# WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

## Worksheet author(s)

<table>
<thead>
<tr>
<th>Name</th>
<th>Date Submitted for review</th>
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<tbody>
<tr>
<td>Maaret Castrén</td>
<td>06.08.2009</td>
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## Clinical question.

**In adult and pediatric patients with ROSC after cardiac arrest (P), does the use of seizure prophylaxis or effective seizure control (I) as opposed to standard care (no prophylaxis) (C) improve outcome (O)?**

**Is this question addressing an intervention/therapy, prognosis or diagnosis?** Intervention/therapy

**State if this is a proposed new topic or revision of existing worksheet:** This worksheet is new

## Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? None

## Search strategy (including electronic databases searched).

- **Cochrane Library**
  - N = 0

- **PubMed**: "Heart Arrest"[Mesh] and cardiac arrest and seizures and survival N = 40, 8 abstracts, "Seizures"[Mesh] AND ("heart arrest"[MeSH Terms] OR ("heart"[All Fields] AND "arrest"[All Fields])) OR "heart arrest"[All Fields])
  - N = 243 topics, 14 abstracts

- **EMBASE**
  - Cardiac arrest and seizures
  - N = 310 topics, of these N = 36 abstracts

- **Hand picked from PubMed from Related articles**
  - N = 5

## State inclusion and exclusion criteria

**Inclusion:** only human, adult or pediatric cardiac arrest with ROSC, reporting on effect on survival, comparing seizure treatment to no treatment on survivors

**Exclusion:** animal studies, comments or letters or editorials or only abstracts

## Number of articles/sources meeting criteria for further review: 553 abstracts were reviewed for relevance, 25 articles were reviewed in depth, 8 articles were used to formulate this worksheet
# Summary of evidence

## Evidence Supporting Clinical Question

Treatment of seizures is beneficial

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
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<tr>
<td>Good</td>
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<tr>
<td>Fair</td>
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<td>Rossetti A, 2009 C</td>
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<td>Poor</td>
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**Level of evidence**

- **A** = Return of spontaneous circulation
- **B** = Survival of event
- **C** = Survival to hospital discharge
- **D** = Intact neurological survival
- **E** = Other endpoint
- **Italics** = Animal studies
### Evidence Neutral to Clinical question

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<thead>
<tr>
<th></th>
<th>Good</th>
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<tbody>
<tr>
<td>Good</td>
<td>Brain Resuscitation Clinical Trial I Study Group, 1986&lt;sup&gt;C&lt;/sup&gt;</td>
<td></td>
<td>Longstreth, 2002&lt;sup&gt;C&lt;/sup&gt;</td>
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<tr>
<td>Fair</td>
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<td>Rundgren M, 2006&lt;sup&gt;C&lt;/sup&gt;</td>
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<tr>
<td>Poor</td>
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<td>Hui AC, 2005&lt;sup&gt;C&lt;/sup&gt;</td>
<td>Sunde K, 2007&lt;sup&gt;C&lt;/sup&gt;</td>
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<td></td>
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<td>Krumholz A, 1988&lt;sup&gt;C&lt;/sup&gt;</td>
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<td>Wijdicks EF, 1994</td>
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**Level of evidence**

A = Return of spontaneous circulation  
C = Survival to hospital discharge  
E = Other endpoint  
B = Survival of event  
D = Intact neurological survival  
*Italics = Animal studies*

### Evidence Opposing Clinical Question

Treatment of seizures is not beneficial

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**Level of evidence**

A = Return of spontaneous circulation  
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B = Survival of event  
D = Intact neurological survival  
*Italics = Animal studies*
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

The question: In adult and pediatric patients with ROSC after cardiac arrest (P), does the use of seizure prophylaxis or effective seizure control (I) as opposed to standard care (no prophylaxis) (C) improve outcome (O) ?

There was no studies looking at seizure treatment and the outcome of these treatments. One randomized study looked at the effects of thiopental when given randomly to all survivors of CA, the results showed that this prevention of seizures decreased the amount of seizures and that early seizures did not compromise the survival. Patient groups were really small. The use of thiopental for brain resuscitation was not supported (Brain Resuscitation Clinical Trial I Study Group, 1986, LOE 1, fair). One study (LOE 5, poor) shows that using a protocol including seizure medication when needed is beneficial for patients, but it does not report on results of treatments in general (Sunde K, 2007). Four studies (Hui AC 2005, Krumholz AC 1988 and Wijdicks EF 1994, all LOE 4, poor and Rundgren M 2006, 836, LOE 5, fair) stated that seizures were really hard to control even if many drugs were used aggressively, and the outcome was grim for the patients with seizures. One study (Longstreth WT 2002. 506, LOE 5 good) gave all ROSC patients randomized either magnesium, diazepam or both. This did not increase the proportion of awakenings. Only one study (Rossetti A 2009, 744) showed a benefit in treatment in five of six patients with PSE when monitored with EEG and treated as status epilepticus.

Unfortunately, no studies directly address the given question in a controlled way, so any firm conclusions can not be drawn. It looks like seizures are hard to control, even with multiple drugs. No statement on effects on survival can be given.

Acknowledgements:

Citation List


Comments: A randomized trial from 12 hospitals in nine countries, 262 patients. The thiopental loading group received a single dose of up to 30 mg per kg intravenously. Incidence of seizures was 13 % vs 21 % and good recovery was 35 % vs 21 %. The occurrence of early seizures did not compromise survival. LOE 1, fair (was not targeted to look at seizures).


Comments: Reulst from 18 patients with seizures after CA. Multiple antiepileptic drugs were required, 2.3 drugs per patient. 16/18 died so no outcome figures could be stated for different treatments. LOE 4, poor.


Comments: Seizures were treated aggressively with benzodiazepines, phenytoin and barbiturates. The seizures were often difficult to stop. Outcome did nod seem to improve even if seizures were controlled. LOE 4, poor.

**Comments**: A randomized study were all patients with OHCA were randomized to get bentsodiatzepin, Mg or placebo. Aim to look at survival, not seizure treatment. LOE 5, good.


**Comments**: The study was not aimed for seizure treatment. Six patients were studied. All were treated with hypothermia. All of them had PSE in the EEG, three also clinically. All patients received benzodiazepines, five got levetiracetam and valproate, three propofol and two phenytoin. One died, four out of five had a favourable outcome. Hypothermia might have increased the possibility for survival for these patients. LOE 5, fair.


**Comments**: Did not address seizures primarily. All seven patients with clinical seizures received propofol, and four also fentanyl infusion. Four where treated with midazolam, two in combination with fosfenytoin. Only transient effects on seizures could be seen. All died. LOE 5, good.


**Comments**: A study looking at the benefit of a protocol. The protocol also states that seizures have to be treated with increased sedation or specific anticonvulsive medication. Patients treated with this protocol had an increased survival compared to historical controls not treated wit a protocol. 5% of patients in the control group had status epilepticus and 8% in the intervention group. Outcome specificaly of these patients were not addressed. LOE 5, poor.


**Comments**: 107 cardiac arrest patients, 67 had myoclonus and only 20 of them woke up. Half of the patients were treated with phenytoin, phenobarbital and benzodiazepines without any effect. LOE 4, poor.

**Not included in the final recommendation:**


**Comments**: Describes chronic situations.

**Comments:** Does not study the treatment of seizures.


**Comments:** Does not study the treatment of seizures.


**Comments:** A review only stating that seizures should be treated with standard medication.


**Comments:** A review only stating that seizures should be treated with standard medication.


**Comments:** Does not study the treatment of seizures.


**Comments:** Review. Does not study the treatment of seizures.


**Comments:** Review. Does not address the treatment of seizures.


**Comments:** Review. Intravenous loading with phenytoin was not as effective in patients with anoxic status than in other patients (40% vs 80%). Does not address outcome of treatments, only states that outcome is not as good if the patient has seizures.


**Comments:** Review. Seizures place the brain in risk for secondary injury. Aggressive treatment is indicated to prevent progression to status epilepticus.

**Comments:** Does not address seizure treatment. No seizures was a factor associated with survival.


**Comments:** Does not address seizures.


**Comments:** Seizures can delay the recovery and should be treated aggressively.


**Comments:** Review.


**Comments:** Does not address seizures after cardiac arrest.


**Comments:** Does not address seizure treatment.


**Comments:** Review. Not systematically looking at seizure treatment. Seizures should be treated. Seizures are predictors for bad outcome.