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

Worksheet author(s)

Thomas Rea

Date Submitted for review: January 25, 2010

Clinical question.

In adult patients suffering from a cardiac arrest (P) does the calling of EMS and the provisions of chest compressions without ventilations (hands-only CPR) by untrained laypersons (I) compared with calling EMS only (C) improve survival to hospital discharge (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 question

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? Worksheet author is involved in an ongoing randomized trial of dispatcher CPR instruction comparing chest compression plus ventilation versus chest compression alone.

Search strategy (including electronic databases searched)

PubMed MESH search for “Cardiopulmonary Resuscitation” (MESH) (6671) or “Resuscitation” (MESH) (55651) or “Heart Arrest” (MESH) (23395) with mostly irrelevant cases. Therefore the search was approached using non-MESH terms including::

- chest compression AND resuscitation (933)
- chest compression AND resuscitation AND human (645)
- chest compression AND resuscitation AND animal (351)
- chest compression AND CPR (795)
- compression only CPR (210)

Embase was also searched using the terms:

- resuscitation and compression (1156)
- resuscitation AND chest compression (379)
- resuscitation AND chest compression and human (251)
- resuscitation AND chest compression and human and randomized trial (5)

Cochrane database was searched using the terms “resuscitation AND chest compression” which yielded no relevant results.

State inclusion and exclusion criteria

Per the question, I excluded (when possible) reports of pediatric patients and patients where CPR provision by EMS or other trained persons with a duty to respond.

Number of articles/sources meeting criteria for further review:

Abstracts were reviewed based on the initial search strategy detailed above. Articles were then reviewed to determine whether they included a primary exposure group (chest compression [CC] alone) and the control group (no bystander CPR). There are multiple other articles – mostly animal – that compare CC alone versus CC plus ventilation. These were not included in the primary evidence accrual though the 2 human studies comparing CC alone and CC plus ventilation are reviewed in the citation section for completeness purposes. Collectively 11 studies – 6 human and 5 animal – met the inclusion criteria and were reviewed in detail with full citations at the end of this document.
## Summary of evidence

### Evidence Supporting 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

### Evidence Neutral to Clinical question

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### Evidence Opposing Clinical Question

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

In adult patients suffering from a cardiac arrest (P) does the calling of EMS and the provisions of chest compressions without ventilations (hands-only CPR) by untrained laypersons (I) compared with calling EMS only (C) improve survival to hospital discharge (O)?

The question is important but not definitively answered by the current published literature. Importantly, the current worksheet does not address compare CC alone CPR to CC plus ventilation CPR.

There are some limitations with respect to the question itself, which uses the terms “untrained” and “layperson” when evaluating the relationship between CC alone and outcome. These terms are difficult to define and open to interpretation. Some simulation and survey studies indicate that untrained lay providers may be more apt and able to provide CC alone (hands-only) CPR than traditional CC plus ventilations. However, none of the clinical human studies are able to adequately describe the training status or occupation (true layperson versus some type of medical professional without a specific duty to respond). As a consequence, the enclosed studies include bystander CPR generically without regard to training status or layperson status. Whether operationally such a strategy of CC alone could be specifically directed and measured among previously untrained (or trained) laypersons is not clear.

Importantly, CPR is sometimes performed in patients who are not experiencing cardiac arrest. Evidence indicates that the risk of injury from CC alone in this group is very low (White 2010, 91).

There are no randomized trials (nor will there likely ever be) comparing CC alone versus no bystander CPR. There are 6 human observational studies using concurrent controls have compared (in some form) CC alone versus no bystander CPR. These studies each demonstrate at least a trend toward survival benefit associated with CC alone compared to no bystander CPR. Each of the studies is a solid effort but each has limitations. These limitations include the specific characteristics of the study population (i.e. restricted to witnessed arrests or arrests due to cardiac etiology – Iwami 2007, 2900; SOS KANTO 2007,920; Waalewijn 2001, 273), analytical methods to assess for independent association (no adjustment for confounders – Holmberg 2001, 511; Van Hoeyweghen RJ 1993, 47; Waalewijn 2001, 273), completeness of outcome and covariates (i.e. missing information which leads to a case dropping out of the analysis - SOS KANTO 2007,920), or modest outcome numbers (Ong 2008, 119; Waalewijn 2001, 273). These limitations again have practical considerations when considering how you might implement CC alone instructions. For example, in some cases, the etiology of the arrest will not be obvious to a lay bystander; or witness status may not be apparent or considered when trying to implement lay CPR. In these cases, CC alone for non-cardiac etiology or unwitnessed arrest may not provide benefit.

Results of animal studies indicate a survival benefit of CC alone compared to no bystander CPR in cardiac arrest due to a primary cardiac cause (Berg 1993, 1907; Berg 1997, 1635; Berg 1997, 4364) There was no clear benefit of CC alone compared to no bystander CPR in asphyxial animal model of arrest (Berg 1999, 1893; Berg 1997, 1635).

Thus the recommendation regarding this worksheet question is made appreciating that there are limitations in the current evidence but that the question is quite relevant and practical given the challenges of increasing the proportion of cardiac arrest victims who receive (effective) bystander CPR. On balance, the evidence suggests that CC alone CPR performed by lay providers compared to no bystander can improve survival in adult cardiac arrest.

Additional investigation is needed to determine the magnitude of the benefit across different systems, identify operationally- and clinically-relevant subgroups for whom CC alone benefits the most and the least (not at all), and evaluate whether a strategy of CC alone can truly increase the proportion of adult victims who receive bystander CPR (from laypersons).

Acknowledgements: Dr Peter Morley who provided a constructive worksheet review.
Citation List

(Please see the comments at the end of the animal studies section that pertain to the animal studies collectively.*)


Review
Level 5, Supportive, Good
The study is a randomized swine study of CC alone versus CC plus ventilation versus no CPR in a simulated witnessed model of cardiac arrest due to heart disease. The model used a relatively short duration of untreated, electrically-induced VF. The primary outcomes were 24-hour survival. 24-hour survival was 100% (CC plus ventilation – 8/8), 100% (CC only – 8/8), and 13% (no CPR - 1/8). CC alone produced statistically significant better 24-hour survival that no bystander CPR.

Limitation is that the arrest etiology simulates cardiac etiology. This model may be pertinent to primary cardiac mechanisms but not respiratory mechanisms of arrest.


Review
Level 5, Supportive, Good
The study is a randomized swine study of CC alone versus CC plus ventilation versus no CPR in a simulated witnessed model of cardiac arrest due to heart disease. The model used a relatively long duration of untreated, electrically-induced VF. The primary outcomes were 24-hour survival and neuro-intact 24 hour survival. Neuro-intact 24-hour survival was 60% (CC plus ventilation – 6/10), 50% (CC only – 5/10), and 13% (no CPR – 0/6). CC alone produced statistically significant better 24-hour survival that no bystander CPR.

Limitation is that the arrest etiology simulates cardiac etiology. This model may be pertinent to primary cardiac mechanisms but not respiratory mechanisms of arrest.


Review
Level 5, Supportive, Good
The study is a randomized swine study of CC alone versus CC plus ventilation versus no CPR in a simulated witnessed model of cardiac arrest due to heart disease. The model used a relatively long duration of untreated VF precipitated by ischemia. The primary outcomes were 24-hour survival. 24-hour survival was 20% (CC plus ventilation – 3/15), 36% (CC only – 5/14), and 0% (no CPR - 0/6). CC alone produced a trend toward better 24-hour survival that no bystander CPR.

Limitation is that the arrest etiology simulates cardiac etiology. This model may be pertinent to primary cardiac mechanisms but not respiratory mechanisms of arrest.


Review
Level 5, Neutral, Good
The study is a randomized swine study of CC alone versus CC plus ventilation (versus ventilation alone) versus no CPR in a simulated asphyxial model of cardiac arrest. The primary outcomes were 24-hour survival and neuro-intact 24 hour survival. Neuro-intact survival was 70% (CC plus ventilation - 7/10), 7% (CC only - 1/14), 14% (ventilation only - 1/7), and 0% (no CPR - 0/8). CC alone was no better that no bystander CPR. Survival was better for CC plus ventilation compared to the other 3 groups.
Limitation is that the arrest etiology is asphyxia. This model may be pertinent to respiratory mechanisms but not primary cardiac mechanisms of arrest.


Review
Level 5, Neutral, Good
The study is a randomized swine study of CC alone versus CC plus ventilation (versus ventilation alone) versus no CPR in a simulated asphyxial model of respiratory shock – near arrest.
The primary outcomes were 24-hour survival and neuro-intact 24 hour survival.
Neuro-intact survival was 80% (CC plus ventilation - 8/10), 40% (CC only - 4/10), 60% (ventilation only - 6/10), and 0% (no CPR - 0/8). 24-hour survival was statistically better for CC alone compared to no bystander CPR, was no better that no bystander CPR. Survival was better for CC plus ventilation compared to the combined groups of CC alone and ventilation alone as well as better than the no bystander CPR group.

Limitation is that the clinical model is near-arrest though this may clinically be consistent with human arrest in many instances. The arrest etiology is asphyxia so that this model may be pertinent to respiratory mechanisms but not primary cardiac mechanisms of arrest.

* These animal studies are well-conducted. There are however some issues to consider. Given the nature of the comparison, the intervention assignment is not blinded providing some potential for bias. With regard to how well animal studies translate to human experience, the investigations work hard to provide some correspondence to real-world human circumstances. On one specific issue, the animals appear to be pre-oxygenated with 100% oxygen prior to inducing the arrest, whether this pre-oxygenation simulates the human clinical experience is debatable. Like most of the published literature, the studies were performed using prior resuscitation protocols. Finally, this body of work comes largely from a single, high-achieving animal laboratory with a career interest in this topic. The robustness of any conclusion is always improved when multiple, separate centers arrive at similar results with independent operations. (This last issue is of course outside the control of the studies’ authors.)


Review
Level 2, Supportive, Fair
The study was prospective cohort human study with concurrent controls.
Population was treated cardiac arrest regardless of etiology or witness status. The study was conducted in Sweden prior to the 2005 guidelines.
The study provides an explanation of how the primary exposure - bystander CPR - was determined/ascertained (arriving ambulance crew assessed type of bystander CPR).
Some potential confounders were assessed and reported.
The primary outcome was alive at 1 month. Outcomes were standardly ascertained but there do appear to be upwards of 10% missing based on the numbers provided in the text.
Relative to this worksheet, 278 persons (~3% of the cohort) received CC only CPR. Survival at 1 month was 6.8% for CC alone compared to 2.5% when no bystander CPR was performed. Multivariable adjusted odds ratio of survival at 1 month were not reported.

The primary limitations include that the study appears to have incomplete ascertainment of outcome, the study is observational (like the others comparing CC alone to no bystander CPR) so there is likely confounding, and the study does not assess the independent association of CC alone compared to no bystander CPR through multivariable adjusted models.


Review
Level 2, Supportive, Fair
The study was prospective cohort human study with concurrent controls.
Population was restricted to cardiac arrests that were bystander-witnessed and deemed to be due to cardiac etiology (n=4092).
The study was conducted in Japan prior to the 2005 guidelines.
The study provides an explanation of how the primary exposure - bystander CPR - was determined/ascertained (arriving EMS assessed type of bystander CPR).
Multiple potential confounders were assessed and included in multivariable logistic models.
The primary outcome was 1-year survival with favorable neurological function. Outcomes are comprehensively ascertained.
Relative to this worksheet, 544 persons (~13% of the cohort) received CC only CPR. Survival at 1 month was 6.9% for CC alone compared to 5.9% when no bystander CPR was performed. The multivariable adjusted odds ratio of survival at 1 month for CC alone versus no bystander CPR was 1.19 (0.83,1.71). Neuro-intact 1-year survival, the primary outcome, was 3.5% for CC alone and 2.1% when no bystander CPR was performed. The multivariable adjusted odds ratio of 1-year neuro-intact survival for CC alone versus no bystander CPR was 1.70 (1.02,2.84). In the VF subgroup, 1-year survival Neuro-intact 1-year survival, the primary outcome, was 11.5% for CC alone and 8.2% when no bystander CPR was performed. The multivariable adjusted odds ratio of 1-year neuro-intact survival for CC alone versus no bystander CPR was 1.45 (0.77,2.73).

The primary limitations include that the population is restricted to arrests that are bystander-witnessed due to a cardiac cause. Importantly over 17,000 of the arrests were excluded because they were unwitnessed and attributed to a non-cardiac cause – this group is 4-fold larger that the study group. Importantly, an equal number of survivors were observed in this group. Hence, we cannot make inference regarding the role of CC alone in 80% of treated cardiac arrests in this setting. This limitation detracts from the study’s generalizability. Given there distinct etiology (non-cardiac) or un-witnessed status exclusions, CC alone may have different effects and potentially be less favorable. From a practical perspective, analyses that restrict to a cardiac cause use an artificial restriction that may often not be apparent to the bystander.

Other comments - Traditional bystander CPR that includes ventilation and compression was also included in the study. The association between traditional bystander CPR and outcome was similar to that of CC alone bystander CPR. The distribution of initial rhythms is not typical compared to most prior reports. In the Iwami study, the prevalence of ventricular fibrillation was 6% among all treated arrests and 20% among bystander-witnessed events due to heart disease.


Review
Level 2, Supportive, Fair
The study was prospective cohort human study with concurrent controls.
Population was treated cardiac arrest regardless of etiology or witness status. The study was conducted over 3 years in Singapore prior to the 2005 guidelines.
The study provides an explanation of how the primary exposure - bystander CPR - was determined/ascertained (arriving ambulance crew assessed type of bystander CPR). There was no validation of bystander CPR performance (review of dispatch tapes) or information about the CPR process measures.
Potential confounders were assessed and reported.
The primary outcome was survival to hospital discharge (or alive at 1 month if still hospitalized). Information was also available regarding functiona/neurological status at discharge. Outcomes were standardly ascertained.
Of the 2428 eligible for analysis, 154 persons (6% of the cohort) received CC only CPR. Survival to hospital discharge was 2.6% for CC alone compared to 0.5% when no bystander CPR was performed. Multivariable adjusted odds ratio of survival for CC alone compared to no bystander CPR was 5.0 (95% CI 1.5-16.4).

The primary limitations include the observation nature of the study and the very modest survival. The CC alone group had only 4 survivors and the CC plus ventilation group had only 8 survivors. Thus although the results are statistically significant, the findings are not robust and could change substantially with the addition or subtraction of one or two survivors.

Other comments: A similar point estimate for the odds ration of survival was also observed for chest compression plus ventilation compared to no bystander CPR 5.4 (2.1-14.0).


Review
Level 2, Supportive, Fair
The study was prospective cohort human study with concurrent controls.
Population was restricted to cardiac arrests that were bystander-witnessed (n=4068).
The study was conducted in Japan prior to the 2005 guidelines.
The study provides an explanation of how the primary exposure - bystander CPR - was determined/ascertained (arriving EMS assessed type of bystander CPR).
Multiple potential confounders were assessed but approximately 30% of the cases appear to be missing 1 or more confounders. The primary outcome was 30-day survival with favorable neurological function. Outcomes are comprehensively ascertained. Relative to this worksheet, 439 persons (~11% of the cohort) received CC only CPR. Neuro-intact survival at 30 days was 6% for CC alone compared to 2% when no bystander CPR was performed. No multivariable model is presented that would provide the independent association of CC alone versus no bystander CPR. The study also reports outcomes for the witnessed VF subgroup. Neuro-intact survival at 30 days was 19% for CC alone compared to 8% when no bystander CPR was performed

Limitations include 1) the population is restricted to arrests that are bystander-witnessed, such that the role of CC alone in unwitnessed arrests cannot be evaluated, and 2) no multivariable model is presented that would provide the independent association of CC alone versus no bystander CPR. (A follow-up author response to letter to the editor does provide a multivariable adjusted odds ratio 2.7 [1.6,4.4] however it is still unclear what the effect of missing cases is since likely about a quarter of cases drop out of the analysis.)

Other comments - Traditional bystander CPR that includes ventilation and compression was also reported in the study. The association between traditional bystander CPR and outcome was also favorable compared to no bystander CPR. There was no statistical difference in the primary outcome between the traditional versus CC alone. Only ~10% had a history of coronary disease, only ~3% had a history of heart failure. The prevalence of these underlying conditions is much greater in other reports of persons who suffer out-of-hospital cardiac arrest.


Review
Level 2, Supportive, Poor
The study was prospective cohort human study with concurrent controls.
Population was restricted to cardiac arrests that were deemed to be due to cardiac etiology (n=3306).
The study is conducted in a European setting prior to 2005 Guidelines.
The study provides an explanation of how the primary exposure - bystander CPR - was ascertained (assessment upon arrival of MICU nurse and/or physician).
The outcome was alive and awake at 14 days following the arrest.
Relative to this worksheet, 265 persons (~8% of the cohort) received CC only CPR. Hospital admission was 21% for CC alone compared to 20% when no bystander CPR was performed. Awake survival at 14 days was 10% for CC alone compared to 7% when no bystander CPR was performed. Among those with an initial rhythm of ventricular fibrillation, awake survival at 14 days was 20% for CC alone compared to 15% when no bystander CPR was performed. No direct statistical comparison between CC alone and no bystander CPR is provided.

Primary limitations include 1) the study population is restricted to cardiac cause 2) the outcome is unknown in 271 persons, or ~8% of the cohort, 3) there is no attempt to account for potential confounders (i.e. logistic regression) in evaluating the independent association of CC alone and survival compared to no bystander CPR. From a practical perspective, analyses that restrict to a cardiac cause use an artificial restriction that may often not be apparent to the bystander.


Review
Level 2, Supportive, Poor
The study was prospective cohort human study with concurrent controls.
The study population was restricted to bystander-witnessed (922). The study is conducted in a European setting prior to 2005 Guidelines.
The study provides an explanation of how the primary exposure - bystander CPR - was ascertained (interviews of bystanders). The outcomes were hospital admit and survival to discharge.
Relative to this worksheet, only 41 persons (~5% of the cohort) received hands-only CPR. Hospital admission was 32% for CC alone versus 24% when no bystander CPR was performed. Survival was 15% for CC alone versus 6% when no bystander CPR was performed. No direct statistical comparison was provided.

Primary limitations include 1) the population is restricted to witnessed arrests, 2) the very small numbers in the chest compression only group (n=41 with a total of 6 survivors), and 3) the study was not primarily designed to determine whether hands-only CPR was associated with better outcomes. Hence analytical models (i.e. logistic regression) do not focus on this exposure (hands-only CPR) to evaluate whether CC alone is independently associated with outcome.

Other studies reviewed in detail but ultimately not directly pertinent to the specific worksheet question


Review
Level of evidence 2, Supportive, Fair
Reason for exclusion - The study classifies bystander CPR as CC alone and CC plus ventilation but does not report survival in patients who did not receive any bystander CPR.
The study was a retrospective human study with concurrent controls.
Population was out-of-hospital cardiac arrest patients who received bystander CPR from 1990 – 2005 who are captured in the voluntary national cardiac arrest registry.
The study was conducted in Sweden prior to the 2005 guidelines.
The study does not provide an explanation of how the primary exposure - bystander CPR with CC alone or CC plus ventilation - was determined/ascertained (though the text leads one to believe that arriving EMS assessed the type of bystander CPR).
Multiple potential confounders were assessed and included in multivariable logistic models. However, information regarding missing values is not provided though the analysis stratified on response time indicates ~7% missing response intervals.
The primary outcome was 1-month survival. The report is unclear regarding the whether outcomes were missing.
Relative to this worksheet, 8209 persons received CC plus ventilations while 1145 received CC alone. Survival at 1 month was 7.2% for CC plus ventilation compared to 6.7% for CC alone. The multivariable adjusted odds ratio of survival at 1 month for CC plus ventilation versus CC alone was 1.18 (0.89,1.56).

The primary limitations include that 1) the study does not report survival for those who receive no bystander CPR. If one accepts that traditional CPR is better than no CPR, then by the commutative property one would contend that CC alone also provides benefit compared to no CPR since the 2 CPR groups in this study have comparable survival. The study does not report the extent of missingness for covariates or outcome, which could affect the relationships and conclusions.


Review
Level of Evidence 1, Supportive, Good
Reason for exclusion - The study classifies bystander CPR as CC alone and CC plus ventilation but does not report survival in patients who did not receive any bystander CPR (no bystander CPR group).
The study is the only randomized human trial evaluating chest compression alone versus chest compression plus ventilation (15:2 ratio).
The study uses dispatchers to randomize CPR instructions.
The study was conducted in a US setting with an exceptionally quick EMS response prior to the 2005 guidelines.
The primary study population and the one featured in the abstract are cardiac arrest patients whose arrest was due to a cardiac etiology (n=520). Another 227 patients were enrolled with presumed arrest due to specific non-cardiac causes (i.e. alcohol or drug intoxication). These results are reported separately.
The study provides an explanation of how the primary exposure - bystander CPR - was determined/ascertained (random assignment with review of the initial telephone encounter).
The outcome was survival to hospital discharge.
Randomization was achieved.
Among the primary comparison group, CC alone was performed by 81% and CC plus ventilation was performed by 62% with the main reason for unsuccessful implementation being EMS arrival on scene. There was a nonsignificant trend toward better survival in the CC alone group (14.6%) compared to CC plus ventilation (10.4%) in the primary comparison group (cardiac etiology). Among those with a specific non-cardiac cause (not the primary comparison group), there was a trend in the opposite direction toward better
survival in CC plus ventilation (80.7%) compared to CC alone (75.7%). When combining these 2 groups, survival to hospital discharge was 32.9% with CC alone and 30.2% with CC plus ventilation (confidence interval of the difference -4.1 to 9.5%). Primary limitations include 1) the very quick response time of the EMS population which make the generalizability of the study less certain, 2) the lack of appreciation by most readers that overall the results are really most consistent with no difference (rather than superiority of CC alone, and 3) the specific character of the dispatchers – most are filed-experienced EMTs and paramedics who subsequently transition to dispatch (in most dispatch systems the dispatchers are not field-experienced EMS personnel) – this may or may not affect the generalizability of the results.

The results indicate that there is no evidence of difference in CC alone compared to CC plus ventilation, though the 95% confidence interval (-4.1 to 9.5%) does not rule out that there may be a clinically-important survival difference between these 2 bystander CPR approaches.


Review
Level of evidence 2, Supportive, Fair
This observational study evaluates the risk of injury due to CPR among persons who receive bystander CPR but who are not experiencing cardiac arrest. These persons are misidentified as cardiac arrest given the clinical circumstances (i.e. hypoglycemia, post-ictal seizure, syncope). The study observed a very low rate of injury due to CPR regardless of the type of CPR (CC alone or CC plus ventilation). The results suggest that CC alone does not produce excess risk among patients who may inadvertently receive CPR because they are misidentified as a cardiac arrest victim.