

Title: Effect of adjunctive therapies for shock reversal in cardiac arrest patients with post-resuscitation shock: An ancillary pre-planned study

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Objectives: Elucidate the effect of adjunctive therapies for shock reversal (e.g. Vasopressin, Methylene Blue, Corticosteroids) in cardiac arrest patients with post-resuscitation shock regarding mortality and neurologic outcome

Hypothesis: Use of adjunctive therapies for shock reversal in cardiac arrest patients with post-resuscitation shock does not impact mortality or neurologic outcome.

Main Outcomes: Primary Endpoints: 30-d Mortality and 6 months neurologic outcome (mRS)

Population: Patients randomized to STEPCARE suffering from post-resuscitation shock within 24 hours from randomization [PMID: 25971391]. Defined as: 1. Hypotension with the need for continuous vasopressors for more than 6 hours despite adequate fluid loading and 2. Lactate Levels >2 mmol/l. The evaluated adjunctive therapies for shock reversal will be: Vasopressin, Methylene Blue and Corticosteroids.

Design/Statistics: Matched, Weighted, G-Estimated adjustment of the study population at randomization, (with time-varying adjustment).

Additional Variables to be included into Database (same as for the inotropic therapy in cardiac arrest patients with post-resuscitation shock sub-study):

- **Hourly Observations (at 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40 hours):**
 - RASS and Drugs -> (We would take the Vasoactive Drugs out of this Section and create a dedicated one)
 - Vasoactive Management
 - Noradrenaline Dose [mcg/kg/min] [mcg/min] [Not used]
 - Vasopressin Dose [IE/min] [Not used]
 - Adrenaline Dose [mcg/kg/min] [mcg/min] [Not used] -> **Instead of the Question Adrenaline Infusion Yes/No**
 - Dobutamine Dose [mcg/kg/min] [mcg/min] [Not used] -> **Instead of the Question Dobutamine Infusion Yes/No**
 - Milrinone Dose [mcg/kg/min] [mcg/min] [Not used]
 - Levosimendan Dose [mcg/kg/min] [mcg/min] [Not used]

- Use of Methylene Blue [yes] [no]
 - Use of Corticosteroids for Shock Reversal [yes] [no]
- Fluid Management
 - Infused crystalloids for a plasma expanding/ resuscitation purpose over the last 4 hours [ml]
 - Infused colloids for a plasma expanding/ resuscitation purpose over the last 4 hours [ml]
- **Hourly Observations (at 48, 56 hours):**
 - RASS and Drugs -> (We would take the Vasoactive Drugs out of this Section and create a dedicated one)
 - Vasoactive Management
 - Noradrenaline Dose [mcg/kg/min] [mcg/min] [Not used]
 - Vasopressin Dose [IE/min] [Not used]
 - Adrenaline Dose [mcg/kg/min] [mcg/min] [Not used] -> **Instead of the Question Adrenaline Infusion Yes/No**
 - Dobutamine Dose [mcg/kg/min] [mcg/min] [Not used] -> **Instead of the Question Dobutamine Infusion Yes/No**
 - Milrinone Dose [mcg/kg/min] [mcg/min] [Not used]
 - Levosimendan Dose [mcg/kg/min] [mcg/min] [Not used]
 - Use of Methylene Blue [yes] [no]
 - Use of Corticosteroids for Shock Reversal [yes] [no]
 - Fluid Management
 - Infused crystalloids for a plasma expanding/ resuscitation purpose over the last 8 hours [ml]
 - Infused colloids for a plasma expanding/ resuscitation purpose over the last 8 hours [ml]
- **Hourly Observations (72, 96, 120 hours):**
 - RASS and Drugs -> (We would take the Vasoactive Drugs out of this Section and create a dedicated one)
 - Vasoactive Management
 - Noradrenaline Dose [mcg/kg/min] [mcg/min] [Not used]
 - Vasopressin Dose [IE/min] [Not used]
 - Adrenaline Dose [mcg/kg/min] [mcg/min] [Not used] -> **Instead of the Question Adrenaline Infusion Yes/No**
 - Dobutamine Dose [mcg/kg/min] [mcg/min] [Not used] -> **Instead of the Question Dobutamine Infusion Yes/No**
 - Milrinone Dose [mcg/kg/min] [mcg/min] [Not used]
 - Levosimendan Dose [mcg/kg/min] [mcg/min] [Not used]
 - Use of Methylene Blue [yes] [no]
 - Use of Corticosteroids for Shock Reversal [yes] [no]
 - Fluid Management
 - Infused crystalloids for a plasma expanding/ resuscitation purpose over the last 24 hours [ml]
 - Infused colloids for a plasma expanding/ resuscitation purpose over the last 24 hours [ml]