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

Worksheet author(s)

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Date Submitted for review: 11 Oct 2008; 03 Aug 2009; 01 Oct 2009

Clinical question.

"In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of passive oxygen delivery during CPR (I) compared with oxygen delivery by positive pressure ventilation (C), improve outcome (eg. ROSC, survival) (O)"

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

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

Conflict of interest specific to this question

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?

None

Search strategy (including electronic databases searched).

Searches were limited to: articles in peer reviewed journals between the years 1966 and 2009, English language, with abstracts.
- ECC Master library Jul 6, 2008
- Cochrane Library (2009) in all Cochrane Databases
- Embase (1988-2009)
- OvidSP “find similar” and “find citing” tools on search engine
- Scopus, Google Scholar
- References from key articles

Related articles and forward to the same author publications search tools from PubMed

Query: "passive oxygen administration" [MeSH Terms] OR "passive oxygen" [All Fields] OR “oxygen delivery” [All Fields] AND "resuscitation" [All Field]
Query: “positive pressure” [All Fields] AND “ventilation” [All Fields] AND "cardiac arrest" [All Fields]

Each query’s items were also checked sequentially

- State inclusion and exclusion criteria

Inclusion: adult and pediatric populations, human and animal studies, metanalyses, use of devices and / or airways adjuncts.

Exclusion: not English language, reviews articles, guidelines and/or scientific societies position statements, editorials and letters, manikin models, newborns setting.

articles excluded: 501 not matching the specific query.

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

Searches narrowed after title / abstract review to 13 articles.
### Summary of evidence

#### Evidence Supporting Clinical Question

"In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of passive oxygen delivery during CPR (I) compared with oxygen delivery by positive pressure ventilation (C), improve outcome (eg. ROSC, survival) (O)?"

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| **Poor**          | Kellum 2006<sup>C,D</sup>  
                   | Kellum 2008<sup>C,D</sup>  
                   | A = Return of spontaneous circulation  
                   | C = Survival to hospital discharge  
                   | E = Other endpoint  
                   | B = Survival of event  
                   | D = Intact neurological survival  
                   | Italics = Animal studies  

Color code: **Adult** Pediatric **IHCA** **OHCA** **Extrapolated** (Manikin, Review, Animal…)
### Evidence Neutral to Clinical question

*In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of passive oxygen delivery during CPR (I) compared with oxygen delivery by positive pressure ventilation (C), improve outcome (eg. ROSC, survival) (O)*

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<td>Saissy 2000&lt;sup&gt;A,E&lt;/sup&gt;</td>
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**Level of evidence**

- **A** = Return of spontaneous circulation
- **B** = Survival of event
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- **D** = Intact neurological survival
- **E** = Other endpoint

**Color code:** Adult Pediatric IHCA OHCA Extrapolated (Manikin, Review, Animal…)

### Evidence Opposing Clinical Question

*In adult and pediatric patients in cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of passive oxygen delivery during CPR (I) compared with oxygen delivery by positive pressure ventilation (C), improve outcome (eg. ROSC, survival) (O)*

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Acknowledgements

Kellum 2006

associated with an significant improvement in neurologically intact survival in adult patients with witnessed CA and an initial ly shockable rhythm,

Two non randomized observational trials confirmed that a new OH protocol based on the principles of cardiocerebral resuscitation (MICR) was

group,

and less complications when compared with standards MV and ETI, as showed by

associated to CCC (with or without ACD device) determined no differences on ROSC, hospital admission and ICU discharge, but better oxygenation

On a clinical RCT, not blinded, of 696 OHCA patients in VF, ASY or PEA, the use of a Bousignac tube for continuous oxygen delivery at 15 L/min

could impact the weigh of this results.

compared with a standard MV or hyperventilation strategy during CPR, but the survival rate that belong to small number (about 2-4/12 pigs per group)

According to

survival on a 22 swine model, where precordial compression and spontaneous gasping yielded minutes volumes that exceeded 5 L.

Earlier,

Okomoto 1993

were equivalent, but hemodynamic were better if compared with positive pressure ventilation.

Okomoto 1990

on 12 cardiac arrest patients observed on a IHCA setting, where

hyperventilation affect significantly the hemodynamic parameters and survival rates on a 9 swine model, mainly by decreasing coronary perfusion pressure, with an inversely proportional relationship between mean intratracheal pressure and coronary perfusion pressure during CPR, despite supplemental of CO2 to prevent hypocapnia.

Aufderheide 2004

showed that even well trained professional rescuers consistently hyperventilate 13 consecutive patients in cardiac arrest, during out-of-hospital CPR (none survived) as confirmed by O'Neill 2007 on 12 cardiac arrest patients observed on a IHCA setting, where

hyperventilation is mostly related to high respiratory rates rather then high tidal volumes. The detrimental effect of hyperventilation on hemodynamic parameters and outcome has been demonstrate in two animal models by Aufderheide 2004 and Hayes 2007.

On a 21 large mongrel dogs model, Kern 1992 showed 73% successful resuscitation in 8/11 dogs ventilated during 20 min of standard CPR with continuous O2 flow via a pharyngeal-tracheal lumened airway, rate similar to the result of historical control with ETI. During the CA period, pO2 and pCO2 were not statistically different from prearrest values. Moreover, excellent ventilation was possible in 10 apneic dogs in NSR from the “bellow effect” of chest compressions, readily correcting hypercapnia and respiratory academia resulting from 5 min of complete apnea.

Earlier,

Okomoto 1998, demonstrated on a canine model that during CPR transtracheal O2 insufflation, at flow 0.5 and 1.0 L/Kg/min, was adequate to maintain oxygenation, but not ventilation according to the level of post-CPR hypercapnia get in successfully resuscitated animals.

Brochard 1996, on a 9 swine model in NSR, confirmed that constant flow oxygenation alone didn’t significantly alter the decrease of pO2 and increase of pCO2 observed during apnea, but the addition of precordial compression maintained arterial blood gases over 4 min period at the level obtained during mechanical ventilation, highlighting the importance of the “bellow effect” on the passive ventilation. During CA, ventilation parameters were equivalent, but hemodynamic were better if compared with positive pressure ventilation.

Okomoto 1993, showed in 27 dogs that tracheal oxygen insufflation at 10 L/min during standard CPR ensure adequate gas exchanges when compared with IPPV, without significant differences in arterial, pulmonary artery and diastolic right atrial pressures, between groups even when a 5 cmH2O CPAP was added to continuous O2 delivery. The addition of CPAP anyway lowered coronary perfusion pressure.

Noc 1995, suggested that during CPR positive pressure ventilation compared with passive oxygen delivery did not improve ROSC and 48h survival on a 22 swine model, where precordial compression and spontaneous gasping yielded minutes volumes that exceeded 5 L.

According to Hayes 2007, 24h neurological normal survival for 36 swine can be equivalent when a continuous oxygen delivery at 10 L/min is compared with a standard MV or hyperventilation strategy during CPR, but the survival rate that belong to small number (about 2-4/12 pigs per group) could impact the weigh of this results.

On a clinical RCT, not blinded, of 696 OHCA patients in VF, ASY or PEA, the use of a Bousignac tube for continuous oxygen delivery at 15 L/min associated to CCC (with or without ACD device) determined no differences on ROSC, hospital admission and ICU discharge, but better oxygenation and less complications when compared with standards MV and ETI, as showed by Bertrand 2006. Same data were already showed by the same group, Saissy 2000, for 95 OHCA asystolic patients.

Two non randomized observational trials confirmed that a new OH protocol based on the principles of cardiocerebral resuscitation (MICR) was associated with an significant improvement in neurologically intact survival in adult patients with witnessed CA and an initially shockable rhythm, Kellum 2006 and Kellum 2008.

Acknowledgements:

The proposed research strategy according to PICO identified many papers for the newborn setting (excluded from this review because considered not in scope being a special population). Cochrane review available at the present moment focus on the same patient's setting. The main focus and results from these excluded papers are on the detrimental metabolic effects related to hyperventilation.

Some of these data could be anyway considered as a general pathophysiological background that highlight the potential detrimental effect of the higher production of radicals and markers of neuron damage, during ventilation with high oxygen concentration as described during positive pressure ventilation, that can conceptually contrast the use of a positive pressure ventilation, at least on a neonatal setting (papers not included on this WS).

There are no RCT or comparable data in human that specifically addressed the topic of a better outcome associated with passive oxygen delivery strategy vs standard positive pressure ventilation.

According to Aufderheide 2004, hyperventilation affect significantly the hemodynamic parameters and survival rates on a 9 swine model, mainly by decreasing coronary perfusion pressure, with an inversely proportional relationship between mean intratracheal pressure and coronary perfusion pressure during CPR, despite supplemental of CO2 to prevent hypocapnia.

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Citation List on alphabetical order


Citation List with Comments

[Aufderheide 2004]

Aufderheide TP, Lurie KG.
Death by hyperventilation: a common and life-threatening problem during cardiopulmonary resuscitation.

Supporting; LOE 4-5; Fair
Extrapolation about the harm associated with hyperventilation. Result might be biased being not a direct comparison on a randomized setting. The study confirm the high prevalence of hyperventilation on real OHCA ALS scenarios, despite adequate training of professional rescuers, and detrimental effect of hyperventilation on survival and hemodynamic parameters (animal model). This evidence suggests the importance to identify alternative way of ventilation vs standard positive pressure MV at least equivalent in efficacy but less potentially harmful.

Human Adult OHCA ALS setting + Animal (swine model) to confirm and quantify the level of hyperventilation on real ALS settings and detrimental effect on survival. Positive pressure ventilation has a detrimental effect on blood flow during CPR.

[Bertrand 2006]

Constant flow insufflation of oxygen as the sole mode of ventilation during out-of-hospital cardiac arrest.

Neutral; LOE 1; Poor
According to statistical description the study lack the predefined power (slow enrollment, protocol amendment for simplification; not addressing “unbias” direct comparison with passive oxygen delivery: the CFIO @15 L/min generate a intratracheal positive pressure of about 10 cmH2O, possible confounding related also to ACD, used only in some cases (not specified on the results), and to other resuscitation treatments (i.e. epinephrine). An evaluation of the role of the quality of CC on the efficacy of the ventilation has not been addressed (inter-individual confounding). The study suggests better oxygenation with CFIO but no improvement on hard endpoints.

Human, Adult, OHCA in VF, ASY and PEA. 696 analysed /1,042 patients (vs 1,884 expected for 80% power and p=0.029); RCT non-blinded; 15 sites, observational period 2000-2003 by SAMU (France) ALS setting (including drugs) comparing passive oxygenation delivered by CFIO (with Boussignac tube) during CCC vs standard MV with ETI (TV 12 mL/Kg, RF 12/min, FiO2=1) and CCC 100/min. Survival to ICU discharge, ROSC and hospital admission rate: no differences between groups; SpO2 legible and >70%; significantly better level of oxygenation with CFIO.

[Brochard 1996]

Brochard L, Boussignac G, Adnot S, Bertrand C, Isabey D, Harf A.
Efficacy of cardiopulmonary resuscitation using intratracheal insufflation..

Neutral; LOE 5; Fair
Animal model, small number, not addressing “unbias” direct comparison with passive oxygen delivery: CFI @15 L/min generate a intratracheal positive pressure of about 10 cmH2O, possible confounding. The model confirm the importance of CC to ensure “passive” ventilation, but the role of CC quality on the ventilation efficacy has not been addressed. The study suggests better hemodynamic effect with CFI with equivalent ventilatory parameters. No data on hard end points.

Animal, Adult porcine model, OHCA in VF. 9 swine; ALS equivalent setting, comparing passive oxygen delivery by CFI (with Boussignac tube) alone and during CPR vs standard MV with ETI (TV 12 mL/Kg, BF 12/min, FiO2=1) and CCC 100/min. Survival to ICU discharge, ROSC and hospital admission rate: no differences for ventilatory parameters but better hemodynamic (systolic Ao pressure and systolic mean carotid flow) for CFI+CPR during VF scenario.

[Hayes 2007]

Hayes MM, Ewy GA, Anavy ND, Hilwig RW, Sanders AB, Berg RA, Otto CW, Kern KB
Continuous passive oxygen insufflation results in a similar outcome to positive pressure ventilation in a swine model of out-of-hospital ventricular fibrillation.

Neutral; LOE 5; Fair
Animal model, relatively small numbers related to neurological outcome (2-4/12), possible confounding related to intratracheal pressure generated by continuous insufflation and role of the quality of CC on ventilation efficacy not addressed. The study shows no difference on hard endpoints, but better hemodynamic effect with passive O2 delivery.

Animal, Adult porcine model, OHCA in VF. 36 swine; ALS equivalent setting, comparing 3 different ventilation scenarios I: standard MV @ 10/min; TV 10ml/Kg; FiO2=1; II: hyperventilation @ 35/min; TV 20 ml/Kg; FiO2=1; III: continuous O2 insufflation at oropharynx level by nasal flexible cannula @ 10 L/min, no ETI; 24h neurological normal outcome; ROSC and survival: no differences between groups; Passive O2 delivery better coronary perfusion pressure during the first 2
minutes of CPR, but not thereafter. Passive insufflation may be an acceptable alternative to positive pressure ventilation, considering procedure simplification (EMS training, administration, less complications due to positive pressure).

[Kellum 2006]

Kellum MJ, Kennedy KW, Ewy GA.
Cardiocerebral resuscitation improves survival of patients with out-of-hospital cardiac arrest.

Supporting; LOE 3; Poor
Non-randomized observational study with retrospective/historical control group, many potential confounding related to different CPR protocols and guidelines in place between intervention and control groups; moreover the study is not addressing only passive ventilation role on patient’s outcome. Preliminary study, need to be confirmed in RCT. The study suggest better outcome with MICR that includes passive oxygen delivery.

Human, Adult, OHCA in VF, AST and PEA, EMS in rural counties in Wisconsin. MICR vs standard CPR. 33 witnessed CA. Survival to hospital discharge, and neuro outcome, improved by MICR. CCC-CPR without ventilation, but passive oxygen delivery and basic airways. Significant better results for survival vs control group (before AHA 2000 GLs).

[Kellum 2008]

Cardiocerebral resuscitation improves neurologically intact survival of patients with out-of-hospital cardiac arrest.

Supporting; LOE 3; Poor
Non-randomized observational study with retrospective/historical control group (same of the previous study), many potential confounding related to different CPR protocols and guidelines in place between intervention and control groups; moreover the study is not addressing only passive ventilation role on patient’s outcome. Preliminary study, need to be confirmed in RCT. The study suggest better survival with MICR that includes passive oxygen delivery.

Human, Adult, OHCA in VF, ASY and PEA, EMS in two rural counties in Wisconsin. MICR vs standard CPR. 89 witnessed CA. Survival to hospital discharge, and neuro outcome, improved by MICR (39% vs 15%). CC only CPR is the same population from the previous paper by Kellum 2006 (duplicate patients). Significant better results for survival vs control group (before AHA 2000 GLs).

[Kern 1992]

Kern KB, Nelson JR, Norman SA, Milander MM, Hilwig RW.
Oxygenation and ventilation during cardiopulmonary resuscitation utilizing continuous oxygen delivery via a modified pharyngeal-tracheal lumened airway.

Supporting; LOE 5; Fair
Non-randomized, historical control, possible confounding, The model confirm the importance of CC to ensure “passive” ventilation, but the role of CC quality on the ventilation efficacy has not been addressed. The study suggest equivalent ventilation parameters and ROSC.

Animal Adult, OHCA in VF, 21 dogs; ALS equivalent setting, evaluating efficacy/safety of a modified pharyngeal-tracheal lumened airway for continuous oxygen delivery. In 10 dogs in apnea and NSR, hyper-CO2 and acidosis (after 5 min apnea) corrected by “bellow effect” of CC. In 11 dogs during 20 min CPR in VF, pO2 and pCO2 not statistically different from pre-CA values from the same animals. ROSC in 8/11 (73%) dogs, equivalent to historical control with IOT.

[Noc 1995]

Noc M, Weil MH, Tang W, Turner T, Fukui M.
Mechanical ventilation may not be essential for initial cardiopulmonary resuscitation

Supporting; LOE 5; Fair
Relatively small number, extrapolation from result of not added value related to positive pressure ventilation; possibly biased being not addressing the role of CC quality on ventilation efficacy. The study shows a tidal volume of >5L generated during CC or gasping, equivalent pO2 and moderate increase on CO2 with passive oxygenation during CPR. ROSC and 48h survival almost equivalent between groups.

Animal Adult, OHCA equivalent scenario in VF, 22 swine; aimed to quantify tidal volumes generated by gasping and CC. Direct comparison of positive pressure vs passive oxygen delivery during CPR. ROSC, 48h survival and blood gases parameters: no differences between groups. CC and spontaneous gasping generate minute volumes >5L.

[O’Neill]

O’Neill JF, Deakin CD.
Do we hyperventilate cardiac arrest patients?

Supporting; LOE 4; Fair

Extrapolation about the harm associated with hyperventilation. Result might be biased being not a direct comparison on a randomized setting. The study confirm the high prevalence of hyperventilation on real IHCA ALS scenarios. No direct inferences on relationship between hyperventilation and hard outcome has been showed. This evidence suggests the importance to identify alternative way of ventilation vs standard positive pressure MV at least equivalent in efficacy but less potentially harmful.

Human, Adult, IHCA, ALS UK setting; 12 ICU pts.,aimed to evaluate ventilation variables using self-inflating bag. Hyperventilation and high airway pressures are common on a real setting. Possible detrimental effect on blood flow during CPR.

[Okomoto 1990]

Okamoto K, Morioka T
Transthacheal O2 insufflation (TOI) as an alternative method of ventilation during cardiopulmonary resuscitation..

Neutral; LOE 5; Fair

Possible confounding related to the role of CC quality on the ventilation efficacy. Study suggest continuous O2 flow >0.5 L7Kg/min to ensure enough oxygenation during CPR.

Animal Adult, OHCA in VF, dogs; ALS equivalent setting. evaluating efficacy of continuous transthacheal insufflation. Flow rate of 0.5 and 1 L/Kg/min was enough to maintain adequate oxygenation during CPR. Flow of 0.2 was ineffective. Post-CPR hyper-CO2 not prevented.

[Okomoto 1993]

Okamoto K, Kishi H, Choi H, Morioka T.
Cardiopulmonary resuscitation without intermittent positive pressure ventilation.

Neutral; LOE 5; Fair

Possible confounding related to the role of CC quality on the ventilation efficacy. Study suggest continuous O2 tracheal insufflation without CPAP is almost equivalent to IPPV during CPR.

Animal Adult, OHCA in VF, 27 dogs; ALS equivalent setting. IOT performed, evaluating efficacy on gas exchange, airways pressure and hemodynamic.of tracheal O2 insufflation @ 10 L/min +/- CPAP (5 cmH2O) vs IPPV during CPR. Tracheal insufflation without CPAP almost equivalent to IPPV during CPR. The role of CC quality on the ventilation efficacy has not been addressed.

[Saissy 2000]

Saïssy JM, Boussignac G, Cheptel E, Rouvin B, Fontaine D, Bargues L, Levecque JP, Michel A, Brochard L.
Efficacy of continuous insufflation of oxygen combined with active cardiac compression-decompression during out-of-hospital cardiorespiratory arrest.

Neutral; LOE 1; Fair

Not addressing “unbias” direct comparison with passive oxygen delivery: the CIO @15 L/min generate an intratracheal positive pressure of about 10 cmH2O, possible confounding; active decompression during ACD may affect ventilation quality, these result can’t be generalized when standard CPR is in place (more frequent then ACD devices). The study suggests better oxygenation with CIO at hospital admission, but no improvement on hard endpoints.

Human, Adult, OHCA in ASY. 95 patients; RCT non-blinded; SAMU (France) ALS setting comparing passive oxygenation delivered by CIO (with Boussignac tube) vs standard IPPV with ETI (TV 12 mL/Kg, RF 12/min, FiO2=1) during ACD. Blood gas parameters: no differences after resuscitation; better pH, pO2 and pCO2 after hospital admission for CIO group. ROSC and time to ROSC: no differences.

[Steen 2004]

Continuous intratracheal insufflation of oxygen improves the efficacy of mechanical chest compression-active decompression CPR.

Supporting; LOE 5; Fair

Result related to the use of a Boussignac tube and ACD (possible confounding). CC quality variability associated to rescuers performance could affect the ventilation efficacy and the overall outcome results. The study confirm the importance of CC to ensure “passive” ventilation, but the role of CC quality on the ventilation efficacy in a “real” setting without ACD device could jeopardise the results.

Animal Adult, OHCA in VF, 16 swine; ALS equivalent setting. evaluating efficacy of CIO (Boussignac tube) vs IPPV during ACD-CPR (LUCAS). ROSC on 8/8 pigs after 8 min ACC and 30 min ACD-CPR. Better gas exchange and hemodynamic values with CIO.