WORKSHEET for Evidence-Based Review of Science for Veterinary CPCR

1. Basic Demographics

Worksheet author(s)

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Mailing address:	**Phone:**
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2. Clinical question:

In dogs and cats with cardiac arrest (P), does providing ventilation with a 1 second inspiratory time and tidal volume of about 10 mL/kg (I), compared with other inspiratory times and tidal volumes (C), improve any outcomes (including ventilation, oxygenation) (O)?

3. Conflict of interest specific to this question:

None

4. Search strategy (including electronic databases searched):

4a. Databases

PubMed: Search Strategy (textword search): Can you give us an idea how many of each of these total search numbers were actually relevant (included) to this worksheet

1) Inspiratory time during cardiopulmonary resuscitation – 6 relevant hits out of 78 records
2) Tidal volume during cardiopulmonary resuscitation – 4 relevant hits out of 198 records
3) Cardiopulmonary resuscitation in dogs – 0 relevant out of 514 records
4) Tidal volume in dogs – 0 relevant out of 1072 records
5) Tidal volume in resuscitation in dogs – 0 relevant out of 222 records
6) Inspiratory time in dogs – 0 relevant out of 889 records
7) Cardiopulmonary resuscitation in cats – 0 relevant out of 32 records
8) Tidal volume in cats – 0 relevant out of 505 records
9) Tidal volume in resuscitation in cats – 0 relevant out of 26 records
10) Inspiratory time in cats – 0 relevant out of486 records
11) CPR AND Hyperventilation - 1 relevant out of 73 records

Cab Abstracts (1910 to Feb 2011) (performed on June 10, 2011)
1) Cardiopulmonary resuscitation
2) Tidal volume
3) Inspiratory time
4) Hyperventilation
1) and 2) No further relevant hits
1) and (3) no further relevant hits
1) and (4) no further relevant hits

Google Scholar (performed on June 16, 2011)
CPR and tidal volume – no additional relevant hits
CPR and inspiratory time – no additional relevant hits
CPR and hyperventilation – no additional relevant hits

4b. Other sources

None

4c. State inclusion and exclusion criteria for choosing studies and list number of studies excluded per criterion

Inclusion criteria

Evaluation of inspiratory time and/or tidal volume in cardiopulmonary resuscitation.

Exclusion criteria

Abstracts only (1) Editorials (3)

4d. Number of articles/sources meeting criteria for further review: 11

- 4 randomized trials were identified: (Dorges et al 2000 [not CPR cases only those undergoing GA]), (Langehell et al 2000), (Wenzel et al 1999 [not CPR cases, only those undergoing GA]), (Droges et al 1999 [not CPR cases only those undergoing GA]),

- 4 relevant human (mechanistic) studies were identified: (Von Goedecke et al 2005), (Von Goedecke et al 2006), (Herff et al 2009), (Herff et al 2008)

-2 relevant Human studies were identified (Dorph et al 2004), (Pytte et al 2008)
- 1 combined human clinical observational study and experimental pig study (Aufderheide 2004)

5. Summary of evidence

Evidence Supporting Clinical Question

Good						
Fair						
Poor						*Dorph 2004; E=blood gases Von Goedecke 2005;E=stomach Inflation, tidal volumes, peak airway pressure Von Goedecke 2006; E= airway pressure, TV, stomach inflation Herff 2009; E=TV Herff 2008; E=TV Aufderheide 2004; B, E=CPP*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

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

Evidence Neutral to Clinical question

Good						
Fair						
Poor						*Dorges 2000;E = PCO2* *Langhelle 2000;E = blood gases* *Dorges 2000;E = blood gases*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

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

Evidence Opposing Clinical Question

Good						
Fair						
Poor						*Wenzel 1999; E = ETCO2, blood gases, stomach inflation* *Pytte 2008;E = blood gases*
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

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

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

No study could be identified that addressed this question in dogs and cats. There are several studies in human patients and bench top models that provide some insight on the optimal tidal volume and inspiratory time during cpr.

It is critical to maintain normocapnia and normoxia during CPR via ventilation, inspiratory time and oxygen supplementation as evident through the effects of hypoxia and/or hypercapnia on outcome in CPR studies (Kerber RE, 1979; Idris, 1995, Yeh, 2009). In addition, hyperoxia appears to have detrimental effect on outcome as well for CPR (Kilgannon, 2010; Zwemer, 1994). There are no studies that this author could find that directly relate tidal volume and/or inspiratory time to outcome in CPR as there are an almost infinite number of variables that likely affect outcome. Consequently the best one can aim for is to maintain normoxia and normocapnia with ventilation. It is difficult to compare many of the studies as there is inconsistent patient selection, inconsistent airway maintenance (some are intubated, some are mask ventilation) and inconsistent oxygen supplementation (21% vs 50% vs 100%). However a majority of the studies suggest that there is a benefit to aim for 10 ml/kg.

Two neutral studies indirectly suggest that 10 ml/kg of tidal volume may be the optimal target ventilation Langhelle states 7ml/kg causes hypercapnia and 13 ml/kg caused hypocapnia; Dorges *et al* suggested tidal volumes of 11 ml/kg would be necessary for adequate ventilation.

In anesthetized adult human patients a smaller tidal volume (365±55ml versus 779±122ml) was found to maintain adequate blood gases suggesting a 10ml/kg tidal volume is larger than necessary (Wenzel 1999). The relevance of this finding to patients during CPR has not been investigated. One study was identified that reported a 10ml/kg tidal volume at 12 breaths/minute was associated with hypercapnia and hypoxemia in a small group of human CPR patients. Given the small number of people included in this study and inconsistencies in the methodology the validity of these results are of question (Pytte 2008).

There is insufficient evidence to determine the optimal tidal volume during CPR for dogs and cats. Given the evidence available a10 ml/kg tidal volume appears appropriate in an intubated dog or cat to provide the optimal ventilation strategy to achieve normoxia and normocapnia and therefore likely improve outcome in veterinary CPR cases.

During CPR with only a single rescuer present, shorter inspiratory times are preferred to increase the time available for, and consequently the actual number of, chest compressions during CPR without risking an excessive increase in stomach inflation.[Von Goedecke 2005; Von Goedecke 2006] In addition, extended duration of positive intrathoracic pressure may negatively impact hemodynamics during CPR and maintaining short inspiratory times will minimize this effect. [Aufderfeide, 2004] Furthermore, lower tidal volume will lead to lower mean intrathoracic pressure. Inspiratory times of 1 second were found to provide sufficient tidal volumes compared to 2 seconds in bench-top experiments while shorter inspiratory times were insufficient to maintain adequate tidal volumes.[Herff 2008; Herff 2009] Further studies are necessary to evaluate inspiratory time effect on oxygenation and subsequently outcome but as such, optimization of tidal volume is the main end point evaluated.

There is insufficient evidence to determine the optimal tidal volume and inspiratory time during CPR for dogs and cats. Given the current evidence available it would appear reasonable to recommend a10 ml/kg tidal volume with a 1 second inspiratory time.

7. Conclusion

DISCLAIMER: Potential possible wording for a Consensus on Science Statement. Final wording will differ due to other input and discussion.

CONSENSUS ON SCIENCE:
A majority of the studies suggest that there is a benefit to aim for 10 ml/kg tidal volume during CPR. Langhelle et al (LOE 6) and Dorges et al (LOE 6) which are considered neutral findings may indirectly suggest that 10 ml/kg of tidal volume may be the optimal target ventilation to achieve normoxia and normocapnia and therefore possibly improve outcome in veterinary CPR cases. Two studies suggested that a 10ml/kg tidal volume was not optimal but the validity of these studies are questionable (LOE 6)(Wenzel 1999; Pytte 2008). All of the investigations into inspiratory time evaluate the relationship to tidal volume and do not assess oxygenation as they utilize bench top models (LOE 6)(Von Goedecke 2005; Von Goedecke 2006; Herff 2008; Herff 2009). A 1 second inspiratory time is sufficient to provide adequate tidal volume although it is unclear how this will affect oxygenation when tidal volume is fixed at 10 ml/kg. No studies were identified that evaluated tidal volume or inspiratory time during CPR in dogs or cats.

8. Acknowledgement

9. Citation list

EFFECTS OF HYPERCARBIA AND/OR HYPOXIA ON OUTCOME:

Circulation 1979 Aug;60(2):226-30.
Factors influencing the success of ventricular defibrillation in man.
Kerber RE, Sarnat W.
Abstract
To define the factors influencing the success of emergency ventricular defibrillation, we identified 52 patients defibrillated at the University of Iowa Hospital during 1974--1976. Thirty-eight patients were successfully defibrillated at least once; 14 could not be defibrillated, despite multiple attempts. Comparisons between these groups revealed no significant differences in body weight, heart weight, energy per kilogram of body weight and energy per gram of heart weight. Factors that militated against successful defibrillation included a prolonged delay before the first defibrillatory shock (successful 7 +/- 7 minutes (SD); unsuccessful 17 +/- 13 minutes, p less than 0.001), acidosis (successful pH 7.36 +/- 0.22; unsuccessful pH 7.23 +/- 0.12, p = 0.05) and hypoxia (successful PO2 100 + 98 torr; unsuccessful PO2 40 +/- 67 torr; p = 0.06). These three conditions tended to occur together in individual patients. Metabolic factors are important in determining defibrillation success; however, the role of high-energy doses is uncertain.
Key points: Retrospective study, success was defined as at least one successful conversion to “another rhythm” and even asystole was considered “another rhythm.” In addition ABGs were variably measured “during resuscitation and defibrillation or within 1 hour of start of procedures” so is not consistent. However it is reasonable evidence that hypoxia and hypercarbia needs to be minimized for a successful CPR outcome.

Chest 1995 Aug;108(2):522-8.
Does hypoxia or hypercarbia independently affect resuscitation from cardiac arrest?
Idris AH, Wenzel V, Becker LB, Banner MJ, Orban DJ.
STUDY OBJECTIVE:

In a previous cardiopulmonary resuscitation (CPR) study in swine, ventilation was associated with improved rate of return of spontaneous circulation (ROSC) compared with nonventilated animals, which had greater hypoxia and hypercarbic acidosis. We used the same model to determine the independent effect of hypoxia and hypercarbic acidosis on ROSC after cardiac arrest.

DESIGN:

Laboratory model of cardiac arrest.

SETTING:

University teaching hospital laboratory.

PARTICIPANTS:

Domestic swine (23 to 61 kg).

INTERVENTIONS:

Twenty-four swine were randomly assigned to three groups receiving ventilation during CPR with 85% O2/15% N2 (control), 95% O2/5% CO2 (hypercarbia), or 10% O2/90% N2 (hypoxia). All animals had ventricular fibrillation for 6 min without CPR, then CPR with one of the ventilation gases for 10 min, then defibrillation. Animals without ROSC received epinephrine, 85% O2, CPR for another 3 min, and defibrillation.

MEASUREMENTS AND RESULTS:

During the tenth minute of CPR, the hypercarbic group had more mean (SD) arterial hypercarbia than the control group (PCO2, 47 +/- 6, compared with 34 +/- 6; $p < 0.01$), and greater mixed venous hypercarbia (PCO2, 72 +/- 14, compared with 59 +/- 8; $p < 0.05$), while mean arterial and mixed venous PO2 was not significantly different. The hypoxic group had significantly less mean arterial (43 +/- 9 compared with 228 +/- 103 mm Hg) and mixed venous (22 +/- 5 compared with 35 +/- 7 mm Hg) PO2 when compared with the control group ($p < 0.01$), while mean arterial and mixed venous PCO2 were not significantly different. Thus, the model succeeded in producing isolated hypercarbia without hypoxia in the hypercarbic group and isolated hypoxia without hypercarbia in the hypoxic group. The rate of ROSC was 6/8 (75%) for the control group, 1/8 (13%) for the hypercarbic group, and 1/8 (13%) for the hypoxic group ($p < 0.02$).

CONCLUSIONS:

Both hypoxia and hypercarbia independently had an adverse effect on resuscitation from cardiac arrest. In this model with a prolonged interval of untreated cardiac arrest, adequate ventilation was important for resuscitation.

Key points: Laboratory study in in pigs only. However it does define success as ROSC and not as a “change in rhythm” as previously.

Resuscitation 2009;80:951-955.

Oxygen requirement during cardiopulmonary resuscitation (CPR) to effect return of spontaneous circulation.

Steve T. Yeh, Rebekah J. Cawley, Sverre E. Aune, and Mark G. Angelos

Background

Recent scientific evidence has demonstrated the importance of good quality chest compressions without interruption to improve cardiac arrest resuscitation rates, and suggested that a de-emphasis on minute ventilation is needed. However, independent of ventilation, the role of oxygen and the optimal oxygen concentration during CPR is not known. Previous studies have shown that ventilation with high oxygen concentration after CPR is associated with worse neurologic outcome. We tested the hypothesis that initial ventilation during CPR without oxygen improves resuscitation success.

Methods

Sprague–Dawley rats were anesthetized with ketamine/xylazine (IP), intubated and ventilated with room air. A KCl bolus (0.04 mg/g) was given (IV) to induce asystolic cardiac arrest and ventilation was stopped. At 6 min, CPR was started with an automated chest compressor at a rate of 200–240/min and epinephrine (0.01 mg/kg)

was given 1 min later. During CPR, the ventilation rate was 50% of baseline with one of three oxygen concentrations: (1) 0% O_2 (100% N_2), (2) 21% O_2, or (3) 100% O_2. The prescribed oxygen concentration was continued for 2 min after return of spontaneous circulation (ROSC) and then all animals were switched to 100% oxygen for 1 h prior to extubation. Blood gases were measured at baseline, 2 min and 1 h after ROSC. Group comparisons were done using Fisher's exact test and ANOVA.

Results

ROSC was achieved in 1/10 (0% O_2), 9/11 (21% O_2) and 10/12 (100% O_2, $p < 0.001$). ROSC times after starting CPR were 80 s in the 0% O_2, 115 ± 87 s in the 21% O_2 group and 95 ± 33 s in the 100% O_2 group (mean ± SD, $p = 0.5$). Aortic end-diastolic pressure before ROSC was not different among groups. 100% oxygen ventilation in the first 2 min resulted in higher PaO_2 at ROSC 2 min (109 ± 44 mm Hg vs. 33 ± 8 mm Hg, $p < 0.001$). Survival to 72 h was 0/1 (0% O_2), 7/9 (21% O_2) and 8/10 (100% O_2) with a low neurologic deficit score in both O_2 groups (NDS range 5–25).

Conclusions

In a mild cardiac arrest model with generally good neurologic recovery, initial CPR ventilation with no O_2 did not allow for ROSC. In contrast, CPR coupled with room air or higher oxygen levels result in a high rate of ROSC with good neurologic recovery. During CPR, the level of oxygenation must be considered, which if too low may preclude initial ROSC.

Key points: Experimental study in rats only. Is not a clinically relevant study since as there was no difference in survival between the two more "normal" O2 supplementation groups. (i.e. you will either have 21% vs 100% O2 during CPR, you are not going to be giving 0% O2).

EFFECTS OF HYPEROXIA ON OUTCOME

JAMA 2010 Jun 2;303(21):2165-71.

Association between arterial hyperoxia following resuscitation from cardiac arrest and in-hospital mortality.

Kilgannon JH, Jones AE, Shapiro NI, Angelos MG, Milcarek B, Hunter K, Parrillo JE, Trzeciak S; Emergency Medicine Shock Research Network (EMShockNet) Investigators.

OBJECTIVE: To test the hypothesis that postresuscitation hyperoxia is associated with increased mortality.
DESIGN, SETTING, AND PATIENTS: Multicenter cohort study using the Project IMPACT critical care database of intensive care units (ICUs) at 120 US hospitals between 2001 and 2005. Patient inclusion criteria were age older than 17 years, nontraumatic cardiac arrest, cardiopulmonary resuscitation within 24 hours prior to ICU arrival, and arterial blood gas analysis performed within 24 hours following ICU arrival. Patients were divided into 3 groups defined a priori based on PaO(2) on the first arterial blood gas values obtained in the ICU. Hyperoxia was defined as PaO(2) of 300 mm Hg or greater; hypoxia, PaO(2) of less than 60 mm Hg (or ratio of PaO(2) to fraction of inspired oxygen <300); and normoxia, not classified as hyperoxia or hypoxia.
MAIN OUTCOME MEASURE: In-hospital mortality.
RESULTS: Of 6326 patients, 1156 had hyperoxia (18%), 3999 had hypoxia (63%), and 1171 had normoxia (19%). The hyperoxia group had significantly higher in-hospital mortality (732/1156 [63%; 95% confidence interval {CI}, 60%-66%]) compared with the normoxia group (532/1171 [45%; 95% CI, 43%-48%]; proportion difference, 18% [95% CI, 14%-22%]) and the hypoxia group (2297/3999 [57%; 95% CI, 56%-59%]; proportion difference, 6% [95% CI, 3%-9%]). In a model controlling for potential confounders (eg, age, preadmission functional status, comorbid conditions, vital signs, and other physiological indices), hyperoxia exposure had an odds ratio for death of 1.8 (95% CI, 1.5-2.2).
CONCLUSION: Among patients admitted to the ICU following resuscitation from cardiac arrest, arterial hyperoxia was independently associated with increased in-hospital mortality compared with either hypoxia or normoxia.

COMMENTS: Obviously very good numbers, human study and survival was the main end-point. Raises the question about the notion of oxygen supplementation during CPR which indirectly relates to tidal volume and inspiratory time.

Resuscitation 1994 ;27(2):159-70.
Cardiopulmonary-cerebral resuscitation with 100% oxygen exacerbates neurological dysfunction following nine minutes of normothermic cardiac arrest in dogs.
Zwemer CF, Whitesall SE, D'Alecy LG.
This study investigated the effects of normoxic (FIO2 = 0.21), hyperoxic (FIO2 = 1.0), and hyperoxic (FIO2 = 1.0) plus antioxidant pretreatment (tirilazad mesylate) [corrected] resuscitation on neurologic outcome following 9 min of normothermic (39 +/- 1.0 degrees C) cardiac arrest. Physiologic variables including arterial blood gases and neurologic outcome, which was assessed using a standardized scoring system, were followed over a 24-h period following resuscitation from cardiac arrest. Hyperoxically resuscitated dogs sustained significantly worse neurological deficit at 12 and 24 h (mean scores: 39 +/- 3 and 49 +/- 8, respectively) than did antioxidant pretreated hyperoxically resuscitated dogs (mean scores: 22 +/- 1, P = 0.0007 and 22 +/- 1, P = 0.004, respectively) and normoxically resuscitated dogs (mean scores: 28 +/- 4, P = 0.025 and 33 +/- 8, P = 0.041 respectively). These data suggest that oxidant injury has a major role in central nervous system dysfunction following successful resuscitation from 9 min of cardiac arrest. Also, resuscitation from cardiac arrest with hyperoxic FIO2's may contribute to and further exacerbate neurologic dysfunction
Key points: Another paper that questions the importance of oxygen supplementation and subsequent hyperoxia during CPR. The main weakness of the paper is the question regarding neurological outcome as we have a clinical study (Waldrop JVECC 2004) which states the most cases are neurologically normal by 48 hours post-arrest so therefore was enough time given to adequately assess neurological function (i.e. if they re-examined at 48 hours, would there have been such a difference between the two groups).

TIDAL VOLUME ON HYPERCARBIA AND/OR HYPOXIA:

Resuscitation 2004 Apr;61(1):23-7.
Arterial blood gases with 700 ml tidal volumes during out-of-hospital CPR.
Dorph E, Wik L, Steen PA.

The optimal tidal and minute ventilation during cardiopulmonary resuscitation (CPR) is not known. In the present study seven adult, non-traumatic, out-of-hospital cardiac arrest patients were intubated and mechanically ventilated at 12 min(-1) with 100% oxygen and a tidal volume of 700 ml (10 +/- 2 ml kg(-1)). Arterial blood gas samples were analysed after 6-8 min of unsuccessful resuscitation and mechanical ventilation. Mean PaCO2 was 5.2 +/- 1.3 kPa and mean PaO2 30.7 +/- 17.2 kPa. The patient with the highest (14 ml kg(-1)) and lowest (8 ml kg(-1)) tidal volumes per kg had the lowest and highest PaCO2 values of 2.6 and 6.8 kPa, respectively. Linear regression analysis confirmed a significant correlation between arterial pCO2 and tidal volume in ml/kg, r2 = 0.87. We conclude that aiming for an estimated ventilation of 10 ml kg(-1) tidal volume at frequency of 12 min(-1) might be expected to achieve normocapnia during ALS.
Key points: LOE 6, supportive, poor: Inclusion criteria of adult, sudden, non-traumatic out-of-hospital cardiac arrest patients without any period of return of spontaneous circulation. ABG was performed 6-8 minutes after initiation of mechanical ventilation during CPR. Inspiratory time of 1.25s and 100% oxygen at a rate of 12 breaths/min caused mean value normocapnia and no patient was hypoxic. Mean tidal volume was 694 +/- 10 ml and median estimated body weight was 75 kg so tidal volume approximately 10ml/kg.

Consistent sampling time, standardized throughout the study. Weaknesses of the paper is that only 7 patients and did not asses effect on survival.

INSPIRATORY TIME ON HYPOXIA AND/OR HYPOCARBIA
Resuscitation 2005;64(3):321-5.
Effects of decreasing inspiratory times during simulated bag-valve-mask ventilation.
Von Goedecke A, Bosden K, Wenzel V, Keller C. Gabrielli A.

During CPR, an inspiratory time of 2 s is recommended when the airway is unprotected; indicating that approximately 30% of the resuscitation attempt is spent on ventilation, but not on chest compressions. Since survival rates may not decrease when ventilation levels are relatively low, and uninterrupted chest compressions with a constant rate of approximately 100/min have been shown to be lifesaving, it may be beneficial to cut down the time spent on ventilation, and instead, increase the time for chest compressions. In an established bench model of a simulated unprotected airway, we evaluated if inspiratory time can be decreased from 2 to 1 s at different lower oesophageal sphincter pressure (LOSP) levels during ventilation with a bag-valve-mask device. In comparison with an inspiratory time of 2 s, 1 s resulted in significantly ($p < 0.001$) higher peak airway pressure and peak inspiratory flow rate, while lung tidal volumes at all LOSP levels were clinically comparable. Neither ventilation strategy produced stomach inflation at 20 cmH2O LOSP, and 1 s versus 2 s inspiratory time did not produce significantly higher (mean +/- S.D.) stomach inflation at 15 (8 +/-9 ml versus 0 +/- 0 ml; $p < 0.01$) and 10 cmH2O LOSP (69 +/- 20 ml versus 34 +/- 18 ml; $p < 0.001$), and significantly lower stomach inflation at 5 cmH2O LOSP (219 +/- 16 ml versus 308 +/- 21 ml; $p < 0.001$) per breath. Total cumulative stomach inflation volume over constantly decreasing LOSP levels with an inspiratory time of 2 s versus 1 s was higher (6820 ml versus 5920 ml). In conclusion, in this model of a simulated unprotected airway, a reduction of inspiratory time from 2 to 1 s resulted in a significant increase of peak airway pressure and peak inspiratory flow rate, while lung tidal volumes remained clinically comparable (up to approximately 15% difference), but statistically different due to the precise measurements. Theoretically, this may increase the time available for, and consequently the actual number of, chest compressions during CPR by approximately 25% without risking an excessive increase in stomach inflation.
Key points: LOE, supportive, poor: This is a laboratory experiment (i.e. model of simulated patient) suggesting that similar tidal volumes can be achieved with reduction of inspiratory time while not increasing risk of stomach inflation. The main problem is that it is relating inspiratory time to tidal volume and not oxygenation.

Anaesthesist 2006;55(6):629-34.
Ventilation of an unprotected airway: evaluation of a new peak-inspiratory-flow and airway-pressure-limiting bag-valve-mask.
Von Goedecke A, Paal P, Keller C, Voelckel WG, Herff H, Lindner KH, Wenzel V.

BACKGROUND:
Currently 30 chest compressions and 2 ventilations with an inspiratory time of 1 s are recommended during cardiopulmonary resuscitation with an unprotected airway, thus spending about 15% instead of 40% of resuscitation time on ventilation. Time could be gained for chest compressions when reducing inspiratory time from 2 s to 1 s, however, stomach inflation may increase as well.
METHODS:
In an established bench model we evaluated the effect of reducing inspiratory time from 2 s to 1 s at different lower oesophageal sphincter pressure (LOSP) levels using a novel peak inspiratory-flow and peak airway-pressure-limiting bag-valve-mask device (Smart-Bag).

RESULTS:
A reduction of inspiratory time from 2 s to 1 s resulted in significantly lower peak airway pressure with LOSP of 0.49 kPa (5 cm H2O), 0.98 kPa (10 cm H2O) and 1.47 kPa (15 cm H2O) and an increase with 1.96 kPa (20 cm H2O). Lung tidal volume was reduced with 1 s compared to 2 s. When reducing inspiratory time from 2 s to 1 s, stomach inflation occurred only at a LOSP of 0.49 kPa (5 cm H2O).
CONCLUSIONS:
In this model of a simulated unprotected airway, a reduction of inspiratory time from 2 s to 1 s using the Smart-Bag resulted in comparable inspiratory peak airway pressure and lower, but clinically comparable, lung tidal volume. Stomach inflation occurred only at a LOSP of 0.49 kPa (5 cm H2O), and was higher with an inspiratory time of 2 s vs 1 s.
Key points: LOE6, supportive, poor: Another laboratory style experiment suggesting that 1s of inspiratory time produced clinically similar tidal volumes and therefore theoretically oxygen levels (similar strengths and weaknesses to previous paper).

Anaesthesist 2009;58(7):686-90.
Effect of decreased inspiratory times on tidal volume. Bench model simulating cardiopulmonary resuscitation.
Herff H, Bosden K, Paal P, Mitterlechner T, von Goedecke A, Lindner KH, Wenzel V.

BACKGROUND:
During cardiopulmonary resuscitation (CPR) with a chest compression rate of 60-100/min the time for secure undisturbed ventilation in the chest decompression phase is only 0.3-0.5 s and it is unclear which tidal volumes could be delivered in such a short time.
OBJECTIVES:
Attempts were made to assess the tidal volumes that can be insufflated in such a short time window.
METHODS:
In a bench model tidal volumes were compared in simulated non-intubated and intubated patients employing an adult self-inflating bag-valve with inspiratory times of 0.25, 0.3, and 0.5 s. Respiratory system compliance values were 60 mL/cmH(2)O being representative for respiratory system conditions shortly after onset of cardiac arrest and 20 mL/cmH(2)O being representative for conditions after prolonged cardiac arrest.
RESULTS:
With a respiratory system compliance of 60 mL/cmH(2)O, tidal volumes (mean+/-SD) in non-intubated versus intubated patients were 144+/-13 mL versus 196+/-23 mL in 0.25 s ($p<0.01$), 178+/-10 versus 270+/-14 mL in 0.3 s ($p<0.01$), and 310+/-12 mL versus 466+/-20 mL in 0.5 s ($p<0.01$). With a respiratory system compliance of 20 mL/cmH(2)O, tidal volumes in non-intubated patient versus intubated patients were 128+/-10 mL versus 186+/-20 mL in 0.25 s ($p<0.01$), 158+/-17 versus 250+/-14 mL in 0.3 s ($p<0.01$) and 230+/-21 mL versus 395+/-20 mL in 0.5 s ($p<0.01$).
CONCLUSIONS:
Ventilation windows of 0.25, 0.3, and 0.5 s were too short to provide adequate tidal volumes in a simulated non-intubated cardiac arrest patient. In a simulated intubated cardiac arrest patient, ventilation windows of at least 0.5 s were necessary to provide adequate tidal volumes.
Key points: LOE6, supportive, poor: Bench top model again so still not ideal and in addition is assess effect on tidal volume not oxygen (which is obviously not possible given that it is a bench top model). However is best information available that shows reducing inspiratory time any shorter than 1 second provides inadequate tidal volume and therefore likely inadequate ventilation.

Anesth Analg 2008 Feb;106(2):535-7,

Minimizing stomach inflation versus optimizing chest compressions.
Herff H, Paal P, vonGoedecke A, Mitterlechner T, Danninger T, Wenzel V.

In a bench model, we evaluated a bag-valve device (Smart Bag MO) with limited maximum inspiratory gas flow developed to reduce the risk of stomach inflation in an unprotected airway. During simulated cardiopulmonary resuscitation with uninterrupted chest compressions, ventilation with the "disabled" Smart Bag MO or an adult self-inflating bag-valve device provided only adequate tidal volumes if inspiratory time was 0.5 s. Ventilation with the "enabled" Smart Bag MO, even in ventilation windows of 0.5 s, provided inadequate tidal volumes during simulated cardiopulmonary resuscitation and would result in hypoventilation in a patient.
Key points: LOE6, supportive, poor: Another bench top model and again the main limitation is that the inspiratory time is being equated to tidal volume and not oxygenation levels (which is not possible). However again supports the notion that inspiratory time of 1 second is the optimal time for CPR.

Circulation. 2004;109(16):1960-5
Hyperventilation-induced hypotension during cardiopulmonary resuscitation.
Aufderheide TP, Sigurdsson G, Pirrallo RG, Yannopoulos D, McKnite S, von Briesen C, Sparks CW, Conrad CJ, Provo TA, Lurie KG.

BACKGROUND: A clinical observational study revealed that rescuers consistently hyperventilated patients during out-of-hospital cardiopulmonary resuscitation (CPR). The objective of this study was to quantify the degree of excessive ventilation in humans and determine if comparable excessive ventilation rates during CPR in animals significantly decrease coronary perfusion pressure and survival.
METHODS AND RESULTS: In humans, ventilation rate and duration during CPR was electronically recorded by professional rescuers. In 13 consecutive adults (average age, 63+/-5.8 years) receiving CPR (7 men), average ventilation rate was 30+/-3.2 per minute (range, 15 to 49). Average duration per breath was 1.0+/-0.07 per second. No patient survived. Hemodynamics were studied in 9 pigs in cardiac arrest ventilated in random order with 12, 20, or 30 breaths per minute. Survival rates were then studied in 3 groups of 7 pigs in cardiac arrest that were ventilated at 12 breaths per minute (100% O2), 30 breaths per minute (100% O2), or 30 breaths per minute (5% CO2/95% O2). In animals treated with 12, 20, and 30 breaths per minute, the mean intrathoracic pressure (mm Hg/min) and coronary perfusion pressure (mm Hg) were 7.1+/-0.7, 11.6+/-0.7, 17.5+/-1.0 ($P<0.0001$), and 23.4+/-1.0, 19.5+/-1.8, and 16.9+/-1.8 ($P=0.03$), respectively. Survival rates were 6/7, 1/7, and 1/7 with 12, 30, and 30+ CO2 breaths per minute, respectively ($P=0.006$).
CONCLUSIONS: Professional rescuers were observed to excessively ventilate patients during out-of-hospital CPR. Subsequent animal studies demonstrated that similar excessive ventilation rates resulted in significantly increased intrathoracic pressure and markedly decreased coronary perfusion pressures and survival rates.
Key points: LOE6, supportive, poor: This study includes both clinical observation of adult human CPR and an experimental pig study. It found that hyperventilation is common during clinical CPR and that hyperventilation (RR of 30/min) in the experimental setting was associated with higher intrathoracic pressures, lower coronary perfusion pressure and lower survival compared to a RR of 12/min. The study numbers were small but methodology was otherwise good.

Resuscitation 2000 Feb;43(3):195-9.
Optimisation of tidal volumes given with self-inflatable bags without additional oxygen.
Dorges V, Ocker H, hagelberg S, Wenzel V, Schmucker P.

Abstract

The European Resuscitation Council has recommended smaller tidal volumes of 500 ml during basic life support ventilation in order to minimise gastric inflation. One method of delivering these tidal volumes may be to use paediatric instead of adult self-inflatable bags; however, we have demonstrated in other studies that only 350 ml may be delivered, using this technique. The reduced risk of gastric inflation was offset by oxygenation problems, rendering the strategy of attempting to deliver tidal volumes of 500 ml with a paediatric self-inflatable bag questionable, at least when using room-air. In this report, we assessed the effects of a self-inflatable bag with a size between the maximum size of a paediatric (700 ml) and an adult (1500 ml) self-inflatable bag on respiratory variables and blood gases during bag-valve-mask ventilation. After induction of anaesthesia, 50 patients were block-randomised into two groups of 25 each. They were ventilated with room-air with either an adult (maximum volume, 1500 ml) or a newly developed medium-size (maximum volume, 1100 ml; Dräger, Lübeck, Germany) self-inflatable bag for 5 min before intubation. When compared with the adult self-inflatable bag, the medium-size bag resulted in significantly lower exhaled tidal volumes and tidal volumes per kg bodyweight (624 + 24 versus 738 +/- 20 ml, and 8.5 +/- 0.3 versus 10.7 +/- 0.3 ml kg(-1), respectively; $P < 0.001$), oxygen saturation (95 +/- 0.4 versus 96 +/- 0.3%; $P < 0.05$), and partial pressure of oxygen (78 +/- 3 versus 87 +/- 3 mmHg; $P < 0.05$). Carbon dioxide levels were comparable (37 +/- 1 versus 37 +/- 1 mmHg). Our results indicate that smaller tidal volumes of about 8 ml x kg(-1) (approximately 600 ml), given with a new medium-size self-inflatable bag and room-air, maintained adequate carbon dioxide elimination and oxygenation during bag-valve-mask ventilation. Accordingly, the new medium-size self-inflatable bag may combine both adequate ventilatory support and reduced risk of gastric inflation during bag-valve-mask ventilation.

Key points: LOE6, neutral, poor: Was a human study in anesthetized patients and not CPR patients and therefore not the same population that we are attempting to study. In addition is bag-masking and not intubation and therefore the difference in tidal volumes is approximate rather than exact as we do not know how much of the air is being given oropharyngeal.

Resuscitation 2000 Jun;45(1):27-33.

Arterial blood-gases with 500- versus 1000-ml tidal volumes during out-of-hospital CPR.

Langhelle A, Sunde K, Wik L, Steen PA.

The correct tidal volume during cardiopulmonary resuscitation (CPR) is presently debated. While the European Resuscitation Council (ERC) and American Heart Association (AHA) previously recommended a tidal volume of 800-1200 ml, the ERC has recently reduced this to 400-600 ml. In a prospective, randomised study of 17 non-traumatic out-of-hospital cardiac arrest patients intubated and mechanically ventilated 12 min(-1) with 100% oxygen, we have therefore compared arterial blood gases generated with tidal volumes of 500 and 1000 ml. Mean time from cardiac arrest to arrival of the ambulance was 13+/-8 and 14+/-8 min in the two groups, respectively. Arterial blood samples were taken percutaneously 5 and 10-15 min after onset of the mechanical ventilation and analysed instantly. Pa(CO(2)) was significantly higher for a tidal volume of 500 than 1000 ml at both 5 and 10-15 min, 7.48+/-2.23 versus 3.70+/-0.83 kPa ($P=0.002$) and 7. 45+/-1.19 versus 3.98+/-1.58 kPa ($P<0.001$). The pH was lower for 500 than 1000 ml at 10-15 min, 7.01+/-0.10 versus 7.20+/-0.17 ($P=0.034$), with a strong trend in the same direction at 5 min ($P=0.06$). There was adequate oxygenation with no differences in Pa(O(2)) or BE at any time between the two groups, and no significant differences in any blood gas variables between the 5- and 10-15-min samples. We conclude that arterial normocapnia is not achieved with either tidal volume during advanced life support with non-rebreathing ventilation at 12 min(-1). What ventilation volume is required for CO(2) removal and oxygenation during basic life support with mouth-to-mouth ventilation cannot be extrapolated from the present data. In that situation the risk of gastric inflation, regurgitation and aspiration must also be taken into account.

Key points: LOE6, neutral, poor: All patients were intubated and mechanically ventilated. Based on estimated body weights, mean tidal volumes of 13 +/- 2 and 7 +/- 1 ml/kg were calculated for the 1000 and 500 ml groups respectively. Those ventilated with 100% O2 at 12/min, tidal volume resulted in stable arterial hypercapnia, 1000 ml in stable hypocapnia, both without hypoxia. Based on this study, neither tidal volume is likely to achieve normocapnia with non-breathing ventilation.

Resuscitation 2000;44(1):37-41.
Smaller tidal volumes with room-air are not sufficient to ensure adequate oxygenation during bag-valve-mask ventilation.
Dorges V, Ocker H, Hagelberg S, Wenzel V, idris AH, Schmucker P.

The European Resuscitation Council has recommended decreasing tidal volume during basic life support ventilation from 800 to 1200 ml, as recommended by the American Heart Association, to 500 ml in order to minimise stomach inflation. However, if oxygen is not available at the scene of an emergency, and small tidal volumes are given during basic life support ventilation with a paediatric self-inflatable bag and room-air (21% oxygen), insufficient oxygenation and/or inadequate ventilation may result. When apnoea occurred after induction of anaesthesia, 40 patients were randomly allocated to room-air ventilation with either an adult (maximum volume, 1500 ml) or paediatric (maximum volume, 700 ml) self-inflatable bag for 5 min before intubation. When using an adult (n=20) versus paediatric (n=20) self-inflatable bag, mean +/-SEM tidal volumes and tidal volumes per kilogram were significantly (P<0.0001) larger (719+/-22 vs. 455+/-23 ml and 10.5+/-0.4 vs. 6.2+/-0.4 ml kg(-1), respectively). Compared with an adult self-inflatable bag, bag-valve-mask ventilation with room-air using a paediatric self-inflatable bag resulted in significantly (P<0.01) lower paO(2) values (73+/-4 vs. 87+/-4 mmHg), but comparable carbon dioxide elimination (40+/-2 vs. 37+/-1 mmHg; NS). In conclusion, our results indicate that smaller tidal volumes of approximately 6 ml kg(-1) (approximately 500 ml) given with a paediatric self-inflatable bag and room-air maintain adequate carbon dioxide elimination, but do not result in sufficient oxygenation during bag-valve-mask ventilation. Thus, if small (6 ml kg(-1)) tidal volumes are being used during bag-valve-mask ventilation, additional oxygen is necessary. Accordingly, when additional oxygen during bag-valve-mask ventilation is not available, only large tidal volumes of approximately 11 ml kg(-1) were able to maintain both sufficient oxygenation and carbon dioxide elimination.
Key points: LOE6, supportive, poor: Human study and in anesthetic patients and not patients with CPR so again not the ideal study. The other problem again is that this is bag valve mask technique so again it is unclear how much of the tidal volume is actually being deliver to the lung and how much is being delivered to the stomach. It does suggest that 11 ml/kg provides more optimal delivery than 6 ml/kg which doesn't prove per se that 10 ml/kg is the optimal tidal volume but obviously it is very similar in volume.

Resuscitation 1999;43(1):25-9.
Effects of smaller tidal volumes during basic life support ventilation in patients with respiratory arrest: good ventilation, less risk?
Wenzel V, Keller C, Idris Ah, Dorges V, lindner KH, Brimacombe JR.

OBJECTIVE:
When ventilating an unintubated patient in cardiac or respiratory arrest, smaller tidal volumes of 500 ml instead of 800-1200 ml may be beneficial to decrease peak airway pressure, and to minimise stomach inflation. The purpose was to determine the effects of small (approximately 500 ml) versus large (approximately 1000 ml) tidal volumes given with paediatric versus adult self-inflatable bags and approximately 50% oxygen on respiratory parameters in patients during simulated basic life support ventilation.
METHODS:

While undergoing induction of anaesthesia, patients were randomised to three minutes of ventilation with either an adult (n = 40) or paediatric (n = 40) self-inflatable bag.
RESULTS:
When compared with an adult self-inflatable bag, the paediatric bag resulted in significantly lower mean (+/- standard deviation) exhaled tidal volume (365 +/- 55 versus 779 +/- 122 ml; P < 0.0001), peak airway pressure (20 +/- 2 versus 25 +/- 5 cm H2O; P < 0.0001), but comparable oxygen saturation (97 +/- 1% versus 98 +/- 1%; NS (nonsignificant)). Stomach inflation occurred in five of 40 patients ventilated with an adult self-inflatable bag, but in no patients who were ventilated with a paediatric self-inflatable bag (P = 0.054).
CONCLUSION:
Administering smaller tidal volumes with a paediatric instead of an adult self-inflatable bag in unintubated adult patients with respiratory arrest maintains good oxygenation and carbon dioxide elimination while decreasing peak airway pressure, which makes stomach inflation less likely.
Key points: LOE6, opposing, poor: Prospective clinical study in anaesthetized patients, not in cardiac arrest. Reasonably good numbers (80 patients total). Two blocks of 50 SAS I and ASA II patients each, block randomized. Reduced tidal volume resulted in higher respiratory rate (15+/-4 vs 22 +/- 3), end-tidal CO2 (26 +/- 8 mm Hg vs 33 +/- 6 mm Hg), lower exhaled tidal volume (779 +/- 122 ml vs 365 +/- 55 ml), lower peak airway pressure (25 +/- 5 cm H_2O vs 20 +/- 2 cm H_2O) and similar O2 saturation (98% +/-1 vs 97% +/-1). Stomach inflation occurred in 5/40 patients with larger tidal volumes vs 0/40 with smaller tidal volumes although not significant (p = 0.054). Did not measure inspiratory time or peak flow rate. Patients were ventilated with 50% oxygen but not room air (21% O2) or mouth-to-mouth ventilation (16% O2 and 4% CO2)

Resuscitation 2008;77(1):35-8.
Arterial blood gases during basic life support of human cardiac arrest victims.
Pytte M, Dorph E, Sunde K, Kramer-Johansen J, Wik L, Steen PA. .

BACKGROUND:
Ventilation with tidal volumes sufficient to raise the victim's chest is an integral part of guidelines for lay-rescuer basic life support, but optimal tidal volume, frequency and ratio to chest compressions are not known.
METHODS:
Adults with non-traumatic, out-of-hospital cardiac arrest, who were not successfully resuscitated following advanced life support by the staff of a physician-manned ambulance, were included. Advanced life support comprised tracheal intubation and mechanical ventilation with tidal volume of 700 ml and 100% oxygen, 12 times per min. An arterial blood sample was drawn at the end of the resuscitation attempt and analysed on the scene. After the victim was declared dead, basic life support was initiated with chest compressions and mouth-to-mask or mouth-to-tracheal tube ventilation (15:2), with volumes sufficient to make the chest rise. The tracheal tube was equipped with an impedance valve to avoid passive ventilation secondary to chest compressions. Arterial blood samples were drawn after 7-8 min of basic life support and analysed on the scene.
RESULTS:
Six men and two women, median (range) age 72 (32-86) years, were included in the study. Four of these received mouth-to-mask ventilation and four mouth-to-tracheal tube ventilation. Mean (S.D.) arterial blood carbon dioxide and oxygen tension during advanced life support were 6.4 (1.4)kPa and 22 (15)kPa, respectively. Similar values during basic life support were 9.6 (1.9)kPa and 8.5 (1.6)kPa, respectively, with no differences between the ventilation methods.
CONCLUSION: .
Ventilation during basic life support performed according to international guidelines (2000) resulted in arterial hypercapnia and hypoxia.

Key points: LOE6, opposing, poor: Tidal volume of 700 ml was used with frequency of 12 ventilations/min and 100% O2. Arterial blood sample was drawn at end of resuscitation attempt. (7-8 minutes of resuscitation). Median age was 72 years, ventricular fibrillation most common rhythm. Very small sample size and inconsistent ventilation means (there were 4 in each group).