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

**Worksheet author(s)**

<table>
<thead>
<tr>
<th>Dr Csaba Dioszeghy MD FCEM</th>
<th>Date Submitted for review:</th>
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<tbody>
<tr>
<td></td>
<td>21 October 2009</td>
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</table>

**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 (e.g. 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:** NEW TOPIC

**Conflict of interest specific to this question**

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? **No COI**

**Search strategy (including electronic databases searched).**


Search of the references listed in all reviews, animal study and clinical trial articles.

**State inclusion and exclusion criteria**

Inclusion criteria: all clinical trials, human studies and animal studies with an intervention of passive oxygen delivery during chest compressions and patient population of cardio-respiratory arrest and endpoints of survival (ROSC, 24 hr survival, discharge) or hemodynamic values or oxygenation values.

Exclusion criteria: abstract only references, non cardiac arrest trials, trials with endpoints not related to survival or oxygenation or hemodynamic values of resuscitation.

Duplicate results are removed.

**Number of articles meeting initial search criteria from the Databases (last updated on 21 Oct 2009):**

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<tr>
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<tbody>
<tr>
<td>Oxygen delivery AND resuscitation:</td>
<td>M: 634 E: 570 C: 39 A: 100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passive oxygen AND resuscitation:</td>
<td>M: 13 E: 9 C: 3 A: 4</td>
<td></td>
<td></td>
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<tr>
<td>Passive oxygen AND CPR:</td>
<td>M: 7 E: 6 C: 1 A: 2</td>
<td></td>
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<tr>
<td>Oxygen delivery AND CPR:</td>
<td>M: 57 E: 51 C: 4 A: 27</td>
<td></td>
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<tr>
<td>Transtracheal oxygen:</td>
<td>M: 202 E: 154 C: 13 A: 8</td>
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<td></td>
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<tr>
<td>No ventilation AND resuscitation:</td>
<td>M: 764 E: 579 C: 72 A: 7</td>
<td></td>
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</tbody>
</table>

NB: “passive oxygen delivery” as Intervention was meant by any form of supplemental oxygen given to the patient without positive pressure ventilation. Resuscitations without ventilation and without supplemental oxygen were not included as these are dealt with the sections about chest compression only CPR.

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

7 animal studies, 5 clinical trials
### Summary of evidence

**Evidence Supporting Clinical Question**

<table>
<thead>
<tr>
<th>Level of Evidence</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>Steen 2004 E (1,2)</td>
</tr>
<tr>
<td></td>
<td>Brochard 1996 E (1,2)</td>
</tr>
<tr>
<td>Fair</td>
<td>Kellum 2006 D</td>
</tr>
<tr>
<td></td>
<td>Bobrow 2009 D (for witnessed VF/VT)</td>
</tr>
<tr>
<td>Poor</td>
<td>Bobrow 2008 C</td>
</tr>
</tbody>
</table>

**Level of evidence**

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

*Italic* = Animal studies

(1 – ACD-CPR; 2 – Boussignac tube; 3 – Other airway device; 4 – Percutaneous tracheal insufflation)

**Evidence Neutral to Clinical question**

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<tr>
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<tbody>
<tr>
<td>Good</td>
<td>Hayes 2007A</td>
</tr>
<tr>
<td></td>
<td>Okamoto 1993 E</td>
</tr>
<tr>
<td>Fair</td>
<td>Saissy 2000 A,E (1,2)</td>
</tr>
<tr>
<td></td>
<td>Bobrow 2009 D (for non-witnessed arrests and for witnessed nonVF/VT)</td>
</tr>
<tr>
<td>Poor</td>
<td>Bertrand 2006 A,E (1,2)</td>
</tr>
<tr>
<td></td>
<td>Kern 1992 E (3)</td>
</tr>
<tr>
<td></td>
<td>Okamoto 1990 E</td>
</tr>
<tr>
<td></td>
<td>Branditz 1989 E (4)</td>
</tr>
</tbody>
</table>

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**Evidence Opposing Clinical Question**

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

There are earlier studies confirming the effect of passive oxygen delivery on gas exchange during different procedures or respiratory arrest. Chest compressions provide a “bellow” effect which makes it more likely to increase the beneficial effect of passive oxygen insufflation without the unwanted effects of positive pressure ventilation during resuscitation. Unfortunately by this time we do not have too much evidence supporting this theory. Kellum and co-workers presented a prehospital study where patients received passive oxygen delivery during the first 12 minutes of resuscitation along with a significantly modified protocol (CCC-CPR, compressions before defibrillation). The intact neurological survival was better compared to the historical control treated according to the 2000 AHA protocol (Kellum 2006). However the passive oxygen delivery was just a part of a group of treatment changes compared to the control group so it is not clear how much role this intervention actually played in the outcome. This result is similar to the one published by Bobrow et al, where the “Minimally Interrupted Cardiac Resuscitation” (MICR) protocol resulted a better survival to discharge after out-of-hospital cardiac arrest compared to historical control resuscitated according to AHA 2000 guidelines. This MICR protocol included an initial and pre- and post-shock compressions, early adrenalin and either passive oxygen delivery (via face mask and oropharyngeal airway) or a bag-valve-mask ventilation with a frequency of no more than 8/min (Bobrow 2008). In a later retrospective analysis the outcome (neurologically intact survival) was compared in the two groups of patients who received MICR and either passive oxygen or bag-valve-mask ventilation. In this paper Bobrow demonstrated a better chance for neurologically intact survival for patients suffered witnessed VF/VT cardiac arrest and received passive oxygen compared to those received bag-valve-mask ventilation. However, for patients suffered non-witnessed cardiac arrests or those with a witnessed arrest of a non-shockable initial rhythm survival was similar in the passive oxygen and bag-valve-mask groups (Bobrow 2009).

Most of the other available data are from animal studies using different adjuncts to enhance the passive oxygen delivery. Brochard and Steen had used the Boussignac tube (Brochard 1996, Steen 2004), Branditz used percutaneous tracheal cannulation (Branditz 1989), Okamoto used endotracheal intubation and then two different placement for the oxygen tube (above the carina or below the top of the tube, Okamoto 1990, Okamoto 1993) and Kern used a special pharyngotracheal tube (Kern 1992) to deliver the oxygen. Hayes et al inserted the oxygen catheter in the oropharynx during CPR (Hayes 2007). The animal studies also used different oxygen flow rates ranging from 0,2 L/kg/min to 20-23 L/kg/min. Steen used mechanical ACD-CPR while other animal studies used conventional CPR. The overall results of the animal studies are generally neutral (Hayes 2007, Okamoto 1990,1993, Kern 1992) showing no difference in oxygenation or hemodynamic values compared to standard CPR+ventilation or simply just demonstrating adequate oxygenation. Steen et al demonstrated favorable oxygenation and hemodynamics in the animal model using passive oxygen delivery via Boussignac tube combined with ACD-CPR (Steen 2004) but in this study the oxygen flow was 20-23 l/min (about the double of what was used in most studies.) Brochard demonstrated better haemodynamics with passive oxygen delivery compared to IPPV (Intermittent Positive Pressure Ventilation) ventilation in pigs (Brochard 1996) without differences in ventilatory parameters. Survival was not measured. There are only two clinical trials evaluating the use of passive oxygen delivery during out of hospital resuscitation and comparing it to conventional CPR with IPPV ventilation (Saissy 2000, Bertrand 2006). Both studies are out-of-hospital adult cardiac arrest trials and both used Boussignac tube. Saissy et al used only ACD-CPR for both the experimental and the control group while Bertrand had both ACD-CPR and standard CPR mixed in both groups. The results showed no statistical differences in the ROSC (Saissy 2000, Bertrand 2006) or ITU discharge (Bertrand 2006). However in the trial by Bertrand et al patients receiving standard CPR (without ACD-CPR) and passive oxygen insufflation tended to have poorer outcome compared to the control group.

In summary: passive oxygen delivery during cardiopulmonary resuscitation has not yet been proved to be more effective than CPR with positive pressure ventilation. Some evidence suggest that passive oxygen delivery via a special adjunct which helps to maintain open airway and ensure adequate transtracheal oxygen flow (like the Boussignac tube) combined with ACD-CPR is at least not worse than conventional (or ACD-CPR) with IPPV ventilation but no convincing evidence exists regarding to survival.

Acknowledgements:
### Citation List

**Bertrand 2006**


**LOE 1, poor quality, Neutral (using Boussignac Tube)**

Randomized controlled non-blinded trial; study population is adult OHCA patients; the intervention is passive oxygen delivery via Boussignac tube. Confounder is the use of ACD-CPR. The non ACD-CPR (standard CPR) group has not been separated and assessed. The study also lacks of statistical power. 730 randomized adult OHCA patients were included. Oxygen insufflations via Boussignac tube versus conventional ET tube and ventilation were assessed. Both the control and the intervention group had patients with standard and also with ACD-CPR. Endpoints are ROSC, hospital admission and ITU discharge. Overall results show no significant difference between the groups. However considering the ACD-CPR and the Standard CPR as separate groups, patients received standard CPR had slightly (but not significant) worse tendency for ROSC, hospital admission and ITU discharge as well. The study demonstrated that the CPR with continuous oxygen delivery using Boussignac endotracheal tube is not worse than CPR with ventilation especially when combined with ACD-CPR. Alos the study has lacked the power as instead of 1884 patients needed for 80% confidence only 730 could have been included mainly due for the generally poor prognosis.

**Bobrow 2008**


**LOE 3, Low quality (confounders, study group is mixed with bag-valve-mask and passive oxygen), Supportive**

This study essentially compared two different CPR protocols: one (historical control) according to the AHA guideline prior 2005 (!) and the other is the MICR (Minimally Interrupted Cardiac Resuscitation) which – among a number of differences – consist of passive oxygen delivery with an oropharyngeal airway. However, more than half of this group have also received bag-valve-mask ventilation by the paramedics. Results showed a better survival to discharge in the MICR group. The main limitation of this study is the number of confounders (different chest compression regime; different defibrillation protocol) as well as the mixture of passive oxygen delivery and bag valve mask ventilation in the sudy group.

**Bobrow 2009**


**LOE 2, Fair quality (confounder), Supportive for witnessed out-of-hospital VF/VT and Neutral for all other out-of-hospital arrests**

A retrospective analysis of the out-of-hospital cardiac arrests received “minimally interrupted cardiac resuscitation” (MICR) either with bag-valve-mask ventilation or passive oxygen insufflation via non rebreathing face mask and oropharyngeal airway. Results shows better neurologically intact survival for those with witnessed cardiac arrest of a VT or VF when received passive oxygen delivery compared to those received bag-valve-mask ventilation. However, the non-witnessed cardiac arrests or those with a witnessed arrest of a non-shockable rhythm had similar outcome in both groups. The limitation of this study is that both the control (bag-valva-mask) and the study group (passive oxygen) have been resuscitated according to the MICR protocol which is different of the current guidelines.
Branditz 1989

LOE 5, Poor quality, Neutral (with percutaneous tracheal catheter)
Non-controlled animal study (21 dogs) using percutaneously placed intratracheal catheter to deliver 15 l/min oxygen during chest compressions during induced VF. The insertion technique of this catheter was modified during the study. Blood gases, aortic and right atrial pressures were measured and coronary perfusion pressures calculated. Results show that oxygen delivery via percutaneously inserted tracheal catheter is an effective method for resuscitation.

Brochard 1996

LOE5, good quality, Supportive (with Boussignac tube)
Animal study (pigs) comparing the effects of 15 l/min oxygen delivery via Boussignac tube (CFI-CPR Group) and conventional ventilation (Control Group) on oxygenation and haemodynamics during CPR. Results shows significantly better systolic aortic pressure, systolic and mean common carotid pressure in the CFI-CPR and also similar ventilator parameters between the two groups.

Hayes 2007

LOE5, Good quality, Neutral
Randomized, controlled animal (swine) study comparing the effects of CPR with (1) passive oxygen insufflation, (2) conventional ventilation and (3) hyperventilation on 24 hour neurological survival after VF arrest and resuscitation. The experimental group was not intubated and oxygen was delivered via flexible tube placed in the oropharynx. Secondary endpoints were ROSC, hemodynamic variables, intrathoracic pressures and blood gases. Results showed no significant differences in ROSC, 24 hrs survival and neurological scores among the three groups. The passive oxygen delivery group had a better coronary perfusion pressure measured during the first two minutes of ALS compared to the other groups but this difference has disappeared after two minutes. No other differences in the hemodynamic variables were detected. Limitation of the swine model is that the airway usually remains patent in these animals without any intervention which is not the case in humans.

Kellum 2006

LOE 3 Fair evidence (confounders), Supportive
Non-randomized clinical observational study with historical control; the intervention is a different CPR protocol as compared with the 2000 AHA guideline. The study group involves CCC-CPR for the first 12 minutes without ventilation and only basic airway maneuver and passive oxygen delivery afterwards (witnessed arrests and trained first responders and EMS personnel). Results confirm significantly better
survival with this protocol compared to the historical control (before 2003).

Kern 1992

LOE5, Fair Quality, Neutral
Animal study (dogs) with historical control. Used a special airway device (Pharyngeal-tracheal airway) to deliver 10L/min oxygen during chest compressions. Results showed no significant difference in blood gases and hemodynamic values compared to the same animals’ pre-arrest values and no significant difference in ROSC compared to historical controls with endotracheal intubation and ventilation.

Okamoto 1993

LOE5, good quality, Neutral
Animal study (dogs) comparing the effect of tracheal oxygen delivery (with and without CPAP) and intermittent positive pressure ventilation during CPR on the gas exchange, airway pressures and hemodynamic values. Animals are intubated and oxygen delivered via a catheter placed 1 cm distal to the top of the ET tube. Results show that CPR with passive oxygen delivery without CPAP has similar effect on hemodynamic values or gas exchange than CPR with IPPV.

Okamoto 1990

LOE5, Fair quality, Neutral
Animal study (dogs) investigating the effect of different flow rates of transtracheal oxygen insufflation on oxygenation during and after CPR. Results show that flow rates above 0.5 L/Kg/Min resulted adequate oxygenation during CPR but not after the chest compression. No control group with IPPV and CPR was investigated.

Saissy 2000

LOE1, Fair quality, Neutral for ACD-CPR and Boussignac Tube
Randomized, non-blinded, controlled trial. Patient population: adult OHCA (only asystole or extreme bradycardia). ACD CPR was used for all cases. Intervention: passive oxygen delivery via Boussignac tube with 15 L/min flow rate (CIO). Control group was intubated and manually ventilated. Endpoints are ROSC, arterial blood gases taken after ROSC, Hospital admission and ABGs after admission. Percutaneous oxygen saturation was also measured during CPR however its reliability is questionable. Results show no significant difference between the two groups in oxygen saturations during CPR, ROSC, early ABG and hospital admission. The CIO group had a significantly better post-admission blood gas which might be explained by the preventive effect of continuous positive airway pressure created by CIO on the development of pulmonary atelectasis.
The study lacks the statistical power due to the poor outcome and small number of patients enrolled. (8 of 47 control and 10 of 48 CIO assessed after ROSC)

**Steen 2004**

**LOE 5, Good Quality, Supportive for ACD-CPR and Boussignac Tube**
Animal study: after induced VF arrest 16 pigs were resuscitated using LUCAS (ACD-CPR) and either pressure regulated ventilation with PEEP or 20-23 l/min continuous intratracheal oxygen insufflation via Boussignac tube (CIO). Results show better hemodynamic values and gas exchange with CIO. The limitation is the unusually high oxygen flow needed to achieve this result.