Clinical question.

In adult and pediatric patients with cardiac arrest due to VF (prehospital or in-hospital) (P), does the use of CPR before defibrillation (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: Revision of Guidelines 2005 worksheets W68 and W177.

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).

Pubmed:


: 215 hits, of which 32 were selected for further review based on the abstract

Cochrane library:

search term: defibrillation (Ti, Ab, keywords) 1 hit, not relevant for the question.

Embase:

(cardiopulmonary resuscitation.m_titl. OR resuscitation/ OR exp Compression/ or exp thorax compression/ or exp Heart Massage/) AND survival.m_titl. AND (cardioversion/ or defibrillation/ OR defibrillation.m_titl.)

92 hits of which 2 were not found in Pubmed

A number of papers were identified from references cited in studied papers and from the results of the Guidelines 2005 Worksheets 86 and 177

Re-search for Revision R3 yielded one relevant new animal paper.

• State inclusion and exclusion criteria

Included were papers that focussed on outcomes after defibrillation, with an emphasis on relation to CPR but also papers that looked for other markers of successful outcome, such as VF characteristics. In the final analysis I only included VF characteristics studies if comparison of the two strategies (CPR first or shock first) were presented.

Reviews without new data were not included.

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

31 papers were studied in detail. Papers that not study the relative sequence of CPR and defibrillation, such as papers analysing the effect of CPR on phenomena as VF characteristics but without comparison of strategies were excluded.

Eventually, 17 papers were selected for final inclusion.
### Summary of evidence

**Evidence Supporting Clinical Question**

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<td><em>Niemann 1992 A</em></td>
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<td><em>Kolarova 2003 A</em></td>
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Level of evidence

*: analysis yielded p=0.04 in single tailed Fisher exact test. Conventional two-tailed p would be 0.082 and make the study “neutral”.

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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<td>Jacobs 2005 A, C, E</td>
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<td>Rittenberger 2008 A, B</td>
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**Level of evidence**

- **A** = Return of spontaneous circulation
- **B** = Survival of event
- **C** = Survival to hospital discharge
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- **E** = Other endpoint

**Italics** = Animal studies

## Evidence Opposing Clinical Question

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

Numerous studies including epidemiological studies with multivariate analysis of potential determinants have established that rapid institution of (bystander) Basic Life Support (BLS) and early defibrillation independently increase the probability of survival to discharge after out-of-hospital cardiac arrest (OOH CA). This well accepted concept was first challenged in a clinical study (Cobb 1999, 1182, LOE 3) when a modification of the AED protocol and introduction of 90 seconds pre-shock CPR (and therefore delaying defibrillation for the same 90 seconds) was associated with an increase in survival (odds ratio of survival of 1.42; 95% CI 1.07-1.90). The change in protocol was inspired by an animal study of Niemann (1992, 281, LOE 5), who in a canine VF model randomized immediate defibrillation with a preceding treatment with epinephrine and 5 minutes of CPR. In that study the RR for ROSC was approx. 3 (95% CI 1.02-8.8) but the contribution to improved survival by pretreatment with epinephrin or by CPR could not be analysed separately.

One earlier animal study (Yakaitis 1980, 157, LOE 5) and numerous later animal studies allowed assessment of the potential value of administering CPR before defibrillation. An important limitation of many of these animal studies is the fact, that the primary question was only indirectly related to "CPR first or shock first" but related to effects of various defibrillation waveforms (Garcia 2000, 301), VF duration (Niemann 2000, 543)(Campbell 2007, 229), the VF waveform characteristics (Menegazzi 2004, 926), various durations of pre-shock CPR (Rittenberger 2008, 155), variation in timing of defibrillation while CPR is performed (Kolarova 2003, 2022). Particularly difficult to analyse were studies where not CPR was the focus, but pre-defibrillation treatment with various drugs or combinations of drugs, and CPR was given with the purpose to move the drug through the blood stream towards the central circulation and the heart. In that design, following guidelines from before 2000 with limited skills of the ambulance personnel, who could not secure the airway or administer drugs.

One second study was performed between 2005 and 2007. (Baker 2008, 424) This study randomized 202 patients into defibrillation first or 3 minutes CPR before defibrillation. Survival to discharge was 17.1% and 10.3% respectively (OR 0.56; 95% CI 0.25-1.25). For patients with an ambulance delay >5 minutes survival was 12.1% and 7.4%, respectively (OR 0.58; 95% CI 0.21-1.60).

Conclusion.
There is no clear proven benefit from delaying defibrillation to administer CPR for several minutes. Seven animal studies and one human study of OOH CA with historic controls appeared to show a benefit and the first human LOE1 study appeared to confirm this. However, nine animal studies and two LOE1 human OOH CA studies did not confirm the concept of delaying defibrillation in order to give CPR. There are several considerations to go with this conclusion. First, delaying defibrillation for CPR contradicts the long established facts about the importance of early defibrillation. Second, administering CPR “first” by arriving ambulance personnel when they are delayed >5 minutes after call (or when the collapse is not ambulance-witnessed) does not take in consideration that CPR is already given by bystanders in >50% of cases in many places in the world. The “realistic” CA model that is employed in many animal studies includes up to 8 minutes of untreated cardiac arrest, but this does not apply to the many cases where bystander CPR precedes arrival of the ambulance. It is acknowledged that bystander CPR may be not of sufficient quality in rate and depth, but neither is this the case for ambulance personnel, as confirmed in many studies. Prolonging ongoing CPR for another 3 minutes may then not produce the benefit that outweighs the possible disadvantage of the delay in defibrillation.

This analysis did not include studies where the effect of CPR on the VF waveform characteristics are shown. These waveform characteristics may be important in identifying patients where initial CPR may outweigh the benefit of early defibrillation. However, these studies on waveform characteristics have only shown that CPR influences the waveform towards a more “healthy” character, but the relation with successful defibrillation (however defined) is only made in databanks of monitor electrocardiograms from resuscitation efforts and suggested in one LOE5 study (Menegazzi 2004, 926). The concept is not yet prospectively validated in human OOH CA. Therefore, it cannot be used to support the general concept that defibrillation should be delayed to allow administration of CPR.

Acknowledgements:

**Citation List**


   **Comment:** LOE1, good, neutral to negative. RCT stopped after first interim analysis at 90% of intended patient intake for futility and trend to worse outcome in CC first group. Roughly mid-trial the guidelines for management of OOH cardiac arrest were changed in accordance with the Australian Resuscitation Guidelines 2006, based on the ILCOR 2005 Consensus on Science and Treatment Recommendations.


   **Comments:** LOE5, good. RCT animal study, neutral to the question for ROSC and 24h survival as outcome and supportive for the question for the outcome VF waveform characteristic median frequency.


   **Comments:** LOE3, poor, neutral for ROSC, survival and neuro-intact survival. Retrospective analysis, little control for potential confounders. Delays to arrival of EMS were calculated from call (not collapse), nevertheless were interpreted as representing the 3-phase model. CPR as given by bystanders was observed on EMS arrival and not controlled. Conclusions that bystander BLS before EMS arrival and defibrillation is better than no bystander BLS before defibrillation is obvious but does not directly address the question of delaying defibrillation after EMS arrival, as suggested in the discussion.


   **Comments:** LOE3, good, supportive. Before-after study with change of management by introducing a 90-seconds CPR period before defibrillation by EMT’s, irrespective of bystander CPR. Post-hoc finding of benefit when delay to arrival ≥4 minutes.

Comments: LOE5 animal study, good quality, opposing clinical question. This is the only animal study in which prolonged myocardial ischaemia is induced before induction of VF.


Comments: LOE1, fair, neutral. RCT, control protocol old: C:V ratio 5:1, unprotected airway in many patients, no pharmacological treatment, CPR before defibrillation only 90 seconds. Study terminated before intended number of patients were included. Overall survival rates fairly low.


Comments: LOE5, good, supportive/neutral animal study. This is an example of a study where only one of the experimental protocols addressed the issue of CPR first vs shock first. Also, the treatment protocol analysed separately the first shock (“experimental shock”) from later shocks (“rescue shocks”) with different outcomes. While the earlier experimental shocks (less CPR) were hardly successful and later shocks were, rescue shocks almost always could result in ROSC and differences between groups became non-existent. Therefore an outcome supportive for the question for a first shock, becomes neutral for more shocks: a clinically acceptable management.


Comments: LOE5, fair, neutral. RCT animal study. CPR first had better outcome (1 h survival). Experimental protocol always included drugs and contribution of CPR first alone could not be determined.


Comments: LOE5, good animal study, neutral for ROSC, survival event. Study designed for drug treatment, but (part of the) results can be used for the question of our interest. Conclusions of the complete study suggest benefit from CPR first, but only with (some) drugs on board. If only a no-drug subgroup of CPR first was compared with control, there was no benefit from CPR first.


Comments: LOE5, good, neutral animal RCT. When analysed for experimental group without concomitant drugs, outcome of shock success and ROSC neutral.


Comments: LOE5, good, supportive animal RCT. Waveform analysis of VF helps determine best moment of shock when CPR is administered. Only at best scaling exponent (associated with short-lasting VF and no CPR), initial shocks were successful. For worst scaling exponents, a period of CPR before shock gave better outcome.


Comments: LOE5 good animal study, supportive for ROSC.


Comments: LOE5, fair, neutral animal study. Historic controls from previous study. Outcome 30 minutes ROSC.

Comments: LOE5, poor, neutral animal study. Study poor because there was no real control of shock first. Study indicates that duration of CPR before shock cannot be prolonged too much. In this study there was an indication that CPR should not exceed 180 seconds before a shock is given.


Comments: LOE5, good, neutral animal study. This study studies a drug cocktail, a group with Mg only and CPR before shock and shock first without drugs. The Mg only group can be considered a “treatment” with CPR first, if we consider Mg as inactive.


Comments: LOE1, fair, supportive human RCT. Study is considered the most convincing study, with great influence on thinking about this question. However, the study has several important design problems, that are generally not recognized. First, the study was terminated at a (first?) interim analysis after 36 months with 40% (200) of expected cases (500) included. Overall survival was not improved, only in a subgroup of 91 patients with response times >5 minutes, with conventional statistics, not correcting for interim analysis. Therefore, the results could be considered a chance occurrence that must be confirmed independently by other studies. Second, by design drug treatment in CPR first group was given much earlier before shock. Additional comment: CPR first was given, irrespective if CPR was already given by bystanders before ambulance arrival.


Comments: LOE5, good, neutral animal study. Outcome ROSC