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

Worksheet author(s)

Michael T. Cudnik, MD, MPH

Date Submitted for preliminary review: 6/30/2008

Clinical question.

"In adult patients in cardiac arrest (P), does the use of any other specific timing for interruptions to chest compressions to diagnose the cardiac rhythm (I), as opposed to the recommended techniques (ie. every 2 minutes) (C) improve outcome (eg ROSC, survival) (O)?"

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

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

Conflict of interest specific to this question

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

Search strategy (including electronic databases searched).

Pubmed "heart arrest" or "cardiopulmonary arrest" or "death, sudden cardiac" as MeSH headings AND "cardiopulmonary resuscitation" or "heart massage" as MeSH headings or "chest compression" as Title, Abstract, Key Terms
Cochrane database for systematic reviews, Central Register of Controlled Trials, AHA Endnote Database, and review of article references.
Forward search using Google Scholar.
Embase Database search using text words "resuscitation" or "cardiac arrest" or "heart arrest" AND "chest compression" or "heart massage"

- State inclusion and exclusion criteria

The following studies were excluded: used mannequin or simulated models (14), did not assess CPR or compressions i.e. impact of vasopressin,etc. (53), assessed impact of active chest compression vs. standard CPR (11) evaluated skills learned/retained from intervention (16), no outcome data (4), evaluated characteristics of providers/volunteers (3), non-human models (2)

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

29 studies meet criteria for further review. 20 were excluded after abstract review for relevant articles leaving 9 for further review. Of these 9, 4 were LOE 1 (RCTs), 1 was LOE 2 (pseudo-randomized), 1 was LOE 3 (retrospective controls), and 3 were LOE 4 (no controls).

Summary of evidence

Evidence Supporting Clinical Question

Good	Wik, 2003 ABC*	Hallstrom, 2007 CE	Kellum, 2008 BD	Eftestol, 2004 A*	
Fair				Box, 2008, E	
Poor					
	1	2	3	4	5
Level of evidence					

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

Evidence Neutral to Clinical question

Good	**Baker, 2008 ACD Jacobs, 2005 ACE**				**Kudenchuk, 2006 ACDE**
Fair				**Blouin, 2001 E**	
Poor					
	1	**2**	**3**	**4**	**5**
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 Opposing Clinical Question

Good					
Fair					
Poor					
	1	**2**	**3**	**4**	**5**
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

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

Discussion: Definitive evidence in humans assessing the optimal duration of CPR before reanalysis to diagnose the cardiac rhythm to improve survival in cardiac arrest does not yet exist. There were no studies whose primary objective was to assess this specific question. Several animal studies and human studies suggest that this may depend on the duration of time that a person has been in cardiac arrest. Those who are in cardiac arrest for longer durations (i.e. greater than 4 minutes) appear to benefit from CPR first as well as longer durations of CPR prior to reanalysis.

The strongest study to date is that done by Baker et al which performed a methodologically good prospective, randomized study evaluating 3 minutes of CPR prior to defibrillation vs. immediate defibrillation in patients with an unwitnessed arrest with ventricular fibrillation as their initial rhythm and an ambulance response time of greater than 5 minutes. After the initial defibrillation, patients received either 1 minute of CPR or 2 minutes of CPR (pre and post 2006 change in guidelines) in between subsequent defibrillations. In this project they found no difference in any of the outcomes (survival to discharge, admission to ICU, ROSC, survival to ED, cerebral performance categories) between the two groups. This was true for all patients, as well as those with an EMS response time greater than 5 minutes and those with a response time of less than 5 minutes. The major limitations of this study were the failure to randomize and thus exclude 139 patients (37%) and the failure to blind the providers to the intervention, which is unavoidable due to the design of the study.

An additional study with conflicting findings, was that done by Wik et al which performed a methodologically good prospective, randomized trial evaluating the impact of 3 minutes of CPR prior to defibrillation followed by 3 minutes of CPR if defibrillation was unsuccessful compared to standard treatment (i.e. immediate defibrillation followed by 1 minute of CPR in between reanalysis) in those patients with ventricular fibrillation or pulseless ventricular tachycardia. Although there was no overall difference in ROSC or in 1 year survival for all patients, on subgroup analysis, those patients with a EMS response time of 5 minutes or longer, more patients achieved ROSC, survival to hospital discharge, and 1 year survival. The major limitation of this study was the inability to blind providers to the treatment arm (CPR first vs. defibrillation first) and the inability to decipher if the CPR first or the 3 minutes of CPR in between reanalysis and shock was responsible for the findings in those with the longer response times.

Additionally, the Kellum et al study reinforces the need for at least 2 minutes of compressions prior to analyzing subsequent rhythms. In this methodologically good prospective, observational analysis of witnessed arrests with shockable rhythms, with retrospective controls, the authors evaluated the impact of "cardiocerebral resuscitation", defined as 2 minutes of uninterrupted chest compressions at 100 per minute before each rhythm analysis +/- shock. In addition, pulse checks were also only done after the 200 chest compressions were complete. These were compared to a similar cohort who was treated based on the 2000 AHA guidelines. Those patients treated with cardiocerebral resuscitation had drastically improved survival and neurologically intact survival. The major limitations of this study are the lack of randomization of patients and the use of retrospective controls.

Finally, the Hallstrom et al study also assessed the impact of 2 minutes of CPR prior to analysis as well between interim analyses in those patients with PEA or asystole. This was an observational analysis of patients enrolled in the randomized ASPIRE trial. In this methodologically good study, patients were subsequently grouped into either a No Shock group or Shock group based on the ensuing rhythms after the 2 minutes of CPR. Those patients that were shocked for either VF or VT at any point during their course were classified into the Shock group. In this analysis, survival to discharge was greater in the No Shock group compared to the Shock group, with Shock group being a predictor of mortality in the multivariate analysis, suggesting that interruptions to identify and shock VF/VT in patients who convert to such a rhythm from PEA/Asystole are of no benefit. The major limitations of this study are the lack of true randomization of the interventions and the lack of true controls.

Statistical Summary of Important Studies: Baker 2008, Wik 2003, Kellum 2008, Hallstrom 2007

Summary of Baker 2008:

- 3245 assessed, 202 enrolled/included in the analysis, no difference in outcomes between the groups
- Discharged alive from hospital: 10/97 in CPR first group (10.3%) vs. 18/105 in defibrillation first group (17.1%), [OR 0.56, 95% CI 0.25-1.25, NNT=14]
- ROSC: 49/97 in CPR first group (50.5%) vs. 56/105 in defibrillation first group (53.3%), [OR 0.89, 95% CI 0.52-1.55, NNT=33)
- Survival to ED: 40/97 in CPR first group (41.2%) vs. 43/105 in defibrillation first group (41%), [OR 1.01, 95% CI 0.58-1.77, NNT=5000]

In those with EMS time of > 5 minutes:
Discharged alive from hospital: 6/81 in CPR first group (7.4%) vs. 11/91 in defibrillation first group (12.1%), [OR 58, 95% CI 0.21-1.60, NNT=21]
-ROSC: 37/81 in CPR first group (45.7%) vs. 46/91 in defibrillation first group (50.6%), [OR 0.82, 95% CI 0.45-1.50, NNT=20)
-Survival to ED: 32/81 in CPR first group (39.5%) vs. 35/91 in defibrillation first group (38.5%), [OR 1.05, 95% CI 0.57-1.93, NNT=100]

Summary of Wik 2003:

-1357 assessed, 200 enrolled/included in analysis, non-significant trend for improved outcomes
-Discharged alive from hospital: 23/104 in CPR first group (22%) vs. 14/96 in Control group (15%), [OR 1.66, 95% CI 0.80-3.46, NNT=14]
-ROSC: 58/104 in CPR first group (56%) vs. 44/96 in Control group (46%), [OR 1.49, 95% CI 0.85-2.60, NNT=10]
-1 year survival: 21/104 in CPR first group (20%) vs. 14/96 in Control group (15%), [OR 1.48, 95% CI 0.71-3.11, NNT=20]

In those with EMS time of > 5 minutes:
-Discharged alive from hospital: 14/64 in CPR first group (22%) vs. 2/55 in Control group (4%), [OR 7.42, 95% CI 01.61-34.3, NNT=6]
-Sensitivity 22% (95% CI 13%-34%), Specificity 98% (95% CI 90%-99%)
-PPV 93% (95% CI 68%-99%), NPV 78% (95% CI 66%-88%)
-ROSC: 37/64 in CPR first group (58%) vs. 21/55 in Control group (38%), [OR 2.22, 95% CI 1.06-4.63, NNT=5]
-Sensitivity 58% (95% CI 45%-70%), Specificity 62% (95% CI 48%-75%)
-PPV 64% (95% CI 50%-76%), NPV 56% (95% CI 42%-68%)

-1 year survival: 13/64 in CPR first group (20%) vs. 2/55 in Control group (4%), [OR 6.76, 95% CI 1.42-31.4, NNT=6]
-Sensitivity 20% (95% CI 11%-32%), Specificity 96% (95% CI 87%-99%)
-PPV 87% (95% CI 60%-98%), NPV 51% (95% CI 41%-61%)

Summary of Kellum 2008:

-516 assessed for historical controls, 92 included; 478 assessed for prospective group, 89 included
-Survived event: 18/92 in control group (20%) vs. 42/89 (47%) in cardiocerebral resuscitation group [OR 3.67, 95% CI 1.89-7.12, NNT=4]
-Sensitivity 47% (95% CI 37%-58%), Specificity 80% (95% CI 71%-88%)
-PPV 70% (95% CI 57%-81%), NPV 61% (95% CI 52%-70%)

-Survived neurologically intact: 14/92 in control group (15%) vs 35/89 (39%) in cardiocerebral resuscitation group [OR 3.53, 95% CI 1.77-7.35, NNT=4]
-Sensitivity 39% (95% CI 29%-50%), Specificity 85% (95% CI 76%-91%)
-PPV 71% (95% CI 57%-83%), NPV 59% (95% CI 50%-68%)

Summary of Hallstrom 2007:

-1377 assessed, 738 were included; 574 in the No Shock group, 164 in the Shock group
-Survival to hospital discharge: 28/574 in No Shock group (4.9%) vs. 1/164 in Shock group (0.6%) [OR 8.36, 95% CI 1.13-61.91, NNT=23]
-Sensitivity 5% (95% CI 3%-7%), Specificity 99% (95% CI 97%-100%)
-PPV 97% (95% CI 82%-99%), NPV 23% (95% CI 20%-26%)

Two minutes of CPR are the current recommendations prior to reanalysis of the cardiac rhythm for patients in cardiac arrest. Current data suggests that this is the minimum of time that chest compressions should be done. Some studies suggest that even longer durations of CPR might be warranted as well in order to improve survival. Definitive data and/or studies do not yet exist to determine the duration of CPR in order to optimize survival. The current data suggests that the time to EMS response and the type of rhythm a patient is in may also contribute to the duration of CPR that is needed prior to reanalysis. Further studies are essential and warranted to further investigate this area.

Acknowledgements:

Citation List

1. Baker PW, Conway J, Cotton C, et al. Defibrillation or cardiopulmonary resuscitation first for patients with out-of-hospital cardiac arrests found by paramedics to be in ventricular fibrillation? A randomised control trial. Resuscitation. 2008 Dec;79(3):424-31

Level 1, neutral, good. Immediate defibrillation in unwitnessed, out of hospital VF arrest as effective as 3 minutes of CPR prior to first defibrillation.

2. Blouin D, Topping C, Moore S, Stiell I, Afilalo M. Out-of-hospital defibrillation with automated external defibrillators: postshock analysis should be delayed. Ann Emerg Med. 2001 Sep;38(3):256-61.

Level 4, neutral, fair (not randomized). Observational analysis of rhythm strips from VT/VT patients in cardiac arrest. Suggest that post shock analysis should be delayed in order for at least 30 seconds of chest compressions to be completed in order to increase the likelihood of identification of VF/VT.

3. Box MS, Watson JN, Addison PS, Clegg GR, Robertson CE. Shock outcome prediction before and after CPR: a comparative study of manual and automated active compression-decompression CPR. Resuscitation. 2008 Sep;78(3):265-74.

Level 4, supportive, fair (not randomized). Observational analysis of ECG rhythm strips in order to evaluate the usefulness of a cardioversion outcome predictor (COP) to determine the probability of ROSC. Increased length of CPR was predictor of success although no recommendation of specific duration of compressions.

.

4. Eftestol T, Wik L, Sunde K, Steen PA. Effects of cardiopulmonary resuscitation on predictors of ventricular fibrillation defibrillation success during out-of-hospital cardiac arrest. Circulation. 2004 Jul 6;110(1):10-5.

Level 4, supportive, good. Observational analysis of subjects from an RCT. Longer durations of CPR (> 3 minutes) had an improved impact on the waveform in those patients in ventricular fibrillation.

5. Hallstrom A, Rea TD, Mosesso VN, Jr., et al. The relationship between shocks and survival in out-of-hospital cardiac arrest patients initially found in PEA or asystole. Resuscitation. 2007 Sep;74(3):418-26.

Level 2, supportive, good. Observational analysis of patients entered into ASPIRE trial demonstrating that patients in PEA/asystole benefit from chest compressions of at least 2 minutes duration rather than defibrillation of a shockable rhythm. ASPIRE Trial was funded 100% by Revivant Corporation.

6. Jacobs IG, Finn JC, Oxer HF, Jelinek GA. CPR before defibrillation in out-of-hospital cardiac arrest: a randomized trial. Emerg Med Australas. 2005 Feb;17(1):39-45.

Level 1, neutral, good. Randomized trial comparing 90 seconds of CPR before defibrillation or immediate defibrillation in those with VF/VT. Authors did not assess the duration of compressions after the initial analysis and its potential impact on survival/ROSC.

7. Kellum MJ, Kennedy KW, Barney R, et al. Cardiocerebral resuscitation improves neurologically intact survival of patients with out-of-hospital cardiac arrest. Ann Emerg Med. 2008 Sep;52(3):244-52.

Level 3, supportive, good. Before/after analysis comparing 2 minutes of chest compressions before initial defibrillation and after each defibrillation in those with a witnessed, shockable cardiac arrest compared to those treated based on the 2000 AHA guidelines. Those treated with the cardiocerebral resuscitation had improved mortality and neurological outcomes suggesting that 2 minutes of CPR/compressions is the minimum that is needed prior to re-analysis of rhythms.

8. Kudenchuk PJ, Cobb LA, Copass MK, Olsufka M, Maynard C, Nichol G. Transthoracic incremental monophasic versus biphasic defibrillation by emergency responders (TIMBER): a randomized comparison of monophasic with biphasic waveform ascending energy defibrillation for the resuscitation of out-of-hospital cardiac arrest due to ventricular fibrillation. Circulation. 2006 Nov 7;114(19):2010-8.

Level 5, neutral, good. RCT of biphasic vs. monophasic for VF. No assessment was made of the duration of CPR/chest compressions between subsequent shocks.

9. Wik L, Hansen TB, Fylling F, et al. Delaying defibrillation to give basic cardiopulmonary resuscitation to patients with out-of-hospital ventricular fibrillation: a randomized trial. JAMA. 2003 Mar 19;289(11):1389-95.

Level 1, supportive, good. RCT of those in VF comparing 3 minutes of CPR before defibrillation + 3 minutes of CPR after each analysis/defibrillation vs. immediate defibrillation + 1 minute of CPR before additional defibrillation. Increased survival in those with EMS response time > 5 minutes in the 3 minute group suggesting that either the 3 minutes of CPR before or the 3 minutes before additional defibrillation is beneficial.