

**WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care****Worksheet author(s).**

Michael Fries

**Date Submitted for review:** 1/22/2010 **Date of last search:** 1/06/2010**Clinical question.**

"In adult patients (prehospital and in-hospital) with ROSC after cardiac arrest (P), does early hemodynamic optimization (I) as opposed to standard care (C), improve outcome (O) (eg. survival)?"

**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:** new topic

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?

No

**Search strategy (including electronic databases searched).****Initial search:**

Pubmed search using "heart arrest" or "cardiopulmonary resuscitation" as MeSH Terms and "post resuscitation" and/or "h(a)emodynamics" and or "outcome" as textword in any field.

COCHRANE library using "heart arrest" and "cardiopulmonary resuscitation" and "post-resuscitation"; also [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

EMBASE search using "heart arrest" and "cardiopulmonary resuscitation" and post-resuscitation" and/or "hemodynamics" and/or "outcome"

AHA master Library using "heart arrest" and "cardiopulmonary resuscitation" and "post-resuscitation"

- State inclusion and exclusion criteria

**Inclusion criteria:**

Human studies, animal studies, RCT's in which the original question was addressed (i.e. protocols involving strategies to influence post-resuscitation hemodynamics or studies evaluating if hemodynamic alterations per se influence outcome)

**Exclusion criteria:**

Intra-arrest interventions, Resuscitation with cardiopulmonary bypass; in animal models: no true CA models (four vessel occlusion, exsanguination, hypoxia only, etc.); studies with abstract only, case reports, studies not addressing the question

- Number of articles/sources meeting criteria for further review:

11

## Summary of evidence

### Evidence Supporting Clinical Question

<b>Good</b>			<b>Sunde 2007 C, D</b>	<b>Trzeciak 2009 C, D</b>	<i>Huang 2005 B, E</i> <i>Huang 2005 B, E</i>
<b>Fair</b>				<b>Werling 2007 B</b>	<i>Wang 2005 E</i> <i>Vasquez 2004 E</i> <i>Meyer 2002 E</i>
<b>Poor</b>				<b>Krumnikl 2006 D</b>	<i>Angelos 1994 E</i>
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Level of evidence</b>					

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

<b>Good</b>					
<b>Fair</b>			<b>Gaieski 2009 B, C, D</b>		
<b>Poor</b>					
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Level of evidence</b>					

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 Opposing Clinical Question

<b>Good</b>					
<b>Fair</b>					
<b>Poor</b>					
	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
<b>Level of evidence</b>					

A = Return of spontaneous circulation  
 B = Survival of event

C = Survival to hospital discharge  
 D = Intact neurological survival

E = Other endpoint  
*Italics = Animal studies*

**REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:**

Initial survival after OHCA has improved over the recent decades whereas secondary survival, i.e. hospital discharge (most desirably with intact neurological function) has not improved. Interestingly, this discrepancy has received only marginal attention. After the two positive hypothermia trials there seems to be more interest in this area. Besides neurological injury as a result of CA and CPR myocardial dysfunction has been recognized as a major determinant of the postresuscitation syndrome. This syndrome includes decreased cardiac output, systemic hypotension and tissue hypoperfusion. One retrospective study (LOE 3; Trzeciak 2009) demonstrated that arterial hypotension was associated with decreased survival and neurological outcome. Few animal experimental studies (LOE 5) exist that investigate the question if early hemodynamic optimization using inotropic agents improves outcome as opposed to standard care (which apparently does not exist) and demonstrated beneficial effects of some agents including dobutamine and levosimendan (Huang 2005, Huang 2005, Wang 2005, Vasquez 2004, Meyer 2002, Angelos 1994). Furthermore, no prospective human data exists. Only one study (LOE 3; Sunde 2007) could proof that when hemodynamic optimization was introduced as part of a whole bundle of interventions that outcome was improved in comparison to a historical control. This is in analogy to the data of Emanuel Rivers where a hemodynamic optimization protocol improved outcome in septic patients. One study (LOE 4; Gaieski 2009) with only few patients and only comparing historical controls used a design in analogy to the Rivers study and did not find a benefit with regard to outcome. With regard to the assessment of the benefits and risks it has to be taken into account that from a physiological point of view restoration of adequate tissue perfusion seems to make sense. This is mainly achieved by beta-adrenergic agents (epinephrine, norepinephrine, dobutamine) However, to the best of my knowledge there is no data to support that any of these drugs improves outcome in settings of hypoperfusion other than post CPR (i.e. septic or cardiogenic shock). On the contrary beta-adrenergic agents have many downside effects including, arrhythmias, increased oxygen demand, etc. In a nutshell, the available data is far too limited to derive any treatment strategy. In my opinion this is the most challenging question in the next years to come.

**Acknowledgements:*****Citation List***

**Angelos MG**, Ward KR, Beckley PD. Norepinephrine-induced hypertension following cardiac arrest: effects on myocardial oxygen use in a swine model. *Ann Emerg Med.* 1994 Nov;24(5):907-14.

**LOE 5; animal study; no industrial relation**

**Gaieski DF**, Band RA, Abella BS, Neumar RW, Fuchs BD, Kolansky DM, Merchant RM, Carr BG, Becker LB, Maguire C, Klair A, Hylton J, Goyal M. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Resuscitation.* 2009 Apr;80(4):418-24

**LOE 3; Prospective interventional trial with few patients and a historical control in analogy to the Rivers sepsis study; no benefit was found for EGDT; no industry support**

**Huang L**, Weil MH, Tang W, Sun S, Wang J. Comparison between dobutamine and levosimendan for management of postresuscitation myocardial dysfunction. *Crit Care Med.* 2005 Mar;33(3):487-91.

**LOE 5; animal study; sponsored by Abbott**

**Huang L**, Weil MH, Sun S, Cammarata G, Cao L, Tang W. Levosimendan improves postresuscitation outcomes in a rat model of CPR. *J Lab Clin Med.* 2005 Nov;146(5):256-61.

**LOE 5; animal study; sponsored by Abbott**

**Meyer RJ**, Kern KB, Berg RA, Hilwig RW, Ewy GA. Post-resuscitation right ventricular dysfunction: delineation and treatment with dobutamine. Resuscitation. 2002 Nov;55(2):187-91.

**LOE 5; animal study; no industrial influence**

**Sunde K**, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, Draegni T, Steen PA. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. Resuscitation. 2007 Apr;73(1):29-39

**LOE 3; good human study, however with historical control; hemodynamic optimization only as part of several factors to improve outcome; no industrial influence**

**Trzeciak S**, Jones AE, Kilgannon JH, Milcarek B, Hunter K, Shapiro NI, Hollenberg SM, Dellinger P, Parrillo JE. Significance of arterial hypotension after resuscitation from cardiac arrest. Crit Care Med. 2009 Nov;37(11):2895-903

**LOE 4; large retrospective study with data from a large database showing that post CPR hypotension is associated with increased mortality rates; no industry support**

**Vasquez A**, Kern KB, Hilwig RW, Heidenreich J, Berg RA, Ewy GA. Optimal dosing of dobutamine for treating post-resuscitation left ventricular dysfunction. Resuscitation. 2004 May;61(2):199-207.

**LOE 5; animal study; no industry support**

**Wang J**, Weil MH, Tang W, Sun S, Huang L. Levosimendan improves postresuscitation myocardial dysfunction after beta-adrenergic blockade. J Lab Clin Med. 2005 Sep;146(3):179-83.

**LOE 5; animal study; sponsored by Abbott**

**Werling M**, Thorén AB, Axelsson C, Herlitz J. Treatment and outcome in post-resuscitation care after out-of-hospital cardiac arrest when a modern therapeutic approach was introduced. Resuscitation. 2007 Apr;73(1):40-5

**LOE 4; prospective study in which hemodynamic stabilization as part of other interventions improved outcome, no industrial support**