Catastrophic Non-Survivable Brain Injury (CPG ID: 13)
Useful guidelines to manage casualties with catastrophic, non-survivable brain injury at Role 2 and Role 3 facilities.

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BACKGROUND

Catastrophic brain injury, for the purpose of this guideline, is defined as any brain injury that is expected after imaging evaluation and/or clinical exam to result in the permanent loss of all brain function above the brain stem level.

NOTE: For patients with potentially survivable but severe Traumatic Brain Injury (TBI), refer to Joint Trauma System CPG, Neurosurgery and Severe Head Injury, 02 Mar 2017.

1. The intent of this guideline is to provide clinically useful recommendations which will allow providers at all roles of care who encounter these injuries to optimize the opportunity for these casualties to be evacuated safely and appropriately to the next level of care.

2. It is not the purpose of this guideline to address the complexities of brain death determination, or at what role of care and by what types of providers this determination should be made.

3. If appropriately resuscitated and hemodynamically normalized, these patients are more likely to be reunited with their families at Role 4 facilities. Additionally, evacuation from a combat theater of operations preserves the potential to honor the expressed intent of a patient to participate as an organ donor. Experience at Landstuhl Regional Medical Center between 2003 and 2013 demonstrated this opportunity to be on par with higher performing centers in CONUS. (Publication in draft, J. Oh, personal communication, 05 Aug 2016)

Catastrophic brain injury is associated with profound physiologic alterations that result in diffuse vascular regulatory disturbances and widespread cellular injury.\(^1,2\) Severe alterations in metabolism,\(^3-5\) endocrine function,\(^6-9\) immunology\(^10\) and coagulopathy\(^11-17\) also commonly manifest. These disturbances frequently lead to multiorgan system failure, cardiovascular collapse and asystole in up to 60% of patients if not appropriately managed.\(^3\)

It is known from animal studies that this cardiovascular deterioration is associated with impaired oxygen utilization, a shift from aerobic to anaerobic metabolism, a depletion of glycogen and myocardial high-energy stores, and the accumulation of lactate.\(^3,5,9\) This irregular metabolism has been associated with low levels of triiodothyronine (T3), thyroxin (T4), and to a lesser extent cortisol and insulin.\(^6-9\) Therapeutic replacement with T3 has been associated with complete reversal of anaerobic metabolism and subsequent stabilization of cardiac function when applied to human brain dead subjects.\(^5,7\) In addition, the use of T3 and similar thyroid replacement preparations have been associated with significant improvements in cardiovascular status, reductions in inotropic support, and decreases in donors lost from cardiac instability.\(^5,18-20\) The etiology of this functional “hypothyroid state” is poorly understood, but may be a result of lower than normal thyroid stimulating hormone levels caused by the irreversible damage to the hypothalamus and pituitary from ischemia.\(^21\) Another explanation is a decrease in the peripheral conversion of T4 to its more potent analogue T3, similar to the euthyroid sick syndrome. It should be noted that evidence which validates the efficacy of hormonal replacement in this population of patients is not conclusive.\(^22,23\) While this subject matter continues to be evaluated it should be recognized that early, effective, conventional critical care management is the therapeutic mainstay in these patients.\(^24\)
TREATMENT

The clinical management of catastrophic brain injury is focused on hemodynamic stabilization. This consists of three aspects:

1. Early identification of the severity of injury, as severity of the TBI correlates with deficiencies in the pituitary adrenal axis, leading to hemodynamic instability. 

2. Intensive care management to achieve hemodynamic stability based on degree of TBI and associated injuries.

3. Resuscitation with fluids and blood products, early use of vasopressors and consideration for endocrine/hormone therapy in patients with refractory hemodynamic instability.

Vasopressors such as norepinephrine should be utilized if the mean arterial pressure (MAP) remains less than 70 mmHg despite adequate fluid resuscitation. (See Appendix A.) In patients whom Diabetes Insipidus (DI) is suspected, consider adding a vasopressin drip to norepinephrine after initial treatment with DDAVP. (See Appendix A and Appendix B treatment of DI). In casualties with catastrophic head injury who require more than a single vasopressor to maintain a systolic blood pressure of 100 mmHg or have evidence of DI, strong consideration should be given for addressing the endocrine abnormalities associated with these injuries that can contribute to ongoing hemodynamic instability. (See Appendix B.) 

Adjuncts shown to assist with hemodynamic stability include stress dose steroids, IV insulin, and replacement of thyroid hormone.

These adjuncts are:

1. 1 ampule 50% dextrose IV
2. 2 g solumedrol IV
3. 20 units regular insulin IV
4. 20 micrograms of thyroid hormone (T4) IV, if available

This is given as an initial bolus followed by a continuous infusion of 10 mcg/hr of T4, if it is available.

An appropriately aggressive approach should also stress early identification and management of catastrophic brain injury-related complications such as:

1. Disseminated intravascular coagulation (DIC)
2. Diabetes Insipidus (DI)
3. Neurogenic pulmonary edema (NPE)
4. Hypothermia
5. Cardiac arrhythmias

See Appendix C for management points on each.
TRANSFUSIONS CONSIDERATIONS

The use of blood products for these patients is a complex issue involving the proper use of limited resources in theater and the paucity of evidence-based recommendations on this topic. If the patient responds hemodynamically to the previous interventions and appears stable after the initial insult, a reasonably aggressive approach should be taken to correct coagulopathy rapidly and transfuse PRBCs to a level sufficient to optimize oxygen delivery to tissue and organs. There is little to support optimal hemoglobin in this population, but in general critically ill populations, a target above at least 7g/dL has been recommended. In this patient population, however, goal hemoglobin of 10g/dl has been set for this protocol. (See Appendix A.) Other blood products are used as per standard ICU practice to correct pre-existing traumatic coagulopathy or disseminated intravascular coagulation generated by the release of tissue factor from necrotic brain tissue. An International Normalized Ration (INR)<1.5 and platelet count >50,000 should be considered until evacuation occurs.

DETERMINING FUTILITY AND THE APPROPRIATENESS OF TRANSPORT

RESPONSIVE

Within the context of a catastrophic, non-survivable brain injury, if the patient responds to initial resuscitation and treatment and achieves clinical stability, transport to the next higher role of care should be considered. In these circumstances, aggressive effort should be made to re-unite the service member with family at the Role 4 facility. As a secondary priority to be considered only in these otherwise futile situations, service members may also be evaluated for potential organ donation at the Role 4 facility.

NON RESPONSIVE

Within the context of a catastrophic, non-survivable brain injury, if the patient does not respond to initial aggressive resuscitation, continued further efforts should be guided by a combination of clinical judgment and battlefield effects, including: resources available at the current role of care facility (critical care personnel, equipment, and supply resources), other critically injured patients requiring immediate attention, potential for further casualties from active troop contact, and availability and capacity of evacuation to next higher role of care.

The medical evacuation clinical and operational leadership should be engaged early in these circumstances. Clinical discussion and decisions regarding stability for transport should occur between the trauma team and the flight team. The clinical team should also inform medical operations leadership who will be able to provide information about evolving battlefield effects affecting the availability and capacity of transport.

If the patient cannot be clinically stabilized or battlefield effects otherwise preclude transport, no further efforts should be pursued and withdrawal of support with dignity and with comfort measures is the most respectful and appropriate course of action. Providers presented with these patients are always encouraged to discuss patient care with colleagues and medical leadership at their location to achieve a clinical consensus in these very difficult situations. When available and appropriate, they are also encouraged to communicate with trauma providers at the next higher role of care to achieve consensus on the plan to transport or not to transport. These situations are fortunately not common, but constitute the most challenging of clinical and ethical management dilemmas that one can face while deployed.
PERFORMANCE IMPROVEMENT MEASURES

INTENT (EXPECTED OUTCOMES)

In patients identified as meeting criteria for catastrophic care, all efforts are undertaken by protocol to keep the patient hemodynamically stable in an effort to deliver them to the next level of care.

PERFORMANCE/ADHERENCE MEASURES

Early use of goal directed fluid therapy, pressors, and hormone therapy in patients with catastrophic brain injury. These will be monitored by using the patient record and the DoD Trauma Registry.

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for Performance Improvement (PI) monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed. The system review and data analysis will be performed by the Joint Trauma System (JTS) Director, JTS Program Manager, and the JTS PI Branch.

RESPONSIBILITIES

It is the trauma team leader’s responsibility to ensure familiarity, appropriate compliance and PI monitoring at the local level with this CPG.

REFERENCES


APPENDIX A: CATASTROPHIC BRAIN INJURY RESUSCITATION MANAGEMENT FOR PERSISTENT HYPOTENSION

Evaluate Patient in ER ASAP
(follow ATLS guidelines)

1. Labs obtained: ABG/serum lactate/CBC/PT/PTT/lytes head-injured patients
2. Transfuse to maintain Hct > 30
3. Bolus 1 liter NS or 500 ml 3% saline
4. Control active bleeding
5. Place large trauma central line
6. Transfer ASAP to ICU following CT scan

Caution: Patients may go from hypertension to hypotension rapidly

YES
Normotensive patient?

NO

Continue to fluid resuscitate as needed and correct lab abnormalities. See Appendix B.

Continue to fluid resuscitate with NS

YES
SBP>100 or MAP>65?

NO

See Appendix B for further management

Continue to bolus with blood products to H/H of 10/30

YES
Blood pressure & H/H goals met?

NO

1. Norepinephrine drip (0.1-0.5 mcg/kg/min)
2. Look for DI and replace UOP over 200cc with 1/2 NS cc for cc every hour or, if patient is hypertensive, DDAVP 1-2 micrograms of DDAVP IVP (q 2-8 hours as needed)
3. Consider starting vasopressin at 0.01-0.04 units/min titrate to SBP>100/MAP > 65 if DI is suspected after initial treatment with DDAVP
APPENDIX B: MANAGEMENT OF CATASTROPHIC BRAIN INJURY

1. Disseminated Intravascular Coagulation (DIC)

Begin correcting any coagulation lab abnormalities (thrombocytopenia, increased INR) early, before clinical DIC.

2. Diabetes Insipidus (DI)

   - If patient is normotensive, serum sodium > 150 and Urinary Output (UOP) > 600cc/hr, give 1-2 micrograms of DDAVP IVP (q 2-8 hours as needed)
   - Replace UOP cc for cc with 1/2 NS q hour for UOP > 200 (example: for UOP of 1000cc replace with 800cc of 1/2 NS).
   - If patient’s serum sodium > 150 and UOP > 300cc/hr, replace UOP cc for cc with 1/2 NS q hour for UOP > 200cc.
   - If patient is hypotensive, then use protocol in Appendix A, and consider adding a vasopressin drip if DI is suspected.

Pitfalls: Assuming high UOP is from DI, but is really from diuretics and/or Mannitol. Replace diuretic fluid loss with NS or LR if hypotensive. (Another marker of DI: urine specific gravity < 1.005).

3. Tachycardia and Hypertension

This commonly occurs prior to complete herniation and should not be treated. Abrupt fluctuations in blood pressure during the period before and immediately after herniation are common. Aggressive treatment of hypertension will only further exacerbate the hypotension that may follow during the natural physiologic course of the herniation process.

4. Neurogenic Pulmonary Edema

This may occur and results in decreased PaO₂; increase ventilator support as needed. With severe problems of oxygenation, utilize increased Positive End Expiratory Pressure (PEEP) and consider advanced ventilator modes such as Airway Pressure Release Ventilation (APRV) or VDR if available. Increasing PEEP, however, can decrease cerebral venous return and should be considered when managing neurogenic pulmonary edema. Similarly, APRV results in permissive hypercapnia, also detrimental to a head injured patient. Once neurogenic edema has been diagnosed, maintaining a low cardiac filling and limiting intravenous fluids to minimize pulmonary edema would be ideal, however, it must be done while balancing of needs of the other organ systems.

5. Hypokalemia and/or Hyperglycemia

Use sliding scales as needed.

6. T4 Protocol

Many patients have a T-3/T-4 deficiency and require additional thyroxin. Start patients on thyroxin protocol if thyroxine is available in patients with severe TBI that are continually hypotensive despite adequate fluid resuscitation and high dose pressors. (Appendix C: T-4 Replacement Protocol) Be aware that potassium will likely need to be aggressively replaced once thyroxin is started.

7. Cardiac Arrest

Follow ACLS code guidelines.
APPENDIX C: T-4 REPLACEMENT PROTOCOL

PRETREATMENT

1. Fluid resuscitate to predefined endpoints (CVP > 7, SBP > 100)
2. Give blood to achieve an H&H above 10 and 30
3. Correct electrolyte imbalances

PREREQUISITE

Patient is requiring a combined vasopressor need greater than 15 mcg (all VP added) to maintain a systolic pressure of 100 after the pre-treatment is completed or becomes hemodynamically unstable.

T-4 PROTOCOL

- Administer IV boluses of the following in rapid succession:
  - 1 Amp of 50% Dextrose
  - 2 gm of Solumedrol
  - 20 units regular insulin
  - 20 mcg Thyroxin (T-4)
- Start a drip of 200 mcg T-4 in 500cc Normal Saline (0.4mcg/cc). Administer at 25cc (10mcg) per hour initially. Reduce levels of other vasopressors as much as possible and then adjust T-4 as necessary to maintain desired pressure.
  - Donors > 100 lbs give above dose
  - Donors 50-75 lbs. give 13cc = 5.2 mcg/hr
  - Donors 75-100 lbs. give 19cc = 7.6 mcg/hr
- After 30 to 60 minutes, patients may become tachycardic with an increase in temperature and blood pressure.

Monitor K+ levels carefully. The only perceived complication of T-4 identified to this point is an unusually high K+ requirement in some cases.
APPENDIX D: ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of “off-label” uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e. “off-label”) uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing “investigational new drugs.” These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the “standard of care.” Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES

Balanced Discussion

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.