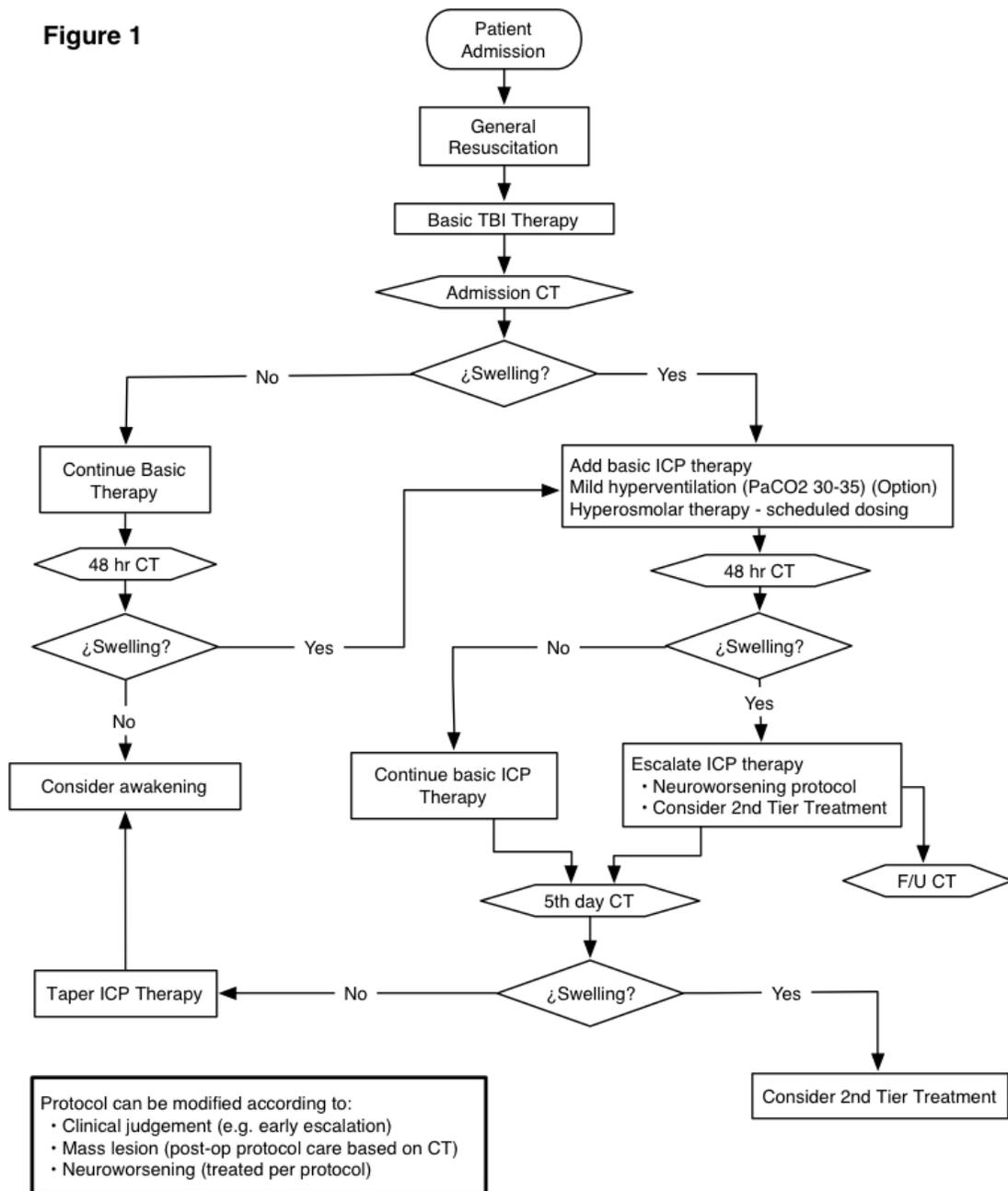


Guidelines for the Management of Severe Traumatic Brain Injury Patients:

Standard Care Group

The guidelines are presented below and are also summarized in Figures 1 and 2.

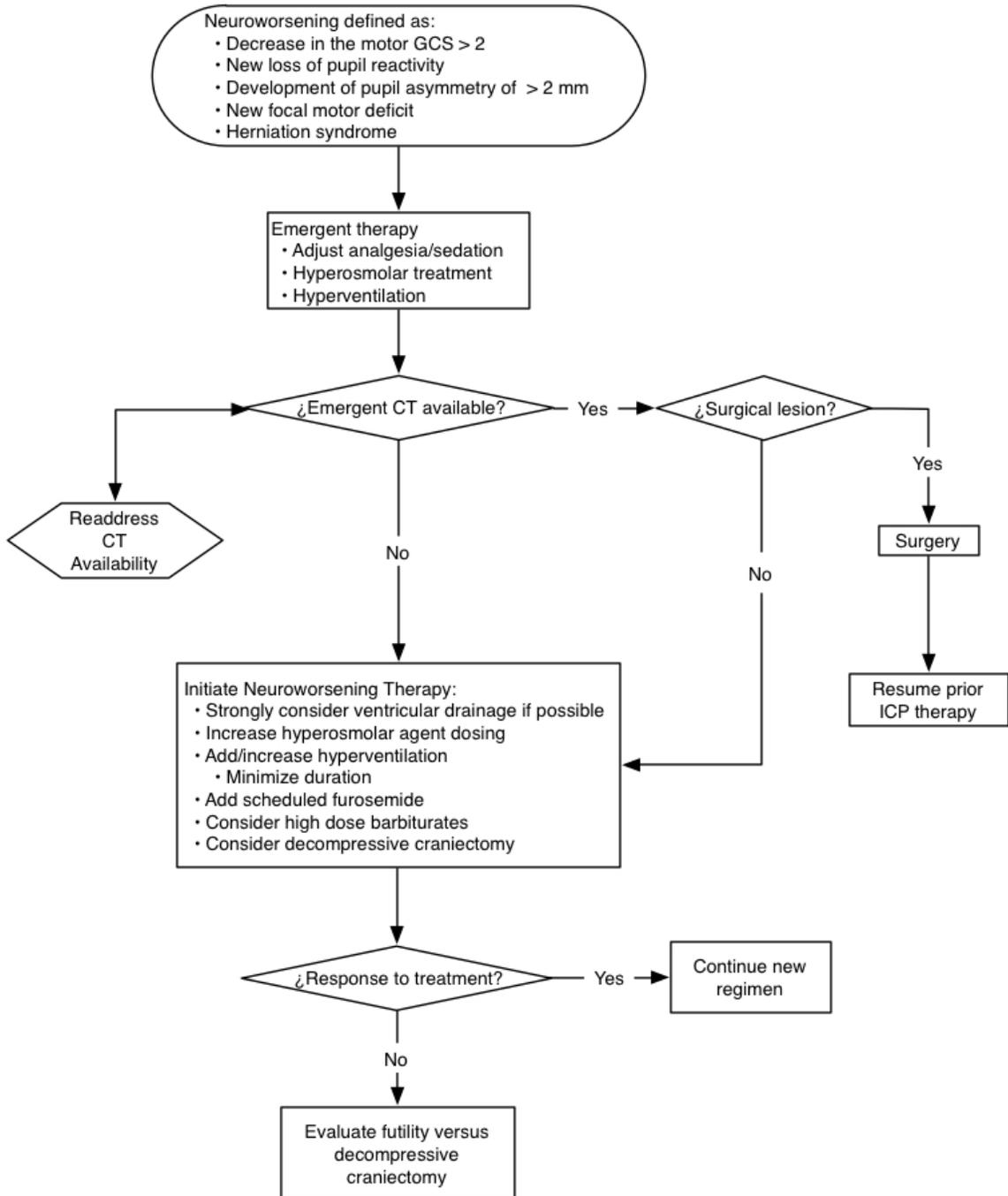


This protocol could be modified:

- By clinical judgment (i.e. DC or barbiturates could be used earlier on)
- Mass lesion on CT scans (procedure to evacuate if it is indicated and then continuing with the protocol based on CT findings)

- Neuroworsening (NW) whenever occurs should be treated as follows (see next)

Figure 2



1. Patient monitoring measures: We strongly suggest using these interventions whenever available and/or possible.
 - a. Place continuous SaO₂ and EtCO₂ monitors

- b. Insert indwelling urinary catheter to monitor urine output
 - c. Insert arterial catheter for arterial pressure monitoring
 - d. Insert central venous catheter for infusion of solution and central venous pressure monitoring
 - e. Monitor clinical neurological status each hour
 - i. Pupil size and reactivity
 - ii. GCS
 - f. Obtain **brain CT**
 - i. To evaluate evolution 48 hours after the admission CT
 - ii. To evaluate evolution 5-7 days after the admission CT
 - iii. As needed based on patient clinical condition
2. General management measures
- a. Place patient on mechanical ventilation, goal SaO₂ > 90% and PaO₂ > 60 mmHg
 - b. Use adequate sedation and analgesia
 - i. Acceptable medications include benzodiazepines, opioids, propofol and low dose barbiturates
 - 1. Low dose barbiturate dosing:
 - a. Thiopental (Pentothal) 1-2 mg/kg/hr IV continuous infusion (approx 1.5-3 gm/day)**
 - c. Maintain head of bed at 30°
 - d. Maintain head and neck aligned and in neutral position
 - e. Actively monitor body temperature and treat hyperthermia
 - f. Hyperthermia defined as central temperature $\geq 38^{\circ}\text{C}$
 - i. Non-pharmaceutical cooling measures
 - 1. Cooling blanket, ice packs
 - ii. Pharmaceutical cooling measures
 - 1. Dipirona (Metamizole sodium)
 - g. Early enteral nutritional support

- i. Initiate within 48 hours of injury
 - ii. Give 25 Kcal/kg patient weight per day
 - h. Pharmacologic prophylaxis for early post traumatic seizures
 - i. Phenytoin (IV or PO)
 - 1. Loading and maintenance doses as per individual hospital guidelines
 - 2. Continue for 7-28 days
 - i. Gastric bleeding prophylaxis
 - i. Ranitidine or Omeprazole (IV or PO)
 - 1. Administer as per individual hospital guidelines
 - j. Prevent decubitus lesions and treat as indicated
 - k. Deep venous thrombosis prophylaxis
 - l. Frequent tracheal suctioning with sterile technique to prevent pulmonary infections
 - m. Maintain Hb \geq 7 mg/dL, use blood transfusions as needed
- 3. CT scans
 - a. First CT: upon hospital admission
 - b. Second CT: 48 hours after the first CT
 - c. Third CT: 5-7 days after the first CT
 - d. Additional CT scans as needed based on patient clinical condition
- 4. Treatment Goals for adequate cerebral perfusion and oxygenation
 - a. Avoid hypotension - systolic blood pressure (SBP) > 90 mmHg, mean arterial pressure (MAP) > 70 mmHg
 - b. Arterial blood oxygen saturation (SaO₂) > 90% or PaO₂ > 60 mm Hg**
- 5. Initial therapeutic interventions
 - a. Normal saline solution (0.9% NaCl) to obtain a CVP of 10-12 cmH₂O
 - b. Vasopressors when necessary to obtain a SBP > 90 mmHg **or mean arterial pressure (MAP) > 70 mmHg**
 - c. Maintain PaCO₂ 35-40 mmHg if CT is normal

- i. In Cochabamba, correct for altitude and maintain PaCO₂ 32-36 mmHg
 - d. If a space-occupying lesion exists, surgical evacuation is indicated if possible
- 6. Specific therapeutic interventions-**Standard (Non-Monitored) Therapy**
 - a. **After optimized sedation and analgesia, hyperventilation and hyperosmotic therapy should be started simultaneously if there is evidence of edema on CT, as indicated as following:**
 - 1. **Compressed peri-mesencephalic cisterns**
 - 2. **Midline shift**
 - 3. **Cortical sulcal compression / effacement**
 - b. Mild hyperventilation
 - i. Maintain PaCO₂ 30-35 mmHg (PaCO₂ 28-32 mmHg in Cochabamba)
 - c. Hyperosmolar/Hypertonic Therapy
 - i. Mannitol should be used first except in the following situations (HHH):
 - a. Arterial Hypotension
 - b. Hypovolemia
 - c. Hyponatremia
 - 2. Hyperosmolar (Mannitol) therapy guidelines and dosing
 - a. Plasma osmolarity **or tonicity** should be monitored at least every 12-**24** hours
 - i. Plasma osmolarity **or tonicity** should be calculated using the following formulae:
 - 1. $\text{Osmolarity} = 2 * (\text{Na}) + (\text{BUN}/ 2.8) + (\text{Glucose}/18)$
 - 2. **Tonicity = 2 * (Na + K) + (Glucose/18)**
 - ii. Hyperosmolar (Mannitol) therapy should be suspended for plasma osmolarity > 320 **or tonicity > 340**
 - b. Mannitol dosing regimen using 20% Mannitol bolus:
 - i. 100ml (20gm) IV every 3-4 hours for the first 3 days, then

- ii. 80ml (16gm) IV every 3-4 hours on day 4, then
- iii. 60ml (12gm) IV every 3-4 hours on day 5, then
- iv. 40ml (8gm) IV every 3-4 hours on day 6 and suspend

3. Hypertonic saline therapy guidelines and dosing

- a. Hypertonic saline should only be used in cases of HHH as described above
- b. Plasma osmolarity **or tonicity** and serum sodium should be monitored at least every 12-24 hours
 - i. Plasma osmolarity **or tonicity** should be calculated using the following formulae:
 - 1. $\text{Osmolarity} = 2 * (\text{Na}) + (\text{BUN}/ 2.8) + (\text{Glucose}/18)$
 - 2. **$\text{Tonicity} = 2 * (\text{Na} + \text{K}) + (\text{Glucose}/18)$**
 - ii. Hypertonic saline therapy should be suspended for plasma **osmolarity > 360 or tonicity > 380 or serum sodium > 160**
- c. Hypertonic saline dosing regimen using 5%NaCl solution bolus:
 - i. 80ml normal saline (0.9%NaCl) + 20ml 20%NaCl = 100ml 5%NaCl solution
 - ii. 100ml IV every 4-12 hours for 6 days then suspend

d. High dose IV barbiturates

- i. Use after hyperventilation and hyperosmolar/hypertonic therapies
- ii. Should be used if second CT shows evidence of compressed PMC
- iii. Dosing: **Thiopental (Pentothal) 2.5-4 mg/kg/hr IV continuous infusion for 3 days (approx 4-6 gm/day)**
- iv. **Hypotension must be avoided**

7. Neuroworsening requires increased therapeutic intensity level, including decompressive craniectomy when necessary and available. Any one or all of the following therapeutic interventions should be utilized based on patient conditions.

- a. Neuroworsening defined as:

1. Decrease in the motor GCS ≥ 2
2. New loss of pupil reactivity
3. Interval development of pupil asymmetry of ≥ 2 mm
4. New focal motor deficit
5. Herniation syndrome

ii. **Hypertonic therapy:**

1. **Additional** mannitol dosing regimen using 20% Mannitol bolus:
 - i. 200ml (40gm) IV every 3-4 hours for 1 day, then
 - ii. 100ml (20gm) IV every 3-4 hours for 2 days, then
 - iii. 80ml (16gm) IV every 3-4 hours on day 4, then
 - iv. 60ml (12gm) IV every 3-4 hours on day 5, then
 - v. 40ml (8gm) IV every 3-4 hours on day 6 and suspend
- b. High dose mannitol at 0.5 – 1 gm/kg per dose should be used in the case of acute neurological deterioration and as a temporizing measure prior to decompressive craniectomy if there is no response to medical management. The above duration of treatment (6 days) should be followed only when neurosurgical intervention is not available.
- c. Contraindicated in patients with HHH
 - i. **Use hypertonic saline**
- d. **Hypertonic saline – doses as above**

iii. Increase hyperventilation (HV)

1. Maintain PaCO₂ of 25-30 mmHg (PaCO₂ 22-28 mmHg in Cochabamba)
2. Use for shortest time period possible to reverse neurological deterioration
3. If no response, stop HV and use barbiturates

- iv. High dose IV barbiturates
 - 1. Thiopental (Pentothal) 2.5-4 mg/kg/hr IV continuous infusion for 3 days**
 - 2. Hypotension must be avoided**
 - v. Furosemide 20mg IV every 8 hours
 - vi. Head CT is strongly suggested if possible
8. Second tier therapy to be considered in salvageable patients **under conditions such as:**
- a. To be considered in case of:
 - i. **Persistent neuroworsening not responding to an increased therapeutic intensity level (as indicated above). CT is recommended, if possible.**
 - ii. **Follow-up CT (eg day 5 CT) showing Inadequate response to treatment such as persistent edema**
 - b. **Primary options**
 - i. **Decompressive craniectomy**
 - ii. **High dose IV barbiturates:**
 - 1. Thiopental (Pentothal) 2.5-4 mg/kg/hr IV continuous infusion (approx. 4-6 gm/day)**
 - 2. Hypotension must be avoided**
 - c. **Other options**
 - i. **Hyperventilation to maintain PaCO₂ 25-30 mmHg (PaCO₂ 22-28 mmHg in Cochabamba), use for shortest time period possible to reverse neurological deterioration**
 - ii. **Hypothermia**
 - iii. **Lund therapy**
9. Management following decompressive craniectomy
- a. Use adequate sedation and analgesia
 - b. Mild hyperventilation to maintain PaCO₂ 30-35 mmHg (PaCO₂ 28-32 mmHg in Cochabamba)
 - c. Hyperosmolar/hypertonic therapy

- i. Use after sedation/analgesia is optimized
 - ii. Mannitol should be used first, except in the following situations (HHH):
 - a. Arterial Hypotension
 - b. Hypovolemia
 - c. Hyponatremia
2. Mannitol therapy guidelines and dosing
- a. Plasma osmolarity **or tonicity** should be monitored at least every 12-**24** hours
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 1. $\text{Osmolarity} = 2 * (\text{Na}) + (\text{BUN} / 2.8) + (\text{Glucose} / 18)$
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 - ii. Hyperosmolar (Mannitol) therapy should be suspended for plasma osmolarity > 320 **or tonicity > 340**
 - c. Continue the pre-operative mannitol dosing regimen using 20% Mannitol bolus:
 - i. 100ml (20gm) IV every 3-4 hours for the first 3 days, then
 - ii. 80ml (16gm) IV every 3-4 hours on day 4, then
 - iii. 60ml (12gm) IV every 3-4 hours on day 5, then
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3. Hypertonic saline therapy guidelines and dosing
- a. Hypertonic saline should only be used in cases of HHH as described above
 - b. Plasma osmolarity **or tonicity** and serum sodium should be monitored at least every 12-**24** hours
 - i. Plasma osmolarity **or tonicity** should be calculated using the following formulae:

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b. **$\text{Tonicity} = 2 * (\text{Na} + \text{K}) + (\text{Glucose}/18)$**

2. **Hypertonic saline therapy should be suspended for plasma osmolarity > 360 or tonicity > 380 or serum sodium > 160**

c. Continue the pre-operative hypertonic saline dosing regimen using 5%NaCl solution bolus:

i. 80ml normal saline (0.9%NaCl) + 20ml 20%NaCl = 100ml 5%NaCl solution

ii. 100ml IV every 4-12 hours for 6 days then suspend

d. High dose IV barbiturates

i. Use after hyperventilation and hyperosmolar/hypertonic therapies

1. Dosing: Thiopental (Pentothal) 2.5-4 mg/kg/hr IV continuous infusion for 3 days

2. Hypotension must be avoided

e. Obtain head CT within 24 hours following decompressive craniectomy

i. If edema improved, stop sedation, hyperventilation, hyperosmolar/hypertonic therapy, and high dose barbiturate therapy and evaluate neurologic exam and GCS

ii. If edema not improved or worse, continue sedation, hyperventilation, hyperosmolar/hypertonic therapy, and high dose barbiturate therapy as above

10. Contraindicated treatments

a. **Corticosteroids for brain injury treatment**

b. **Use of anticonvulsants for prophylaxis of late epilepsy (beyond 28 days)**