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

Clinical question.
In adult and pediatric patients with cardiac arrest (prehospital or in-hospital) (P), does the minimization of hands off time for rhythm analysis including frequency and duration of checks (I) as opposed to standard care (according to treatment algorithm) (C), improve outcome (O) (eg. ROSC, 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: Unknown to worksheet author

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).
Cochrane database for systematic reviews (no hits)
MEDLINE: “cardiopulmonary resuscitation” as MeSH heading AND “English language” AND “clinical trial” (n=425)
MEDLINE: “hands-off” OR “hands off” not as a MeSH heading (n=137)
MEDLINE: (“pre-shock” OR “preshock”) not as a MeSH heading (n=66)
MEDLINE: “cardiopulmonary resuscitation” as MeSH heading AND “interruption” not as a MeSH heading (n=29)
Hand search of all issues of Resuscitation (Volume 47/2001- Volume 78/2008)
ECC EndNote Master Library: searched for terms “pause” and “hands off” and “hands-off” and “pre-shock” and “pre shock”
Manual search of references of all articles identified with above strategies
Forward search of key articles using OVID (see below in Citation List)

• State inclusion and exclusion criteria
The following were included: studies examining the hands off time in the “pre-shock” interval of CPR (time between the cessation of chest compressions, and the delivery of the shock).
The following were excluded: 1) studies examining other parameters of CPR quality (e.g. depth of compressions; rate of compressions; adequate recoil) that either did not examine hands off time in the pre-shock interval, or that mentioned this as a parameter of CPR quality but did not actually measure it. 2) studies of pauses for ventilation or other parameters not related to pauses for rhythm analysis. 3) review articles. 4) abstract-only papers.

• Number of articles/sources meeting criteria for further review:
Sixteen studies met criteria for further review: six LOE 3, one LOE 4, and nine LOE 5.
# Summary of evidence

## Evidence Supporting Clinical Question

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td>Steinmetz, 2008 A, C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sato, 1997 AB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yu, 2002 AB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Eftestøl, 2002 E</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Steen, 2003 AB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Berg, 2003 AB</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tang, 2006 AB</td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

**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

<table>
<thead>
<tr>
<th>Good</th>
<th>Olasveengen, 2009</th>
<th>D, E</th>
<th>Walcott, 2009 E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
<td>Ristagno, 2008 E</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

**Level of evidence**

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

### Evidence Opposing Clinical Question

<table>
<thead>
<tr>
<th>Good</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
</table>

**Level of evidence**

A = Return of spontaneous circulation  
B = Survival of event  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other endpoint  
*Italic* = Animal studies
REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

There are very few studies examining any actual outcomes as they relate to “hands-off” or “no-flow” time during CPR.

1. A number of studies have quantified the “hands-off” or “no-flow” time without examining any patient data or outcomes. These studies clearly demonstrate the magnitude of the problem, showing that no chest compressions are performed roughly 50% of the time during both in-hospital and out-of-hospital resuscitations due to a combination of factors, only one of which is the pre-shock rhythm check. These studies thus do not constitute useful evidence in answering the clinical question at hand, and are not reviewed further.

2. A number of papers are frequently cited by other papers examining this clinical question, but do not examine our clinical question directly, and thus are not fully reviewed here:

   - Two animal studies examined interruptions for rescue breathing / ventilation (not for rhythm analysis), and found detriments to hemodynamics (Berg RA. Circulation 2001;104:2465) and to clinical outcomes (Kern KB. Circulation 2002;105:645). Both would be LOE 5, supportive, good if they met the inclusion criteria for this review.

   - Several studies examined the sum of all interruptions, looking at total no-compressions time but not delineating the specific shock analysis time (Valenzuela TD. Circulation 2005;112:1259 – would be LOE 4, supportive good; van Alem AP. Ann Emerg Med 2003;42:449 – LOE 4, supportive, fair).

3. Regarding limiting the frequency of rhythm checks (the first of the two parts of the “I” portion of the PICO question), four studies (one animal: Tang, 2006, 2683-2689; three human: Rea, 2006, 2760-2765 and Bobrow, 2008, 1158-1165 and Kellum, 2008, 244-252) have examined the benefits of a one-shock protocol instead of the three-stacked-shocks protocol, with all three showing clinical benefit. This suggests that limiting the frequency of rhythm checks is beneficial, but the evidence is far from conclusive.

4. Regarding limiting the duration of rhythm checks (the second part of the “I” portion of the PICO question), seven studies (one human, five animal, and one mathematical) have examined the impact of a longer delay between the cessation of chest compressions and the delivery of a shock (the delay being the time needed for either automated or manual rhythm analysis, charging of the defibrillator, and delivery of the shock). All have found that increasing delays were associated with worse outcomes. These studies provide some evidence that limiting the duration of rhythm checks is beneficial, and while this evidence seems better than that for limiting the frequency of rhythm checks, it is similarly not conclusive.

5. Six human before-and-after studies have examined the effect on clinical outcomes of using the new 2005 guidelines, with specific mention of the emphasis on continuous compressions with limited interruptions. Five found improved survival; one found no change. Only three (Bobrow, 2008, 1158-1165; Olasveengeng, 2009, 407-411; Rea, 2006, 2760-2765) reported on whether there were actually any improvements in hands-off time; one of these (Olasveengeng, 2009, 407-411) found no improvement in outcomes. Other protocol changes besides limited interruptions were involved in most of these studies, making it somewhat difficult to assess the contribution of limiting interruptions to the improvements seen in the two papers that reported better survival.

Statistical analysis of key studies: The six LOE 3 studies located in the search.

Rea, 2006, 2760-2765:
- protocol: one shock, then 2 minutes of compressions, then one shock. (134 pts)
- historical controls with usual ACLS protocols. (375 pts)
- survival to discharge: 61/134 (32.8%) vs 122/374 (45.5%), p=0.008, OR 1.75 (95%CI 1.16-2.64)

Bobrow, 2008, 1158-1165:
- protocol: 200 compressions, rhythm analysis with single shock, 200 compressions before next pauses. (668 pts)
- historical controls with usual ACLS protocols. (218 pts)
- survival to discharge: 1.8% (4/218) vs 5.4% (36/668), OR 3.0 (95% CI 1.1-8.9)
- survival in subgroup with witnessed VF arrest (n=174): 4.7% (2/43) vs 17.6% (23/131), OR 8.6 (95%CI 1.8-42.0)

Kellum, 2008, 244-252:
- protocol: same as for Bobrow, 2008 (230 pts)
- historical controls with usual ACLS protocols. (268 pts)
- survival to discharge: 18/92 (20%) vs 42/89 (47%)
- neurologically intact survival: 14/92 (15%) vs 35/89 (39%)
- only a 95% CI for each "group comparison" is given: 0.1 to 0.4 for survival, and 0.1 to 0.4 for intact survival

Steinmetz, 2008, 908-913:
- protocol: ALS according to ERC 2005 guidelines; Zoll AutoPulse; mild therapeutic hypothermia
- historical controls: ALS according to ERC 2000 guidelines
- 30 day survival (primary outcome): 8.3% vs 16.0%, p=0.001
- ROSC at admission: 23.4% vs 39.1%, p<0.0001
- survival to discharge: 7.9% vs 16.3%, p=0.0048

Olasveengen, 2009, 407-411:
- protocol: Norwegian modification of ERC 2005 guidelines, incl 2 min of CPR before or between shocks
- historical controls: Norwegian modification of ERC 2000 guidelines, incl 1 min of CPR before or between shocks
- survival to discharge: 11% vs 13%, p=0.287
- no benefit in subgroups: good neurologic outcome, cardiac etiology, witnessed with initial rhythm of VF

Garza, 2009, 2597-2605:
- protocol: 50:2 ratio, 200 compressions before shock, single shocks, no pulse check after shocks, no intubation until after third "round" of chest compressions (or ROSC)
- historical controls: standard ACLS- no details given except 5:1 ratio
- survival to discharge: 7.5% vs 13.9%, p<0.001

In summary, while the direct human evidence is limited, a weak recommendation ("should", not "must" or "shall") to limit both frequency and duration of rhythm checks seems reasonable. It seems unlikely that a prospective trial (either LOE 1 or LOE 2) will be conducted that directly addresses either part of the clinical question, though it seems likely that additional LOE 3 before-and-after trials will be conducted, allowing for more rigorous analysis of this clinical question. Such studies should report as much data as possible on the extent to which interruptions were actually limited.

Acknowledgements:
None.

Citation List (alphabetical)


LOE 5 study, supportive. Good. No industry funding. This study focused on the time from defibrillator arrival to the delivery of the first shock, and the first chest compressions. It did not specifically examine any further pauses for rhythm analysis, and the first shock was delivered before any compressions (so this is not technically a study of the pause between compressions and shocks), but the rhythm analysis (either automated or manual) preceding the first shock was studied. [Forward-search: 11 citing articles]


LOE 5, study, supportive. Good. No industry funding. This study examined limiting (eliminating) post-shock rhythm checks (not pre-shock rhythm analysis), and found clinical benefit. [Forward-search: 2 citing articles]


LOE 3 study, supportive. Good. No industry funding. The study protocol tried to minimize all interruptions, and did not specifically focus on the interruptions for shock analysis. However, the protocol included immediately resuming chest compressions after a shock, rather than watching the rhythm to determine if another shock is needed. This appears to be as close as anybody has
come to examining the number of rhythm checks (as opposed to the duration of rhythm checks), though no data are given regarding actual number of shocks given, duration of delays, etc. [Forward-search: 19 citing articles]


LOE 4 study, supportive. Good. Grant funding from Laerdal Medical Corporation. The logistic regression model found that a five-second decrease in the pre-shock pause was associated with an 86% increase in the odds of shock success. Unfortunately, this study was underpowered to address ROSC and survival; the outcome of interest was the success of the first shock in terminating VF. [Forward-search: 5 citing articles]


LOE 5 study (mathematical model), supportive. Fair (used only a mathematical estimate of defibrillation success; no clinical outcomes were studied). No industry funding, but the lead author was a part-time employee of a defibrillator manufacturer, and another author has been a consultant to and a board member of that same company. [Forward-searching: 49 citing articles]


LOE 3, supportive. Good. No industry funding. Authors mention the limitation of not knowing how closely the new protocols were followed, and the lack of neurologic outcome data. Otherwise, provides good support for the benefits of minimizing interruptions.


LOE 3 study, supportive. Good. No industry funding. The use of single shocks in the intervention group (cardiocerebral resuscitation) instead of “stacked shocks” is intended to reduce the frequency of pauses for rhythm analysis (the first part of the clinical question being examined here), though no data are presented regarding the actual number of pauses that occurred in these resuscitation attempts. Note that the “cardiocerebral resuscitation” protocol was reserved for cardiac arrest patients judged by field personnel to be cardiac in origin. Other patients, even during the “after” phase, received “regular” CPR/ACLS. [Forward-search: 9 citing articles]


LOE 3 study, neutral. Good. No industry funding. While there was improvement in both hands-off ratios and pre-shock pauses, no clinical benefit was seen. It will be important to monitor similar “effectiveness” papers to see if the “efficacy” demonstrated in many of the other papers discussed in this review persists with real-world application; this paper suggests that it may not. [Forward-search: 1 citing article]


LOE 3 study, supportive. Good. No industry funding. Again, the use of single shocks instead of stacked shocks reduces the frequency of pauses for rhythm analysis, although the amount of reduction was not quantified. The authors did report on the decrease in delay in resuming CPR after shocks (by not waiting for a rhythm analysis), but did not report on the whether the pauses were any shorter. [Forward-search: 16 citing articles]


LOE 5 (animal model), neutral. Poor (small n, not powered for survival). Industry funded; two authors also employed by industry. The duration of the interruptions (8 seconds) is so brief compared to the duration of interruptions seen in studies of actual CPR as to be practically irrelevant to the study question. [Forward-search: no citing articles]

LOE 5 study (animal model), supportive. Fair (small n, ad hoc hands off intervals assessed). Partially supported by the Laerdal Foundation (as well as another foundation, and a private donation). [Forward-search: 25 citing articles]


LOE 5 study (animal model), supportive. Fair (small n). No industry funding. Examined whether CPR before first defibrillation helped, as well as examining whether giving shocks during ongoing CPR (rather than pausing compressions to give shocks) helped. Difficult to sort out relative contributions of these several variables to the overall findings. [Forward-search: 18 citing articles]


LOE 3, Fair. No industry funding. A number of interventions occurred, including implementation of the 2005 ERC, addition of the Zoll AutoPulse device (used in only 77 patients, and associated with worse 30-day survival), and mild therapeutic hypothermia (used on 60% of patients with ROSC). Also, no data are presented regarding whether there was actually any improvement in hands-off time. These factors make it very difficult to assess the contribution of the new guidelines to the improved survival seen. [Forward-search: one citing article]


LOE 5 study (animal model), supportive. Fair (small n). Grant-in-kind aid was provided by Phillips Medical Systems. This study found both decreases in no-CPR time and improved survival in the swine who received CPR with a one-shock protocol. While the number of pre-shock rhythm analysis pauses is not quantified, it seems likely that there were fewer of these in the one-shock protocol animals. [Forward-search: 4 citing articles]


LOE 5 study (animal model), neutral. Good. Industry funding, and several authors employed by industry. This study complicates things a bit, as it found that once the post-shock pause was eliminated, there was no further clinical benefit to altering the timing of, shortening, or completely eliminating the pre-shock pause. No other studies were found looking at the clinical question from this perspective. [Forward-search: no citing articles]


LOE 5 study (animal model), supportive. Fair (small n, confusing methods). No industry funding. This study seems to most directly address the question of the role of the duration of pre-shock interruptions, but the methods are confusing. [Forward-search: 55 citing articles]

Disclaimer
This review includes information on resuscitation questions developed through the C2010 Consensus on Science and Treatment Recommendations process, managed by the International Liaison Committee on Resuscitation (http://www.americanheart.org/ILCOR). The questions were developed by ILCOR Task Forces, using strict conflict of interest guidelines. In general, each question was assigned to two experts to complete a detailed structured review of the literature, and complete a detailed worksheet. Worksheets are discussed at ILCOR meetings to reach consensus and will be published in 2010 as the Consensus on Science and Treatment Recommendations (CoSTR). The conclusions published in the final CoSTR consensus document may differ from the conclusions of in this review because the CoSTR consensus will reflect input from other worksheet authors and discussants at the conference, and will take into consideration implementation and feasibility issues as well as new relevant research.