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

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<th>Worksheet author(s)</th>
<th>Date Submitted for review:</th>
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<tr>
<td>Peter J. Kudenchuk, MD; Laura S. Gold, PhC</td>
<td>09/11/2009 (revised 11/9/09)</td>
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**Clinical question.**

“In adult patients suffering from a cardiac arrest (P) does calling of EMS and starting chest compressions (without ventilation) by trained laypersons or professionals (I) compared with calling EMS and starting chest compressions plus rescue breathing (C) improve survival to hospital discharge (O)?”

**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 existing worksheet

**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: #1 “Cardiopulmonary Resuscitation” (MESH) (6671) or #2 “Resuscitation” (MESH) (55651) or #3 “Heart Arrest” (MESH) (23395) and #4 “Respiration, Artificial”) MESH (44584). The combination of (#1 or #2 or #3) and #4 yielded 29450, with mostly irrelevant cases. Therefore the search was approached using non-MESH terms including: “resuscitation and ventilation” (17962); “chest compressions and ventilation” (249); “resuscitation and chest compressions and ventilation” (234); “resuscitation and chest compressions and ventilation and survival” (68); “CPR and ventilation” (593); CPR and rescue breathing” (21); “CPR without rescue breathing” (21); “CPR without ventilation” (593).

Embase: “resuscitation and ventilation” (3475); “CPR and ventilation” (551); “CPR and rescue breathing” (14); “CPR and ventilation and survival” (153), “CPR and ventilation and survival” (153).

Cochrane: “resuscitation and ventilation” –yielded no Cochrane reviews

Other: References from published articles gleaned from the searches above were also evaluated, as we re references from the recently published AHA Advisory Statement (Sayre MR et al. “Hand-only (Compression Only Cardiopulmonary Resuscitation) Circulation 2008;117:000-000 (http://www.americanheart.org/presenter.jhtml?identifier=3003999)

Summary: The above searches yielding <600 cases will be screened by title; further screened by abstract content and then by actual article content for relevance to the clinical question. Animal studies will be evaluated for conceptual relevance; pediatric studies will be excluded.

**State inclusion and exclusion criteria.**

Exclusion: pediatric or neonatal  (however cardiac arrest due to asphyxiation was taken from animal literature, if felt to be potentially applicable to some adults with cardiac arrest)

Other limitation: It was presumed that the question under evaluation was directed at BLS-level care by professional or trained providers. Therefore the impact of ALS-level care (specifically endotracheal intubation) and its impact on outcome was not considered to be within the domain of the question under evaluation.

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

1. Human clinical studies: 17
2. Animal/tissue preparation science studies: 16
3. Miscellaneous studies: 4
### Summary of evidence

#### Evidence Supporting Clinical Question

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<td>SOS-KANTO 2007, 920 BD; Kern 2002, 645 ABDE; Ewy, 2525 2007 D</td>
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Bobrow 2008, 1158 ABCD, Kellum 2006, 335 BD; Kellum 2008, 244 BD; Bobrow 2009, 656 AD

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Level of evidence

### Evidence Neutral to Clinical question

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<td>Jawan 2000, 133 E; Chandra 1994, 370 E</td>
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Level of evidence

### Evidence Opposing Clinical Question

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<td>Idris 1994, 3063 AB; Tang 1991, 218 E; Idris 1995, 522 A</td>
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<td>Safar 1962, 1 E; Berg 1999, 1893 D; Weil 1958, 437 E</td>
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<td>Bobrow 2009, 656 AD (unwitnessed VF, nonshockable)</td>
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<td>Von Hoeyweghen 1993, 47 ABE; Holmberg 2001, 511 AE</td>
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Level of evidence
The current approach to BLS resuscitation (employing chest compressions and ventilation) is based on the presumption that both circulatory and ventilatory support are required in cardiac arrest for provision of blood flow, oxygenation, and avoidance of CO2 accumulation. Fair-good animal studies support the adverse hemodynamic effects resulting from hypercarbia and acidosis (Weil 1958, 437), the adverse effects of isolated hypercarbia without hypoxia, and of isolated hypoxia without hypercarbia on short-term outcome (ROSC) after induced VF cardiac arrest (Idris 1995, 522). Other animal studies have observed an association between worsening hypoxia and hypercarbia and deterioration of hemodynamic status during CPR (Kern 1998, 179). Although concentrations of oxygen and CO2 differ from expired air as compared with ambient air (Wenzel 1994, 1806), it appears that either mouth-to-mouth or bag-valve-mask ventilation can improve oxygenation and ameliorate hypercarbia in apneic patients (Greene 1957, 313). The two have never been formally compared under cardiac arrest conditions in which CPR by trained lay providers is more likely to involve mouth-to-mouth rescue breathing whereas that by EMS providers typically employs bag valve mask ventilation using room air or supplemental oxygen. Questions as to whether the combined approach of resuscitation using chest compressions and ventilation makes the technique too difficult to learn, perform and remember; whether superimposed ventilation compromises the performance of other important aspects of resuscitation (chest compressions) or makes CPR less likely to be performed by lay providers (trained or untrained) are all important, but will not be addressed here. Rather, the focus of our clinical question is whether outcome from cardiac arrest, survival to hospital discharge, is favorably, unfavorably, or indifferent affected by the provision of chest compressions alone, or in combination with rescue breathing.

Animal studies

Most, but not all animal studies have demonstrated either comparable or better outcomes when resuscitation from cardiac arrest due to VF is initially performed with chest compressions in the absence of active ventilation rather than in its presence. In all these studies, the period of unsupported VF prior to BLS interventions (CPR) has been relatively brief (ranging from 30 seconds to 6 minutes) simulating a scenario in which the cardiac arrest was witnessed, with a relatively short collapse-to-CPR interval. In all instances, provision of BLS care (chest compressions with and without ventilation, typically using 17% O2 and 4% CO2 to mimic expired air) was subsequently performed over a period ranging from 8-12 minutes, thereafter followed by standard ALS interventions including shock, intubation, epinephrine, and ventilation with 100% oxygen. In all but one study, comparison was made against chest compressions and ventilation that adhered to 2000 Guideline recommendations of 15:2 rather than current 2005 Guideline recommendations of 30:2. A number of pertinent observations emerge from these studies:

1. When cardiac arrest was precipitated by asphyxia rather than a primary rhythm abnormality, neurologically normal survival was better achieved with the combination of chest compressions and ventilation than in the absence of either one or both. Specifically, oxygen saturation, acid-base balance, and hemodynamics during CPR were significantly better when chest compressions and ventilation were performed in combination than with chest compressions alone in this setting (Berg 1999, 1893). Notably, when the period of asphyxia was not as protracted and the resulting hemodynamic as well as metabolic insults less severe, 24 hour survival was not significantly different with the combination of chest compressions and ventilation than with chest compressions or ventilation alone (Berg 2000, 1743), suggesting a time and severity-dependent relationship between anoxic insult and recovery with CPR of one form or the other.

2. Whether intubated or not, it is recognized that airways of animals are less likely to obstruct during CPR than in humans, permitting both spontaneous gasping and passive ventilation during the performance of chest compressions. Conversely, in humans, it has been demonstrated that in the absence of an artificial airway, an unsupported head (which assumes the position of slight anteflexion) produces obstruction of the hypopharynx, resulting in the complete absence of tidal volumes during chest compressions (Safar 1962, 1). In the late stages of cardiac arrest, closed chest massage also produced minimal (less than anatomic dead space) or no ventilation, even in the presence of an endotracheal airway (Safar 1962, 1; Deakin 2007, 53). That is, the ability of a human to passively ventilate during CPR is less predictable than in animals, and in the later phases of arrest ventilation may not be adequate in humans even with a patent airway. Thus the series of experiments comparing chest compression with ventilation against chest compression only in animals may be better characterized as a comparison between active ventilation with chest compression versus passive ventilation with chest compression, with questionable applicability to human cardiac arrest. That in most instances the two techniques achieved comparable outcomes in animals is not surprising, but necessarily transferrable to the human arrest situation.

When the capacity for passive ventilation was eliminated from the animal experiments, a comparable benefit from chest compressions alone as compared with chest compression with ventilation was less evident, or reversed. For example, the prevention of passive inspiration during chest compression-only CPR by use of an impedance threshold valve resulted in the absence of any arterial-venous PO2 difference after only 3 minutes of CPR, and a longer period of time and greater number of shocks to achieve ROSC (Dorph 2004, 309). Conversely, in another study comparing chest compression with ventilation against chest compressions alone, the endotracheal tube in the latter group of animals was deliberately clamped to prevent the occurrence of passive ventilation during chest compressions. Survival at 24 hours was comparable between the two treatment groups. However, attributing this outcome to strictly the absence of passive ventilation was confounded by the hemodynamic effect of a clamped airway, which potentially enhanced forward flow during chest compressions (development of higher intrathoracic pressures) and an ITD-like effect during chest recoil (enhancing venous return). As a result, airway clamping produced significantly higher blood and perfusion pressures.
during the initial minutes of chest compressions in the tracheal tube-clamped animal, preventing the ability to attribute differences between the clamped (nonventilated) and unclamped (ventilated) treatment groups merely to the absence of (passive) ventilation (Kern 1998, 179).

3. Animal studies have suggested a relatively limited time window over which chest compressions can be safely administered in the absence of adequate ventilation before metabolic and hemodynamic deterioration ensues. With ongoing passive ventilation (averaging 80 ml tidal volume/chest compression) during chest compression-only CPR among dogs in VF, oxygen saturation averaged 94%, pH 7.4 and PCO2 24 mm Hg at 4 minutes. However, by 8 minutes, oxygen saturation declined to 75%, pH to 7.29, and PCO2 risen to 34 mm Hg, associated with a significant decline in aortic systolic and diastolic perfusion pressures (Chandra 1994, 370). Among the pigs described above whose airway was purposely clamped during chest compressions, the initial improvement in hemodynamics resulting from a probable compression- and recoil-enhanced hemodynamic effect (compared to the group receiving chest compressions and ventilations via an open airway) had all but disappeared by 6 minutes into CPR, in association with progressively worsening hypoxia, hypercarbia and acidemia (Kern 1998, 179).

4. Perhaps the most important lesson learned from animal experiments is that pauses in compression, not ventilation per se, may be the more critical issue affecting outcome from resuscitation. This principle has been elegantly demonstrated when interruptions in chest compressions (for 2 breath ventilation) were extended from earlier experiments, in which they averaged 2-4 seconds, to later experiments where they averaged 16 seconds. This resulted in differences in outcome (neurologically intact survival) between chest compression with ventilation versus chest compression alone that became significantly improved with chest compressions alone (Ewy 2007, 2525). Notably, these more exaggerated differences during more protracted periods of interrupted chest compression for ventilation were observed when either a 15:2 (Berg 2001, 2464; Kern 2002, 645) or 30:2 chest compression: ventilation ratio (Ewy 2007, 2525) was employed.

5. Over time, chest compression in the absence of ventilation (either active or spontaneous inspiratory gasping) may result in reduced functional residual capacity, with bronchial and alveolar collapse, culminating in lung injury (Kawamae 2001, 165). This may, in part, be the mechanism for the reported absence of significant passive ventilation during chest compressions after protracted CPR (Safar 1962, 1; Deakin 2007, 53).

Clinical studies

Human studies addressing the specific question of provision of chest compression only or standard CPR by trained laypersons or professionals are limited in quantity and most had important methodological limitations. Only 4 have specifically addressed the provision of such care by professionals (formal EMS providers); the remainder of the studies focused on principally on citizens (bystanders), some of whom were trained medical providers. The following observations are pertinent:

1. The 4 studies which specifically addressed provision of chest compression-only CPR by EMS providers had similar methodological limitations. None was randomized (controls were historical), all simultaneously changed numerous aspects of resuscitation protocols including discouragement of early active ventilation (other changes included provision of 200 chest compressions before rhythm analysis, deployment of a single shock analysis followed by a cycle of CPR, and early epinephrine), any one of which (apart from the absence of ventilation) might have influenced the observed outcomes. Later published reports by the same authors included patients reported in their initial publication and thus were an expansion of, rather than confirmatory studies. Notably, studies in other communities have observed a significant improvement in survival from out-of-hospital cardiac arrest when some or most of these other measures have been deployed, even when positive pressure ventilation during CPR has been performed (Rea 2006, 2760). How compliance with any or all of the changes in protocol was observed or enforced was not specifically described, although compliance percentages were provided. In one study, survival deteriorated back to baseline in the months following introduction of the new protocol, raising question whether the earlier observed differences were related to a Hawthorne rather than treatment effect (Bobrow 2008, 1158). Likewise, comparisons of the new treatment protocol were made against EMS agencies that were following different “control” resuscitation protocols (2000 versus 2005 AHA Guidelines), adding more uncontrolled variability in assessing outcomes. Neurological assessment of outcome was potentially subject to bias, in being assessed only in subjects who were willing to participate (potentially selecting out those with more favorable outcomes) and/or whether the investigator was blinded to treatment assignment when assigning a Cerebral Performance Category score. One study (Bobrow 2009, 656) that specifically addressed passive ventilation versus bag valve mask ventilation during the initial 3 cycles of 200 compressions admitted that compliance was self-reported and that evaluation of bag valve mask ventilation was conducted during the earliest stages of implementation of the multiple interventions when “EMS personnel were reluctant to use this strategy”. It is not clear whether this “noncompliant cohort” that deployed bag valve mask ventilation may also have been less compliant to other components of the continuous chest compression strategy. Also of note, while this study reported improved neurologically intact survival in witnessed VF arrest, the trend (not statistically significant) trended toward harm in patients with unwitnessed VF arrest or with arrest due to nonshockable rhythms.

In addition to having many of these same limitations, two additional studies (Kellum 2006, 335; Kellum 2008, 244) did not describe nor adjust for the baseline characteristics of the patients undergoing treatment in the outcome analysis. Thus, that these studies reported significant improvement in survival to hospital discharge, and in neurologically intact survival therefore cannot necessarily be ascribed to the interventions themselves.
2. Six other observational studies primarily assessed the conduct of bystander CPR, 4 of which observed no statistically significant differences in outcome when bystanders initiated chest compression-only as compared with conventional CPR (Ong 2009, 119; Holmberg 2001, 511; Waalewijn 2001, 273; Van Hoeyweghen 1993, 47).

One prospective, population-based study of bystander-witnessed out-of-hospital cardiac arrest observed that 1 year survival with favorable neurological outcome was comparably improved by bystander chest compression-only or conventional CPR, as compared with no CPR (Iwami 2007, 2900). When the interval of bystander CPR was brief (0-5 minutes from collapse to EMS arrival), chest compression-only CPR tended to be superior to conventional CPR (odds ratio 2.22 versus 1.67 compared to no provision of CPR). A potential survival advantage of chest compression-only CPR over conventional CPR was observed when the interval of bystander CPR was brief (0-5 minutes from collapse to EMS resuscitation) (odds ratio 2.22 versus 1.67 as compared with no provision of CPR). Outcomes in chest-compression only and conventional CPR were virtually identical when the interval of bystander CPR was of intermediate duration (6-15 minutes); and the converse was observed when the interval of bystander CPR was more protracted (>15 minutes from collapse to EMS resuscitation) (0.3% in the no CPR, 0% in the chest compression only, and 2.2% in the conventional CPR group (p<0.05). Other aspects such as how well CPR was performed in the comparison groups were not determined in this study

Nor did this study describe whether any trained providers administered CPR

A second non-population based observational EMS study evaluated patients with bystander-witnessed out-of-hospital cardiac arrest who were subsequently transported by paramedics to participating emergency hospitals (SOS-KANTO 2007, 920). The primary endpoint of the study was favorable neurological outcome 30 days after cardiac arrest based on the Glasgow-Pittsburgh cerebral performance category assessed by physicians who were blinded to patients' treatment assignment; no surviving patient was lost to follow-up. Both the chest compression-only and conventional CPR treated patients had better survival with favorable neurological outcome than patients not receiving any bystander intervention, but, overall, did not differ between recipients of either form of CPR. However, an “observation within an observation” post hoc analysis found such survival was improved with chest-compression only CPR in subgroups of patients (which were not prospectively identified) with apnea, VF or tachycardia as the initial cardiac rhythm (p=0.041) and when resuscitation began within 4 minutes of collapse (p=0.02). Multivariate analysis found presenting VF/VT, a shorter time interval between first bystander resuscitation attempt and first AED analysis, and chest-compression only CPR as independent predictors of outcome. This study also did not characterize how conventional CPR was performed by bystanders (compression:ventilation ratio) against which chest-compression only was compared, nor aspects of CPR quality.

3. One prospective randomized trial evaluated dispatch assisted CPR instruction to untrained bystanders, and found a nonstatistically significant trend toward improved survival to hospital discharge among those assigned to chest compression only as opposed to conventional CPR (Hallstrom 2000, 1546).

Summary

Animal studies suggest that when a witnessed cardiac arrest is precipitated by an acute arrhythmia, survival (and favorable neurological outcome) with chest compression-only CPR in the initial minutes of resuscitation is comparable or superior to conventional CPR. It is hypothesized that pre-arrest concentrations of oxygen and CO2 in such circumstances are not significantly altered for a number of minutes by what little circulation is afforded by chest compressions, and ventilation support by rescue breathing is not required. Conversely, when precipitated by a protracted period of asphyxia, concentrations of oxygen and PCO2 are already at critical levels, and ventilation or the combination of chest compressions and ventilation is more likely to improve survival than circulatory support by chest compressions alone. Hence, depending upon the immediate cause of the cardiac arrest, immediate ventilation may or may not be required. Mechanistically, chest compression-only CPR may be comparable or superior to standard CPR in animals because of a more predictably open airway, allowing for gas exchange from the chest compressions themselves as well as from spontaneous gasping, at least in the initial minutes of witnessed arrest. Furthermore, any interruption of chest compressions (as required for rescue breathing) is hemodynamically detrimental in proportion to the duration of the resulting pause, resulting in worsened survival than when CPR is performed without pauses for rescue breathing. Rescue breathing may itself be hemodynamically detrimental in that the resulting transient increase in intrathoracic pressure may impair venous return to the chest. Although this mechanism has been proposed to account in part for the detrimental effects from hyperventilation that has been observed during asynchronous ventilation-compression following endotracheal intubation (Aufderheide 2004, 345, Aufderheide 2004, 1960), it may not play as great a role when chest compressions and relaxation are interrupted for synchronous ventilation since circulation has presumably ceased entirely during this period. Animal studies have not determined an absolute upper interval after which rescue breathing is required to prevent the deleterious metabolic and hemodynamic effects provoked by worsening hypoxia and hypercarbia, perhaps coupled with bronchal and alveolar collapse from relative hypoventilation, but may range from 6-8 minutes after witnessed arrest.

Some, but probably not all, of these principles are operative during arrhythmogenic cardiac arrest in humans, such as the initial preserved state of oxygenation and CO2, and the potentially detrimental effects of interrupting chest compressions. However, because airway obstruction is more common during cardiac arrest in humans than in animals, the absence of passive ventilation during chest compressions (or spontaneous gasping) potentially shortens the time interval during which rescue breathing may be safely avoided without progressive hypoxia and accumulating hypercarbia with its metabolic and hemodynamic consequences. The best data from dispatch-assisted CPR suggests that when the interval from collapse to provision of standard CPR by EMS was relatively brief (averaging 3.1 minutes), survival was comparable in humans (in fact tended to be better) when only chest compressions were provided by bystanders, as compared with standard CPR. Uncontrolled observational studies evaluating the provision of CPR by mainly untrained but including some trained bystanders in witnessed cardiac arrest have suggested a
comparable or improved survival when CPR was performed with chest compressions alone, or in combination with ventilation, when the interval from collapse to provision of standard CPR by EMS was not protracted, and when the presenting arrhythmia was ventricular fibrillation. Three observational (before and after) studies have also suggested a survival benefit from chest compression-only CPR by BLS EMS providers, but were methodologically challenged by having made multiple simultaneous changes in CPR protocol along with the change in ventilation strategy, many of which have been shown to favorably impact survival from cardiac arrest even when standard chest compressions and ventilation are provided. In addition, observational trials have for the most part compared chest compression-only CPR against 2000 resuscitation guidelines, rather than 2005 Guidelines, which place a greater emphasis on not interrupting CPR and changed the compression:ventilation ratio from 15:2 to 30:2. Evidence that these factors likely influenced outcome was apparent in a recent study that noted over a two-fold increase in survival to hospital discharge when a 50:2 compression:ventilation ratio was implemented (Garza 2009, 2597).

**PERSPECTIVE ON SCIENCE:**

Animal evidence suggests that active (positive pressure) ventilation may not be required in the early aftermath of sudden cardiac arrest that has been precipitated by a ventricular arrhythmia, when the airway is not obstructed (This, however, is not likely to be the case in asphyxial pulseless cardiac arrest (particularly when the period of inciting anoxia is protracted). The window of opportunity is finite, perhaps limited to 6-8 minutes following witnessed arrest. Conversely, the patency of an unprotected airway is less predictable in humans than in animals, such that chest compressions may not reliably sustain sufficient tidal volumes for adequate ventilation, particularly in the later phases of cardiac arrest, potentially shortening the window of therapeutic opportunity during which rescue breathing can be safely avoided. Neither animal nor human data suggest that rescue breathing can be avoided during resuscitation, only that it may be postponable, depending upon the arrest circumstances. Important methodologic deficiencies in the observational studies evaluating chest-compression only CPR by untrained bystanders, trained bystanders, and EMS providers in witnessed cardiac arrest do not permit making definite conclusions as to whether a strategy of chest compression-only CPR is more likely to improve survival than traditional CPR. Rather, the data suggest that treatment strategies that minimize interruption of CPR (whether for stacked shocks, pulse checks, repeated rhythm evaluation) in the absence of any change in ventilation strategy can improve outcome from cardiac arrest.

At present, there is insufficient evidence to suggest that the provision of chest compressions (without ventilation) by trained laypersons or professionals, compared with calling EMS and starting chest compressions plus rescue breathing improves survival to hospital discharge, or to advocate a change in treatment recommendations for trained laypersons or EMS providers. Notably, while the combination of rescue breathing with chest compressions has been described as a complex psychomotor task that is difficult to learn, perform and remember, its elimination creates comparable challenges. The elimination of rescue breathing requires (1) recognizing that a cardiac arrest was not precipitated by asphyxia (for which deprivation of ventilation may be harmful), (2) that it be witnessed, and (3) requires a judgment as to when a sufficient time has transpired such that active rescue breathing should be reinstituted.

**Acknowledgements:**
Citation List in alphabetical order


**HUMAN STUDIES**

### Detailed Citation List


   **LOE 3 (retrospective cohort study)**

   **Methodological quality: Poor**

   **Were comparison groups clearly defined?** Not very well. This was a before/after study but the authors admit that many patients treated after the MICR protocol went into effect still received ventilations. They say “because this approach…was such a dramatic change…bag-valve-mask ventilation was still permitted by paramedics and firefighters at an encouraged rate of 8 ventilations per minute.” This implies that even after the protocol was implemented, some (no indication of how many) were still receiving substantial number of ventilations.

   **Were outcomes measured objectively in both groups?** The primary outcome, survival to hospital discharge, was. CPC score to assess neurological outcome: they sent mailings; seems unlikely that those with low scores would have been able to participate.

   **Were known confounders identified and properly controlled for?** They didn’t adjust for age, sex, location, bystander CPR, or arrival time, but said they weren’t significant.

   **Was follow-up of patients sufficiently long and complete?** Yes, followed to hospital discharge.

   **Outcomes assessed:** A (return of spontaneous circulation); B (survival of event [to hospital admission]); C (survival to hospital discharge); D (intact neurological survival).

   **Magnitude of any observed effect:**

   All arrests due to cardiac etiology: Before chest-compression only protocol, survival to hospital discharge was 4/218 (1.8%) [95% CI: 0.7%-4.6%]. After training, 36/668 (5.4%) [95% CI: 3.9%-7.4%]. Absolute risk reduction is 5.4%-1.8%=3.6%. Number needed to treat=1/0.036=28.1.

   Survival from witnessed VF: Before chest-compression only protocol, survival to hospital discharge was 2/43 (4.7%) [95% CI: 1.3%-15.4%]. After training, survival was 23/131 (17.6%) [95% CI: 12-25%]. Absolute risk reduction is 17.6-4.7=12.9%. Number needed to treat=1/0.12=7.75.


   **LOE 3 (retrospective cohort study).** Reporting of additional 1589 patients from *JAMA* publication cited above (Bobrow 2008, 1158). Substudy of 1019 of 5097 total arrests in whom passive ventilation or bag valve mask ventilation was deployed during initial 3 cycles of 200 compressions, at a time when providers were “reluctant to use” passive ventilation.

   **Methodology:** Poor. Study not randomized. Comparison of passive ventilation vs bag valve mask ventilation was self-reported and self-selected by providers; it is likely bag valve mask ventilation was deployed early during the experience of the change in CPR protocol to continuous compression when other details of the protocol that may have also impacted outcome (1) 200 uninterrupted preshock compressions (2) 200 uninterrupted postshock compressions before pulse check or rhythm analysis (3) delayed endotracheal intubation for 3 cycles of 300 compressions and rhythm analysis (4) attempted IV or IO epinephrine) may also not have been fully deployed; compliance with the overall protocol during this time period was not confirmed; quality of CPR was not formally assessed. Hence it is not clear whether the proposed difference in intervention was responsible for the differences in outcome reported. Whether neurological outcome was assessed by investigators blinded to treatment received is not specified. There is also the potential for “survivor bias” in that neurological outcome was only assessed in those who did not refuse to participate in such an assessment.

   **Results:** No difference in ROSC or neurologically intact survival to hospital discharge (defined as CPC 1-2) between passive and bag valve mask ventilation groups (OR 1.2 (0.8-1.9)). Improved outcome in subgroup of patients with witnessed VF/VT arrest (OR 2.5 (1.3-4.6). However, although not highlighted, trend was toward worse outcome in unwitnessed VF/VT (OR 0.5 (0.2-1.6) and in nonshockable arrest (OR 0.3 (0.1-1).

LOE 5 (not the right population because they didn’t look at trained laypeople or EMS) but within that, LOE 3 (retrospective cohort study).

Methodological quality: Fair.

Were comparison groups clearly defined? Yes, one group received chest compression only CPR and the other received standard CPR. However, since chest compression only CPR was not taught in the area, it was unclear why it would have been done.

Were outcomes measured objectively? Yes, the primary outcome was one month survival.

Were known confounders identified and properly controlled for? Yes, they adjusted for variables that were significantly different between the groups receiving the two types of CPR, namely age, gender, initial rhythm, ambulance response time, and whether the bystander performing CPR was trained.

Was follow-up of patients sufficiently long and complete? Probably survival to hospital discharge would have been better but follow-up for one month isn’t bad since most people would have been discharged by then anyway.

Outcome assessed: B (survival of event [to one month and to hospital admission])

Magnitude of any observed effect (survival to one month, all types of arrest): standard CPR: 591/8209 (7.2% [95% CI: 6.7%-7.8%]). Chest compression only: 77/1145 (6.7% [95% CI: 5.4%-8.3%]). Absolute risk reduction=7.2-6.7%=0.5%. Number needed to treat=1/0.005=200.


LOE 5 (using endpoint of tidal volume), but within this category would be classified as:

Methodology: poor (late evaluation in selected patients who were transported to hospital with ongoing CPR)
LOE 4, an observational study to assess tidal volume generated by using an external chest compression device (Lucas, with de-activated active decompression component) late in the course of cardiac arrest in 14 intubated adult patients with out-of-hospital cardiac arrest.

Results: Median inspiratory tidal volume per compression was 41.5 cc (range 33-61.1 cc) whereas median anatomic deadspace was 162.7 cc. That is, in all study patients, passive tidal volume was less than the measured anatomic dead space (averaging 27% of anatomical dead space). This assessment was late in the course of arrest (average time from emergency call to hospital arrival was 39.4 minutes). Relevance of this study may be with respect to poor tidal volumes achieved with manual compression even with an ETT, in concordance to what Safar noted (see Safar P, Brown TC, Holtey WJ. Failure of closed chest cardiac massage to produce pulmonary ventilation. Chest 1962;41:1-8.) late in the course of cardiac arrest, and in distinction to the animal studies where resuscitation occurred earlier and was accompanied by spontaneous gasping.


LOE 5 (non cardiac arrest circumstance), within this category, LOE 4. Sixteen anesthetized paralyzed patients were ventilated with expired air prior to elective surgery. Following expired air resuscitation for time periods varying from 5-65 minutes by operators instructed to approximately double their usual tidal volume during inflations (via oronasal mask or via cuffed tracheal tube), arterial blood samples were evaluated.

Methodology: fair (volumes of inspired air and rates not controlled); no comparison (control groups) evaluated

Results: At moment expired air resuscitation started, alveolar oxygen concentrations had decreased to 10%; reoxygenation to the control oxygenation level occurred with 20 seconds and sustained thereafter; restoration of arterial oxygen saturation occurred within 30 seconds. CO2 in subjects’ alveolar air fell to control level within 15 seconds and continued thereafter. Arterial blood studies showed oxygen saturation >90% with no evidence of respiratory acidosis.


LOE 5 (not the right population because they didn’t look at trained laypeople or EMS) but within this category, LOE 1 (randomized control trial).

Methodological quality: Good.

Were comparison groups clearly defined? Yes, dispatchers randomly assigned bystanders to the two types of CPR.
Were outcomes measured objectively? Yes, the primary outcome was survival to hospital discharge. He also assessed neurological outcome which was assessed by physicians who didn’t even know about the study.

Were known confounders identified and properly controlled for? Yes, they adjusted for age, sex, race, location, witness status, response time, coexisting conditions, and the presence of symptoms before the arrest.

Was follow-up of patients sufficiently long and complete? Yes, assessed survival to discharge.

Outcomes assessed: B (survival of event [to hospital admission]); C (survival to hospital discharge); D (intact neurological survival).

Magnitude of any observed effect (survival to hospital discharge in cardiac etiology arrests): standard CPR: 29/278 (10.4% [95% CI: 7.4%-14.6%]). Chest compression only: 35/240 (14.6% [95% CI: 10.7%-19.6%]). Absolute risk reduction=14.6%-10.4%=4.2%. Number needed to treat=1/0.04=25.

Magnitude of any observed effect (No morbidity following arrest): standard CPR: 22/44 (50% [95% CI: 36%-64%]). Chest compression only: 21/47 (45% [95% CI: 31%-59%]). Absolute risk reduction: 50-45=5%. Number needed to treat=1/0.05=20.


LOE 5 (assessing CPR performance) within this category would be LOE 4 (observational): 24 paramedic firefighters certified to perform BLS CPR evaluated for ability to perform 2 recommended breaths within 4 seconds.

Methodology: Fair

Results: Mean length of time needed to provide two quick mouth to mouth breaths during standard CPR was 10±1 seconds. Mean number of CC/min delivered with standard CPR was 44±2. CCC resulted in 88±5 CC per minute (p<0.0001). Also observed initial delay to providing CC was longer with CPR than with CCC, due to time spent assessing and positioning the manikin and providing 2 initial rescue breaths prior to starting chest compressions. When performing CCC 15/22 paramedics (68%) delivered minimum goal of at least 80 compressions/minute; none did so in conventional CPR group (p<0.001). Asked if, off duty, they would perform CPR with mouth-to-mouth ventilation in a stranger who collapsed in a public place, 2/24 (8%) said they definitely would do so; 22/24 (92%) would definitely be willing to perform CCC without mouth-to-mouth. Trained professionals following AHA guidelines cannot deliver two breaths in less than 10 seconds. Prior studies have shown lay persons pause 16±1 second for 2 ventilations; medical students 14±1 second and now paramedics 10±1 sec.


LOE 4 Prospective observational evaluation of 1 month survival after cardiac arrest in Sweden (14 065 reports in whom resuscitation attempted in 10966 of which of which 1089 occurred after EMS arrival and 9877 [focus of report] of whom bystander CPR was attempted in 36%. Data assembled from Swedish ambulance cardiac arrest registry, based on reports from 60% of the ambulance systems in Sweden (hence not 100% comprehensive).

Methodology: Poor

Results: Of 9877 cases, 898 received “incomplete” bystander CPR (620 ventilation only; 278 compressions only). Survival at 1 month was 4.3% (ventilation only), 6.8% (compression only), 9.7% (complete bystander CPR). Outcome between incomplete (5.1%) vs complete (9.7%) statistically significant p<0.001. Statistical comparison not provided between CC only and complete CPR.

Limitations: Not completely comprehensive; not clear how information about conduct of CPR was obtained or verified; most of data from smaller communities; only 25% of case reports from large cities. Uncertain representation of entire population


LOE 5 (not the right population because they didn’t look at trained laypeople or EMS) but within that, LOE 3 (retrospective cohort study).

Methodological quality: Fair.

Were comparison groups clearly defined? Yes, one group received chest compression only CPR and the other received standard CPR. However, since chest compression only CPR was not taught in the area, it was unclear why it would have been done.
Were outcomes measured objectively? Not really. The primary outcome was neurologically favorable (CPC score 1 or 2) 1-year survival. They don’t say whether the person assessing CPC score was blinded to the type of CPR the patient received, so they probably were not. Some scores were assessed by letter, some by telephone interview.

Were known confounders identified and properly controlled for? They present adjusted odds ratios but don’t say what they’re adjusted for.

Was follow-up of patients sufficiently long and complete? Yes, patients were followed for 1 year.

Outcomes assessed: A (return of spontaneous circulation); B (survival of event [to hospital admission]); D (intact neurological survival); E (1-week, 1-month, 1-year survival).

Magnitude of any observed effect: Favorable neurological outcome for all types of witnessed arrests of cardiac origin: standard CPR: 28/783 (3.6% [95% CI: 2.5%-5.1%]). Chest compression only: 19/544 (3.5% [95% CI: 2.3%-5.4%]). Absolute risk reduction=3.6-3.5=0.1%. Number needed to treat=1/0.001=1000.

Favorable neurological outcome for all types of witnessed VF arrests of cardiac origin: standard CPR: 18/161 (11.2% [95% CI: 7.2%-17%]). Chest compression only: 14/122 (11.5% [95% CI: 7.0%-18%]). Absolute risk reduction=11.5-11.2=0.3%. Number needed to treat=1/0.003=333.


LOE 4 Study was conducted from retrospective collection of data from a control period (2001-2003) compared with a prospective “project” period (early 2004-May 2005) after institution of “new protocol”. “New protocol” consisted of multiple changes including 200 CC before rhythm analysis, a single shock instead of multiple or stacked shocks, elimination of post shock pulse and rhythm analyses, and continuous chest compressions immediately after shock with emphasis on rate and full chest recoil. Initial airway management delayed until second rescuer arrived and then conited only of placement of oral pharyngeal airway and administration of O2 by nonrebreather mask. If arrest was witnessed and down time < 12 min, rescue breaths and ventilations not performed until return of ROSC or until 3 cycles of CC followed by rhythm analysis (with or without shock) were performed. Protocol to be used only in adults with presumed cardiac arrest (unexpected collapse with absent or abnormal breathing); cases of traumatic or presumed respiratory origin were treated with standard CPR protocol. [Not clear how responders could distinguish these.] Protocol instituted in 2 rural Wisconsin counties.

Methodological quality: Poor

Were comparison groups clearly defined? This was a before/after study. They did not assess how well the cardiocerebral resuscitation protocol was carried out by EMS personnel, so we have no idea how different the comparison groups actually were.

Were outcomes measured objectively in both groups? The CPC score was determined from hospital records; blinding of whom was not specified.

Were known confounders identified and properly controlled for? No, and the patients from the two time periods differed significantly in several factors, including age, gender, and time to defibrillation. They don’t present other potential confounders like location of arrest and they made no attempt to control for anything, just present the percentages of neurologically intact survivors in each time period.

Outcomes assessed: Survival at hospital discharge; neurologically intact survival at hospital discharge.

Results: Compared 92 witnessed cardiac arrests with initially shockable rhythm in prior 3 years compared with 33 during treatment period. In prior period 18/92 (20%) survived and 14/92 (15%) survived neurologically intact. In treatment period 19/33 (57%) survived and 16/33 (48%) survived neurologically intact. Both differences p<0.001.


LOE 3 (retrospective cohort study)
Methodological quality: Poor
Were comparison groups clearly defined? This was a before/after study. They did not assess how well the cardiocerebral resuscitation protocol was carried out by EMS personnel, so we have no idea how different the comparison groups actually were.

Were outcomes measured objectively in both groups? The CPC score was determined from hospital records by an “often unblinded” physician.

Were known confounders identified and properly controlled for? No, and the patients from the two time periods differed significantly in several factors, including age, gender, and time to defibrillation. They don’t present other potential confounders like location of arrest and they made no attempt to control for anything, just present the percentages of neurologically intact survivors in each time period.

Outcomes assessed: B (survival of event [but they don’t specify how long they were followed to assess survival]); D (intact neurological survival).

Magnitude of any observed effect:

All witnessed arrests in shockable rhythm of cardiac etiology: Before cardiocerebral resuscitation protocol, survival was 18/92 (19.6%) [95% CI: 12.8%-29%]. After protocol change, survival was 42/89 (47.1%) [95% CI: 37%-57%]. Absolute risk reduction is 47.1-19.6%=27.5%. Number needed to treat=1/0.275=3.6.

All witnessed arrests in shockable rhythm of cardiac etiology: Before cardiocerebral resuscitation protocol, survival with CPC score of 1 was 14/92 (15.2%) [95% CI: 9.3%-24%]. After protocol change, survival with CPC score of 1 was 35/89 (39.3%) [95% CI: 30%-50%]. Absolute risk reduction is 39.3-15.2%=24.1%. Number needed to treat=1/0.241=4.1.


LOE 5 (evaluation of (presumably) untrained layperson CPR) but within this category, LOE 2 (studies using controls without randomization)

Methodological quality: Good

Were the comparisons clearly defined? Paramedics on the scene assessed whether patients received chest compression only, chest compression with ventilations, or no CPR from bystanders. The authors noted that the accuracy of this reporting may have been compromised by the urgency of the situation but the paramedics were required file run reports immediately and therefore were likely to have had fairly accurate recollection of the events.

Were outcomes measured objectively in both groups? Yes, both the primary outcome (survival to hospital discharge or to 30 days post-arrest) and CPC score were assessed in the same way in each group of patients.

Were known confounders identified and properly controlled for? Although significantly more patients who arrested at their residence received chest-compression only CPR, they did not perform logistic regression analysis controlling for this. They did stratify analyses on several variables that were not significantly different between the two groups of patients, including whether the etiology of the arrest was cardiac, the initial rhythm, and the response time.

Was follow-up of patients sufficiently long and complete? Yes, patients were followed to hospital discharge or to 30 days after their arrests.

Outcomes assessed: A (ROSC), B (survival to hospital admission), C (survival to hospital discharge or 30 days post-arrest); D (intact neurological survival).

Magnitude of any observed effect:

All arrests: Chest-compression only: survival to hospital discharge was 4/154 (2.6%) [95% CI: 1.0%-6.5%]. Chest compression with ventilation was 8/287 (2.8%) [95% CI: 1.4%-5.4%]. Absolute risk reduction is 2.8-2.6%=0.2%. Number needed to treat=1/0.002=500.

CPC score of 1: Chest-compression only: 2/154 (1.3%) [95% CI 0.4-1.6%]. Chest compression with ventilation was 6/287 (2.1%) [95% CI: 1.0%-4.5%]. Absolute risk reduction is 2.1-1.3%=0.8%. Number needed to treat=1/0.008=125.


Three studies within 1 publication:

Overall LOE 5 study (using endpoints of tidal volume and oxygen saturation during chest-compression only CPR), but within this category (LOE 5) could be characterized as:
Metholodgy: Fair

LOE 2 (observational/pseudorandomized human with each subject serving as his own control) study in which tidal volumes were measured in 30 anesthetized and paralyzed normal volunteer adults during closed chest sternal compression (1) in the absence of an artificial airway in an unsupported head (which assumed a position of slight anteflexion which is known in the unconscious patient to produce obstruction of the hypopharnyx as the base of the tongue is pushed against the posterior pharyngeal wall) (2) with subjects' shoulders elevated so that unsupported head held tilted backward and mandible held forward. All subjects underwent each procedure (excepting tracheal or oropharyngeal airway which were done in 17 and 13 subjects, respectively). Wright ventilation meter used to minor inspired tidal volumes.

Results: (1) With natural airway and head unsupported all tidal volumes were 0; (2) with backward tilted position due to elevation of shoulders average inspired tidal volume was 53 cc (3) with airway tidal volume averaged 156 cc

LOE 4 (observational human) study of 12 “non-salvageable” patients undergoing chest compression with cuffed tracheal tube

Results: Closed chest massage produced no ventilation (tidal volume 0 in 10/12; 10 in 1 patient; 40 cc in another). In each subject deep intermittent positive pressure inflations were possible through the tracheal tube, however. Authors interpreted results to mean chest may not have sufficient elastic recoil to provide ventilation when pulmonary compliance decreased, or resulting atelectasis.

LOE 4 (observational human) study in which 6 normal adults were anesthesized and paralyzed, intubated. After several minutes of controlled room air ventilation, ventilation stopped and O2 sat allowed to drop to 85%. Sternal chest compression begun for 3 minutes.

Results: Operator unable to move more than 100 cc of tidal volume even with maximal chest compression force. Unable to restore oxygen saturation to 95% in 5/6 hypoxic subjects. In 3/6 further deoxygenation occurred in spite of sternal compression. That is, the tidal volume observed in the first experiment was insufficient to reoxygenate. In all subjects intermittent positive pressure ventilation with air caused a rise in oxygen saturation within 2-4 inflations and restored control saturations in 30-80 seconds.

Limitations: Subjects paralyzed, obviating possibility of gasping. In the initial study, arguably each subject served as his own control but there was no true randomization.


LOE 5 (different study population); within that, LOE 3 (retrospective cohort study)

Methodological quality: Fair

Were comparison groups clearly defined? Yes, one group received chest compression only CPR and the other received standard CPR. However, since chest compression only CPR was not taught in the area, it was unclear why it would have been done.

Were outcomes measured objectively? The primary outcome was favorable (CPC score 1 or 2) neurological outcome 30 days after the arrest. This was assessed by physicians who were blinded to the type of resuscitation the patient received. The authors do not elaborate on how CPC score was assessed (e.g. did physician interview patients personally, speak to them on the phone, look at their charts?). Additionally, the authors report that neurologically intact survival differed between the two groups, but overall survival did not.

Were known confounders identified and properly controlled for? Yes, they adjusted for age, time between first CPR and AED analysis, and initial cardiac rhythm (mention that they also included gender and gasping, but these did not change the estimates). Did not adjust for location of arrest even though it was different in the two groups.

Was follow-up of patients sufficiently long and complete? Patients were assessed after thirty days. Probably this was long enough.

Other comments on the study methodology: This study included only hospitals participating in SOS-KANTO and thus was not a population-based study.

They don’t report overall survival except in a bar graph in Figure 4. In this, it appears that conventional CPR (top part of the bar) led to higher percentage of survivors than cardiac only resuscitation.

Outcomes assessed: D (intact neurological survival).
Magnitude of any observed effect: All types of arrest, witnessed only: Receipt of chest compressions only, neurologically favorable survival to hospital discharge was 27/439 (6.2%) [95% CI: 4.3%-8.8%]. Receipt of standard CPR, 30/712 (4.2%) [95% CI: 3.0%-6.0%]. Absolute risk reduction is 6.2%-4.2%=2.0%. Number needed to treat=1/0.02=50.

VF witnessed events: Receipt of chest compressions only, neurologically favorable survival to hospital discharge was 24/124 (19%) [95% CI: 13-27%]. Receipt of standard CPR, 23/205 (11%) [95% CI: 7.6-16%]. Absolute risk reduction is 19-11=8%. Number needed to treat=1/0.08=12.5.


LOE 5 (not the right population because they didn’t look at trained laypeople or EMS) but within that, LOE 3 (retrospective cohort study).

Methodological quality: Poor.

Were comparison groups clearly defined? Yes, the EMS team assessed the type of CPR that was being provided when they arrived on the scene.

Were outcomes measured objectively? Yes, the primary outcome was survival to 14 days following arrest.

Were known confounders identified and properly controlled for? No, they did not adjust for any confounders.

Was follow-up of patients sufficiently long and complete? No, they only followed the patients for 14 days after arrest. If they were still unconscious after 14 days, they were not considered a long-term survivor.

Outcomes assessed: A (restoration of spontaneous circulation); B (survival of event [to 14 days]); E (survival to hospital admission but died within 14 days or remained unconscious).

Magnitude of any observed effect (survival to 14 days following event of cardiac etiology): standard “good quality” CPR: 71/443 (16% [95% CI: 13%-19%]). Chest compression only: 26/263 (10% [95% CI: 7%-14%]). Absolute risk reduction=16%-10%=6%. Number needed to treat=1/0.06=17.

Magnitude of any observed effect (survival to 14 days following event of cardiac etiology of patients VF): standard “good quality” CPR: 58/188 (31% [95% CI: 25%-38%]). Chest compression only: 23/113 (20% [95% CI: 14%-29%]). Absolute risk reduction=31%-20%=11%. Number needed to treat=1/0.11=9.1.


LOE 5 (not the right population because they didn’t look at trained laypeople or EMS) but within that, LOE 3 (retrospective cohort study).

Methodological quality: Fair.

Were comparison groups clearly defined? It was unclear why anyone would have performed chest compression only CPR (only 8% of bystander CPR was performed this way). Whether chest compressions only or standard CPR were performed was assessed by a med student who interviewed the witnesses immediately after the incident.

Were outcomes measured objectively? Yes, the two outcomes were survival to hospital admission and survival to hospital discharge.

Were known confounders identified and properly controlled for? They did adjust for some confounders, but not all (e.g. did not adjust for age, gender, location of arrest, initial rhythm).

Was follow-up of patients sufficiently long and complete? Yes, assessed survival to discharge.

Outcomes assessed: B (survival of event [to hospital admission]); C (survival to hospital discharge).

Magnitude of any observed effect (survival to hospital discharge in witnessed arrests):
Standard CPR: 61/437 (14.0% [95% CI: 11.0%-17.5%]). Chest compression only: 6/41 (14.6% [95% CI: 6.9%-28.4%]). Absolute risk reduction=14.6%-14.0%=0.6%. Number needed to treat=1/0.006=167.

LOE 5 (expired gas study) within which qualifies as LOE 4 (observational study) involving 33 volunteers who performed simulated 1 or 2 rescuer CPR, but exhaled into gas collection bag for measurement of O2 and CO2 content during mouth-to-mouth ventilation.

Methodology: Good

Results: Oxygen concentration in exhaled gas significantly lower than room air gas (16.4-17.8% vs 20.9%); CO2 concentration significantly higher than room air (3.5-4% vs 0.03%). Possible extrapolation to detrimental effect of higher CO2 concentration from expired air from a prior animal study by one of the authors (Idris AH, Wenzel V, Becker LB, Banner MJ, Orban DJ, Does hypoxia or hypercarbia independently affect resuscitation from cardiac arrest? Chest 1995;108:522-8). The article however also references an older study of 29 normal volunteers (with normal circulatory status) who were paralyzed and received mouth-to-mouth ventilation with resulting mean O2 saturation of 94% and PCO2 of ≤ 50 mm Hg, and were not harmed by receipt of expired air.

**ANIMAL STUDIES**


LOE 5 (animal). Within this category, LOE 1. 30 instrumented, intubated swine (not paralyzed in order to allow spontaneous ventilation) ventilated on 100% O2 → VF induced electrically without support x 30 seconds (downtime for witnessed arrest) → 12 minutes ‘BLS’ with animals randomized to CC+mechanical ventilation (80-100 compressions/min (?asynchronous mechanical ventilation to maintain ETCO2 between 30-40 mm Hg), vs CC only (ETT removed) vs no CPR → ALS (with reintubation of CC only group) and resumption of ventilations in all groups. Essentially a comparison of “normalized” ventilation vs no ventilation (vs No CPR control) in witnessed VF with short “down time”.

Results: All swine in CC+MV and CC groups had ROSC and survived 24 hours. Only 2/8 animals in no CPR group survived to 24 hrs (p<0.001 vs other two groups) one of whom was comatose and unresponsive. All animals in CC+MV and CC groups had normal neurological examination at 24 hours. Blood pressures during CPR in CC+MV and CC groups were comparable, though aortic diastolic pressure and CPP at 6 minutes higher in CC group (27 vs 23 mm Hg, p<0.05, not likely to be clinically significant.) Trend toward increased need for epinephrine in CC vs CC+MV group (p=0.098). During CPR, arterial PO2 and O2 saturation were higher in CC+MV group than CC; pH higher and PCO2 lower in CC+MV than CC only group. In this swine model of witnessed cardiac arrest, survival & neurological outcomes the same with CC+MV vs CC. Of note, this compared mechanical ventilation (presumably asynchronous) with CC alone. No presumed difference in CC rate, and apparently no ill effects on outcome from positive pressure ventilation.

Methodology: Fair. Research technician providing CC was blinded to ETCO2 and vascular pressure measurements during CPR but not to treatment groups; assessment of neurological outcome not blinded to treatment groups. Both groups preoxygenated at baseline (100%) – not mimicking true clinical arrest (BLS) circumstance; animals allowed to breathe spontaneously without measuring minute ventilation (agonal respiration is more unpredictable in humans and does not provide a reliable source of ventilation since upper airway obstruction is common).


LOE 5 (animal). Within this category LOE 1 (prospective randomized). Instrumented, intubated swine ventilated on RA/anesthetic–→VF induced without support x 5 min → (1) standard CC+V @ 15:2 (n=10)(2) CC only (extubated) @ 100 cpm (n=10) (3) no CPR x 8 minutes (n=6) → ALS (shock, epi, reintubation of CC animals, ventilation at 100% on ventilator at 15 breaths/min)

Methodology: Fair (CPR provider not blinded, neurological status assessment not blinded to treatment

Results: ROSC in 9/20 CC+V, 10/10 CC, 4/6 no CPR. 24 hr survival 6/10 CC+V, 5/10 CC, 0/6 no CPR (CC+V vs control 0.03; CC vs control p =0.058). All 24 hour survivors were neurologically normal. During CPR, arterial PO2 and SaO2 higher in CC+V vs CC; but two groups did not differ in mixed venous PO2 or SO2.; arterial pH higher and PCO2 lower in CC+V than CC group. Mixed venous pH of two groups not different. No differences in LV myocardial blood flow, CO, or oxygen delivery between two treatment groups during CPR. 15/26 animals had active gasping or agonal respirations during CPR (making CC group a partly ventilated group (8/10 CC+V; 7/10 CC; none of control animals gasped during CPR). Hence this is more of a study of gasping, vs gasping + ventilation. Questionable applicability to humans in whom airway obstruction makes gasping less predictable.

LOE 5 study (animal, and addressing young pigs, hence possibly a pediatric population – however the importance of inclusion is that the study addresses respiratory arrest and role of CC vs CC+RB in this setting). Within the LOE 5, this study could be categorized as:

LOE 1:  Intubated piglets ventilated on RA + anesthetic before interventions. Asphyxial cardiac arrest produced by clamping ETT of piglets (x 8.9 ± 0.4 min) to aortic pulse pressure < 2 mm Hg → 8 min simulated bystander CPR with CC+RB (15:2) (n=14); CC only (@ 100/min) (ETT removed) (n=14); RB only (20/min using BV endotracheal tube with FiO2 0.17; FiCO2 0.04) (n=7); No CPR (control) (n=7) → ALS (intubation of CC only group. ETT remained clamped in No CPR group

Methodology:  Fair.  Prospective, randomized; research technician blinded to end tidal CO2 and vascular pressure measurements during CPR; however neurological assessment not blinded as to treatment.

Results:  Arterial SO2 markedly lower at 1 and 7 minutes of CPR in CC vs CC+RV only group (26% vs 80%; 17% vs 87%); PCO2 higher (81 vs 56; 97 vs 45) and pH lower (7.07 vs 7.24; 7.21 vs 7.01).  CC+RB had better 24 hr and neurologically normal survival compared with each of the other groups (ROSC 90% vs 71% vs 42% vs 62% for CC+RB, CC, RB, Control); (24 hr survival: 80% vs 21% vs 14% vs 25%); 24 hr neurologically intact survival (70% vs 7% vs 14% vs 0).  Outcomes in all groups p<0.05 or better compared with CC+RB.  During bystander CPR period CPP and aortic relaxation (diastolic) pressures generally higher in CC+ RB than CC; oxygen saturation and pH markedly better also.  These higher pressures possibly due to better maintenance of vascular tone with better oxygenation and pH.  When asphyxial arrest is more prolonged (prior study) CC+RB is preferred resuscitation technique.


LOE5 study (animal) but could be categorized as:

Methodology:  Fair.  Prospective, randomized; research technician blinded to end tidal CO2 and vascular pressure measurements during CPR; however neurological assessment not blinded as to treatment.

LOE 1:  Similar design as Berg RA, Hilwig RW, Kern KB, Babar I, Ewy, GA.  Simulated mouth to mouth ventilation and chest compressions (bystander cardiopulmonary resuscitation) improves outcome in a swine model of prehospital pediatric asphyxial cardiac arrest.  Crit Care Med 1999 but with BV endotracheal tube ventilation at 12-15/min and shorter clamping of ETT (x 6.8 ± 0.3 min) to Ao systolic pressure < 50 mm Hg.

Results:  39/40 animals had PEA with bradycardia or NSR at time of puleslessness; 1 VT none with VF.  Rhythm deteriorated to VF at some point in 17/40 piglets during the experiment.  Hemodynamics during first 30 seconds of CPR tended to be nonsignificantly higher (CPP, Ao diastolic and Ao systolic) in CC+RB group; both CC+RB and CC groups had better hemodynamics than RB only and control (no CPR) groups.  24 hr neurologically normal survival CC+RB 80% vs 40% CC vs 60% V only vs 0% No CPR.  Earlier in the asphyxial process, CC and V are each independently more effective than no bystander CPR in terms of survival at 24 hours (80% CC+RB, 50% CC, 60% V, 0% no CPR; all p<0.05 or better compared with no CPR).  Early in the asphyxial pulseless arrest process, doing something (RB or CC) is better than nothing at all.  When asphyxial arrest is more prolonged (prior study) CC+RB is preferred resuscitation technique.


LOE 5 (animal study reporting survival and neurological outcome).  Within this category could be considered as:

Methodology:  Fair (rescuer providing CC not blinded to treatment; however CPP at end of 15 compression cycle with CC+RB did not differ from CCP with CC only suggesting comparable chest compression vigor.)

LOE 1:  14 instrumented, intubated pigs ventilated with RA and isoflurane→ VF induced with 3 minutes of no treatment (mimicking bystander recognizing arrest and calling for help) → 12 minutes of BLS randomized to CC only (manual) @ 100 ccm vs CC+ rescue breathing 15:2 @ 100 ccm and 2 breaths (presumably over 4 seconds) (17% oxygen 4% CO2).  Animals in both groups gasped during CPR → ALS with shock, volume-cycled ventilator 15 breaths/minute @100%, epinephrine.

Results:  Aortic diastolic pressures (relaxation pressures) decreased during interval of 2 rescue breaths and thus mean value was significantly lower during first 2 compressions in each compression cycle than of the final 2 compressions (14 vs 21 mm Hg).  Presumably longer pause between compressions resulted in greater “runoff” of blood from aorta thereby decreasing aortic volume and pressure.  CPP comparable in both groups early into CPR 2-5 minutes) of 29 (CC) vs 26 (CC+RB) and late CPR (9-12 minutes) 18 vs 21.
13/14 animals survived 24 hrs, 6/7 CC animals and 5/7 CC+RB animals had normal cerebral performance at 24 hrs; 1/7 CC and 1/7 CC+RB in cerebral performance category 1; 1 CC+RB animal in category 3. ABGs: PO2 lower, pH lower and PCO2 higher at 2 and 12 minutes in CC only group than CC+RB group. Left ventricular blood flow during interval between 2 and 5 minutes of CPR was 96 ml/g/min (CC) vs 60 CC+RB (p<0.05) and at 9 –12 minutes (79 vs 52, p=0.11) with no differences in LV myocardial oxygen delivery at those times (590 (CC) vs 560 (CC+RB) early; 590 vs 490 late CPR). That is, CC resulted in better myocardial perfusion but worse oxygen content; net result was no substantial difference in myocardial oxygen delivery. Comparable successful resuscitation and neurological outcome after either resuscitation approach.

Limitations: Relevance: Intubated model does not mimic preALS treatment scenerio; comparison with 15:2 CPR protocol not current 30:2 protocol. Scientific: Not blinded as to treatment assignment.


LOE 5 (animal). Within this category, the study qualifies as LOE 4 (uncontrolled study) with primary endpoint being ABG parameters. 7 dogs intubated and ventilated with room air. VF induced with removal of ETT. Chest compressions performed with serial measurement of tidal volume and ABG.

Methodology: Poor – non randomized, not blinded, observational only without a control group.

Results: At 4 minutes after onset of VF, O2 sat 94% but fell to 87% at 6 minutes. At 4 minutes pH 7.39 but by 6 minutes fallen to 7.36. Arterial PCO2 did not rise above 35 mm Hg until 8 minutes, well after O2 saturation had fallen below 75%. Vascular pressure also did not begin to decline until 8 minutes of CC only (Ao sys 52 → 36; Diastolic Ao pressure 24→21). Tidal volume breath in 70 ml/breath range throughout resuscitation.


LOE 5 (animal study) but within this category, LOE 1 (prospective, randomized study) 13 instrumented intubated swine ventilated with anesthetic and room air—3 minutes untreated VF—randomized to ABC CPR (30:2 with bag mask ventilation using 17% O2 4% CO2 with each inhalation over 1-1.5 seconds) and ABC chest compression device and ITD to prevent passive inspiratory airflow (n=6) vs CCC @ 100 cpm (presumably not extubated) x 10 minutes (ITD used to prevent passive inspiratory airflow in both groups) (n=6) → ALS (defibrillation, epi, ventilation with 100% oxygen). One pig excluded due to inadequate pressure and flow recordings. Primary outcome was calculated carotid and cerebrocortical oxygen delivery during BLS and time to ROSC in ALS period.

Methodology: Fair (small study; exclusion of 1 animal; not blinded to treatment assignment)

Results: No differences in any pressures (Ao, RA, LV, CPP) observed between groups during CPR. After 1 minute BLS, arterial PO@, oxygen saturation and pH significantly higher and arterioal pCO2 significantly lower in ventilated group. For the nonventilated group, there was no arteriovenous difference in PO2 after 3 minutes of CPR. BLS with 30:2 RATIO @ 100 cpm and pausing for 4.8± 0.2 s for two ventilations resulted in average minute ventilation of 3.8±0.3 L/min. During BLS arterial oxygen content and cerebral oxygen delivery significantly higher in ventilated than CC only group. Outcome: significantly more pigs ventilated during BLS achieved ROSC within first 2 minutes of ALS (6/6 vs 1/6). Total ROSC 6/6 vs 5/6 for CC+V vs CC only. Time to ROSC 1.5 vs 6.7 minutes, respectively. More shocks required in CC only group (7 vs 2). If CC were administered alone, arterial blood virtually desaturated within 1.5-2 min; this decline significantly attenuated by the interposition of 2 second pauses for ventilation vs CCC @ 100 cpm (presumably not extubated) x 12 minutes after arrest (i.e. 9, 8, 7 and 6 minutes of BLS in each respective VF group) → ALS (single shock followed by ALS with no pause for AED analysis; ventilation with 100% oxygen; 10 second pause after each 2 minutes of CPR, epinephrine).

Methodology: Fair (CPR provider not blinded; neurological assessment not blinded)

Results: 33 swine in CCC groups and 31 in 30:2 groups. With longer duration of untreated VF before BLS, fewer animals survived with good neurological outcome. Overall normal 24 hour neurological score in 23/33 CCC vs 13/31 30:2 CPR (p=0.025). Both groups comparable in 3
minute VF group (7/8 and 7/8 with normal 24 hr neurological outcome. In the combined 4, 5, 6 minute VF group 16/17 survivors (16/25 of total group) CCC vs 6/11 survivors (6/23 of total group) 30:2 groups survived with normal neurological function (p=0.022). In combined 5, 6 minute VF groups, 10/10 survivors (10/16 of total group) CCC survived with normal neurological function vs 4/9 survivors (4/16 of total group) of 30:2 (p=0.011). Odds ratios for ROSC and 24 hour survival not different in the combined 3, 4, 5, 6 second VF groups between CCC and 30:2.

Perfusing rhythm followed first defib shock in 21/33 (64%) animals in CCC group vs 9/31 (29%) in 30:2 group (p=0.028). Mean integrated CCP during BLS was 20 in CCC vs 14 in 30:2 CPR (p=0.028). Mean number of compressions delivered during BLS period was 746 in CCC groups vs 385 in 30:2 groups (p=0.001). Mean arterial blood saturation after 12 minutes of BLS was 79% for CCC vs 88% for 30:2 group (p=0.28). No significant differences existed in arterial PO2 or arterial PCO2 at 12 minutes of BLS.

Critique: Problem with this model was protracted time for ventilations with “hands off” and providing an open airway for ventilation in CCC only group, making the real difference between the two groups the “hands off” time.


LOE 5 (animal). Within this category, LOE 1 (prospective randomized). 24 instrumented, intubated swine, paralyzed (to prevent spontaneous ventilation) and oxygenated with 0.21 FiO2 10 minutes before VF induced → VF x 6 minutes (untreated) → CC + MV group reconnected to ventilator with prior minute ventilation and FiO2 0.85 (n=12) vs CC only (n=12). (CC performed @ 100 cpm with 60% duty cycle and unsynchronized with ventilation via mechanical device) x 10 minutes → ALS (shock, epi, ventilation with FiO2 85%. Primary endpoint ROSC (Aortic SBP >80 mm Hg for 5 consecutive minutes).

Methodology: Good

Results: After 9 minutes VF, significant differences observed in ABG and mixed venous gases. Unventilated group with greater arterial academia (7.14 vs 7.29), hypoxia (38 vs 216) and hypercarbia (62 vs 35); mixed venous academia (7.07 vs 7.15), hypoxia (15 vs 32) and hepercarbia (74 vs 60). Nonventilated group had substantial ventilation produced by CC alone (3.8 L/min) vs ventilated group (mechanical ventilation 4.8 L/min + CC ventilation 2.3 L/min) or a total of 3.8 vs 7.1 L/min. CPP similar in nonventilated and ventilated groups (16 vs 19), but response to epinephrine resulted in significant increase in CPP in ventilated group, but no nonventilated group. 9/12 (75%) of ventilated animals vs 1/12 (8%) of nonventilated animals had ROSC (p<0.002). CC+MV after 6 minutes of unsupported VF resulted in significantly higher rate of ROSC than CC alone. Decreased return of ROSC in nonventilated group could be due to less CPP caused by peripheral vasodilation associated with increased levels of hypercarbic acidosis and reduced responsiveness to epinephrine.


LOE 5 (animal study) but could be categorized as LOE 1. Randomized assignment of 24 swine receiving ventilation during CPR with 85% O2/15% N (control) vs 95% O2/5% CO2 (hypercarbia) or 10% O2/90% N (hypoxia). All animals had VF x 6 minutes without CPR, then CPR with one of the ventilation gases x 10 min then defibrillation.

Methodology: Good

Results: Model produced isolated hypercarbia without hypoxia in the hypercarbic group and isolated hypoxia without hyercarbia in the hypoxic group. ROSC was 6/8 (75%) in controls, 1/8 (13%) hypercarbic group, 1/8 (13%) for hypoxic group (p<0.02). ABG at 10th minute CPR was 7.3/228/34/17 in control; 7.21/295/47/19 in hypercarbic group, 7.4/43/30/18 in hypoxic roup. Mixed venous gases were 7.14/35/59/20; 7.11/30/72/23, 7.22/22/57/23 respectively (pH, PO2, PCO2, HCO3-)


LOE 5 (animal study using evaluation of aspiration during supine chest compressions). Within this category could be considered as:

Methodology: Poor (unclear that investigators were blinded to treatment assignment)

LOE 2 (concurrent animal controls): 10 dogs anesthesized and paralyzed, 8 of which underwent chest compression only CPR in various head down positions with mouth filled with mixed barium; 2 in the supine position (controls for effect of prolonged external chest compression on aspiration). Aspiration assessed radiographically.

Results: All dogs in the supine position showed barium in both lungs; not observed in dogs placed in the 20 degrees head down position.

LOE 5 (animal study using measure of long injury during chest compression only CPR). Within this category could be considered as:

Methodology: Poor (unclear that investigators were blinded to treatment assignment)

LOE 2 (concurrent animal controls) in which 32 rats with cardiac arrest induced by ketamine-provoked central apnea (resulting in VF with minimal gasping): (A) chest compression without airway management (B) chest compressions with tracheal tube (C) chest compressions with tracheal tube and 100% flow of oxygen (D) chest compressions with tracheal tube and controlled mechanical ventilation and 100% oxygen.

Results: Wet/dry ratio of explanted lungs significantly higher in group A than other groups. Pathological findings also observed more edema, migration of neutrophils and destruction of lung structure in A than the other groups (which had little difference between them). Not clear that pathology or wet/dry ratio determined with investigators blinded to treatment assignment.


LOE 5 (animal). Within this category LOE 1 (prospective randomized). 20 domestic intubated, instrumented swine ventilated with anaesthetic and RA → VF induced without support x 30 seconds → BLS x 6 minutes randomized to CC+ bag-valve endotracheal tube ventilation (15:2; with 17% oxygen and 4% CO2) (n=10) vs CC only with clamped endotracheal tube (n=10) → ALS with shock x 3, unclamping of ETT in CC only group and ventilation with 100% O2, epinephrine. Primary endpoint 24 hour survival

Methodology: Fair (not clear that CPR provider was blinded)

Results: CC only CPR lead to significantly higher pressures than did standard CPR with patent airway, although these differences (including CPP) were gone by 6 minutes (perhaps due to hypoxia 29 vs 82, hypercarbia 82 vs 33 and academia 7.2 vs 7.44 between CC and CC+V groups). Survival 10/10 with CC+V, 9/10 with CC only (p=0.99)


LOE 5 (animal) but within this category, LOE 1 (prospective, randomized study) 30 instrumented intubated swine ventilated with anaesthetic and room air → 3 minutes untreated VF → randomized to ABC CPR (15:2 with bag mask ventilation using 17% O2 4% CO2) with 16 second pauses for ventilation (n=15) vs CCC @ 100 cpm (presumably not extubated) x 12 minutes (n=15) → ALS (defibrillation, epi, ventilation with 100% oxygen).

Methodology: Fair (CPR provider not blinded; neurological assessment not blinded)

Results: Primary endpoint “normal” neurological 24 hour survival 12/15 CCC vs 2/15 ABC CPR (p<0.0001). All other outcomes (ROSC, 30 min survival, 2 hr survival, 24 hr survival, 24 hr with “good” neuro outcome also significantly favored CCC group. Integrated CPP significantly greater with CC group throughout the entire CPR period even though when measured during CPR (not pauses) CCP was comparable between the groups. ABC CPR group had 496 total compressions during 12 minute BLS period vs 111 for CCC group (p<0.0001). Better oxygenation and ventilation with ABC CPR but CCC group also achieved substantial oxygenation and ventilation (probably through spontaneous gasping) (11 vs 6-7.8 L/min in ABC vs CCC groups). pH comparable during CPR 7.55 vs 7.46; PO2 83-87 vs 58-64; PCO2 26 vs 36; MV CO2 and O2 comparable as was MV pH (7.3). Better outcome likely secondary to better hemodynamics from uninterrupted chest compressions.


LOE 5 (animal study) but could be categorized as LOE 2 (concurrent controls). 5 dogs injected with pressor agents under various pH conditions in presence of respiratory acidosis. Then

Methodology: Fair (small study) but unclear if range of pH values tested is relevant to human resuscitation

Results: Pressor responses to metaraminol, epi, norepi all reduced (18% of normal when pH was 6.76; to 36% of normal when increased to 7.27). Same response seen with metabolic acidosis produced by HCl infusion. Animals then placed on cardiopulmonary bypass to isolate heart from
peripheral vascular bed response. Pressor response to epinephrine and norepinephrine uniformly much less if pH depressed (6.67, pressor response was 18% higher than control value; when pH 7.41 it was 40% higher than control value).

**BENCH RESEARCH**


LOE 5 (bench research in isolated perfused rat heart) LOE 2 (concurrent controls): 12 hearts perfused with solution equilibrated with 70% oxygen, 5% CO2 and 25% N2 followed by progressive increase in PCO2; then keeping PCO2 constant and lowering pH from 7.42 to 7.07 to 7.06.

Methodology: Good

Results: When PCO2 of perfusate was progressively increased from 36 to 64, to 64 to 99 to 146 mm Hg, pH declined from 7.4 to 7.12 to 7.06 to 6.78, LV systolic pressure generated by isolated heart and maximum rate of pressure change in LV (dP/dt) decreased to 20% of control values. However comparable acidosis in the absence of hypercarbia produced only minimal decreases in these values. Decreases in oxygen consumption (VO2) were related to concurrent increases in perfusate PCO2 and independent of changes in perfusate H+

**SUPPLEMENTAL ARTICLES** (not formally included in evidence evaluation, but whose information was utilized in the discussion)


