural brain damage if lesions are at high risk of progression; evidence of progression of lesions/clinical deterioration; or patients who would not be examinable for a period of time (e.g. need for general anesthesia, prolonged transport, need for deep sedation/chemical paralysis). However, ICP monitoring can be safely avoided in comatose patients who either have no CT evidence of structural brain injury, or no evidence of elevated ICP on the initial CT scan (e.g. compressed basal cisterns) if close clinical monitoring and repeat CT scanning are feasible[26]. If an ICP monitor is placed, the target ICP should be <22 mmHg, and a goal CPP between 60-70 mmHg[1]. ICP monitors fall into different categories, which include the following: External ventricular drains (EVD), which are placed in the lateral ventricle and connected to a pressure monitor, and can also be used for continuous or intermittent drainage of CSF as a means to decrease the ICP. In contrast, other ICP monitors (intraparenchymal probes, microstrain gauge transducers, fiberoptic catheters, subdural bolts) provide pressure readings but can't be used to drain the CSF[7]. Despite the fact that EVDs provide a therapeutic option, their use has not been shown to be superior to intraparenchymal ICP monitors, and may even be associated with more frequent device related complications[27]. In addition to measuring the ICP, increasing number of centers are now using brain tissue oxygen tension levels (measured by intraparenchymal probes) to guide the management. Addition of brain tissue oxygen monitoring to the

conventional ICP/CPP-guided therapy seems to improve long-term outcomes, but fails to alter the ICP, mortality, or length of hospital stay[28].

c. Response to Treatment: If the ICP can be maintained under 22 mmHg, then supportive care, seizure prophylaxis, nutrition, and strategies for avoiding secondary brain injury should be continued, along with protocol driven critical care and serial exams. Supportive care must also include appropriate pain control, adequate ventilator support (oxygenation and ventilation), appropriate resuscitation, correction of acid-base and electrolyte abnormalities, and proper positioning. A repeat CT scan of the head should be obtained in 6-8 hours in all non-examinable patients, and it should be done sooner (to rule out progression of injury) if there is worsening of clinical exam and/or an increase in the ICP. A short-interval repeat CT scan is also typically obtained after any major neurosurgical intervention such as craniotomy or craniectomy. Earlier imaging is also appropriate for high risk patients (e.g. on antiplatelet or anticoagulant agents) or high risk lesions. If the ICP does not respond appropriately, or responds transiently, and CT scan shows no lesions amenable to operative intervention, then additional medical therapy should be added in a stairstep fashion starting with Tier 1.

d. Tier 1 Interventions: In addition to supportive care, consider deeper sedation, stronger analgesics, controlled CSF drainage (if a ventriculostomy is in place), and address any other reasons for increased ICP such as sub-clinical seizures, and increased intra-thoracic (e.g. pneumothorax) or intra-abdominal pressures. Propofol is recommended for the control of ICP[1], but high dose Propofol must be administered with caution to avoid morbidity. Dexmedetomidine, a highly selective α-2 adrenergic agonist, is commonly used for the control of agitation in the ICU patient population. We now have data to

suggest that in the TBI patients it may control paroxysmal sympathetic hyperactivity[29], and could also have a narcotic and sedative sparing effect[30]. But in the early post-TBI period, it should be administered with caution as its use has been associated with significant hypotension[31].

e. Tier 2 Interventions: In addition to tier 1, administer hyperosmolar therapy, use vasopressors if needed to maintain CPP between 60-70 mmHg, and consider brief periods of mild hyperventilation (pCO_2 30-35 mmHg) and possibly neuromuscular paralysis.

f. Tier 3 Interventions: In addition to tiers 1&2, consider administration of high dose barbiturate or Propofol. Hemodynamic stability is essential during barbiturate therapy to avoid significant morbidity.

g. Rescue/Salvage Interventions: *Early* bifrontal decompressive craniectomy is not recommended in severe TBI patients with diffuse injury (without mass lesion) and difficult to control ICPs[1]. This is based upon the results of the DECRA trial[9] where in adults with severe diffuse traumatic brain injury and refractory intracranial hypertension (ICP>20 mmHg for 15 minutes in a one hour period that was responsive to first trier therapy), early bifrontotemporoparietal decompressive craniectomy (DC) decreased intracranial pressure and the length of stay in the ICU but was associated with more unfavorable outcomes. However, the results were markedly different in the more recent RESCUEicp trial where DC was used in a more pragmatic fashion as a delayed *salvage* intervention[10]. In this large trial, DC in patients with traumatic brain injury and refractory intracranial hypertension (defined as ICP>25 mm Hg for 1 to 12 hours, despite stage 1 and 2 measures) resulted in lower mortality and higher rates of vegetative state, lower severe disability, and upper severe disability than medical care. The surgical

procedures in the RESCUEicp trial were calibrated to the needs of the patients. A large unilateral frontotemporoparietal craniectomy (hemicraniectomy), was performed for patients with unilateral hemispheric swelling, or bifrontal craniectomy, for patients with diffuse brain swelling that affected both hemispheres on imaging studies. Not only DC was done as the last tier intervention for more severe intracranial hypertension, patients with intracranial hematoma (evacuated or nonevacuated) that were excluded from the DECRA trial, represented almost 20% of the patients in the RESCUEicp trial. There has been a healthy debate among the experts about how to best use the data from these two trials that have some similarities, but also have key differences in study design. Most agree that in appropriately resourced settings, 1) early bifrontal DC for mild-moderate intracranial hypertension is not superior to optimal medical management, and 2) unilateral or bifrontal DC used as a last-tier therapy for patients with severe, sustained, and refractory intracranial hypertension leads to significantly lower mortality, but an increase in disability compared to medical management[32].

In patients who have failed all interventions, novel salvage efforts can include experimental therapies under institutionally approved protocols.

In summary, patients with severe TBI require specialized care from providers from multiple disciplines. They often develop intracranial hypertension, which should be managed with a logical, stepwise, and practical approach. This manuscript provides an easily understandable algorithm to streamline the delivery of care for these challenging patients.

Author Contributions

Conception and design – All authors. Data acquisition – HBA; Data interpretation – All authors; Manuscript preparation –HBA; Critical revisions – all authors.

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Figure Legend

An algorithm for the management of increased intracranial pressure (ICP) in patients with severe traumatic brain injuries (TBI)

CT= Computed tomography; Y= yes; N= no. The various decision making points and interventions are explained in the text of the manuscript, and these areas are marked in the figure for easy identifications as follows: * If the patient shows signs of severe intracranial hypertension/impending herniation then it is acceptable to initiate Tier 1 (additional analgesics & sedatives, CSF drainage) and/or Tier 2 interventions (hyperosmolar therapy, neuromuscular paralysis) prior to obtaining a CT scan [section E (b)]; [1] Indications for primary decompressive craniectomy [section E (b)]; [2] Indications for ICP monitor placement [section E(b)]; [3]supportive care and measures to avoid secondary brain injury [section D (b) (c), section E (a), and table below]; [4]Timing for routine repeat CT scan of the head [section E (c)]; [5]Tier 1 interventions [section E (d), and table below]; [6]Tier 2 interventions [section E (e), and table below]; [7]Tier 3 interventions [section E (f), and table below]; [8]Rescue interventions [section E (g)]; [9]Indication for repeat CT scans [section E (c), and table below].

Figure 1

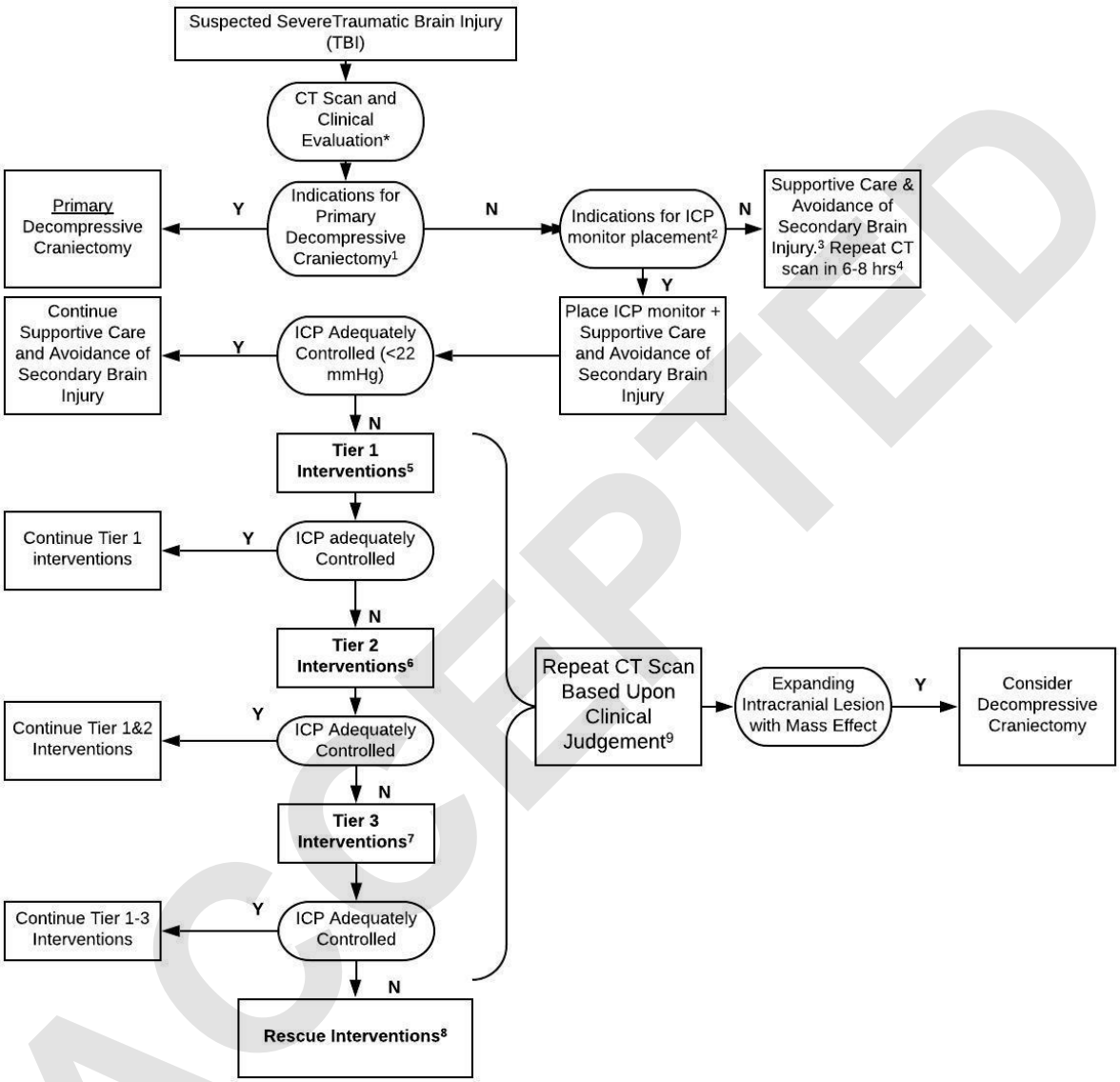

Table 1

Categories	Interventions
Supportive Care and Measures to Avoid Secondary Brain Injury	• Standard Trauma Care • Hemorrhage control • Adequate Resuscitation and Administration of Blood Products • Elevation of the head of bed • Analgesics/Sedatives • Fluid and Electrolyte Management • Avoidance of Hyponatremia • Prevention of Hyperpyrexia • Treatment for Hyper/Hypoglycemia • Supplemental Oxygen to Maintain Oxygen Saturation >90% and pO2 > 60 mmHg • Normocarbic Ventilation (pCO2 35-40 mm Hg) • Correction of Coagulopathy • Early Delivery of Nutrition (Preferentially Enteral) • Treatment of Infections
Tier 1	• Additional Analgesia/Sedation • Cerebrospinal Fluid Drainage
Tier 2	• Hyperosmolar Therapy • Neuromuscular Paralysis
Tier 3	• High Dose Barbiturates • High Dose Propofol
Rescue Strategies	• Decompressive Craniectomy • Experimental Therapies