WORKSHEET for Evidence-Based Review of Science for Veterinary CPCR

1. Basic Demographics

Worksheet author(s)

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[redacted]

2. Clinical question:

For dogs and cats requiring resuscitation (P), does the use of physiological feedback regarding CPR quality (e.g. EtCO2 monitoring) (I) compared with no feedback (C), improve any outcomes (eg. ROSC, survival) (O)?

3. Conflict of interest specific to this question:

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? None

4. Search strategy (including electronic databases searched):

4a. Databases

-MEDLINE via PUBMED

1-cardiopulmonary resuscitation **Limits Activated:** Animals, Clinical Trial, English, MEDLINE, Veterinary Science, Publication Date from 1950/01/01 to 2011/03/01: 20 hits: 0 relevant

2- cardiopulmonary resuscitation monitoring **Limits Activated:** Animals, Clinical Trial, English, MEDLINE, Veterinary Science, Publication Date from 1950/01/01 to 2011/03/01: 0 results

3-cardiopulmonary resuscitation monitoring **Limits Activated:** Humans, Animals, Clinical Trial, English, MEDLINE, Veterinary Science, Publication Date from 1950/01/01 to 2011/03/01: 20 hits: 2 relevant

4- cardiopulmonary resuscitation monitoring **Limits Activated:** Humans, Animals, Clinical Trial, English, MEDLINE: 20 hits, 2 relevant

5-cardiopulmonary arrest end tidal carbon dioxide **Limits Activated:** Humans, Animals, Clinical Trial, English, MEDLINE, Publication Date from 1950/01/01 to 2011/03/01 15 hits, 0 relevant

-PUBMED
6-cardiopulmonary arrest end tidal carbon dioxide pub med search, all years: 142 hits, 23 relevant

7-cardiopulmonary arrest SVO2 monitoring pub med search, all years: 7 hits, 0 relevant

8-cardiopulmonary arrest venous oxygenation monitoring, pub med search, all years: 16 hit, 1 relevant

4b. Other sources

-GOOGLE SCHOLAR (performed on August 5th 2010): cardiopulmonary arrest end tidal carbon dioxide veterinary "veterinary": 982 hits, 8 relevant

-VIN journal abstract search (performed on April 5th 2011): cardiopulmonary resuscitation monitoring: 45 hits, 5 are relevant.

-In addition all references of identified articles and in particular the references of the following relevant review articles were examined:

Cardiopulmonary Resuscitation in Small Animal Medicine: An Update S.J. Plunkett and M. McMichael
J Vet Intern Med 2008;22:9–25: 11 relevant references

Prognostic indicators for dogs and cats with cardiopulmonary arrest treated by cardiopulmonary cerebral resuscitation at a university teaching hospital Erik H. Hofmeister, Benjamin M. Brainard, Christine M. Egger, Sangwook Kang
JAVMA July 1, 2009 (Vol 235; No. 1: pp. 6-88): 8 relevant references

Cardiopulmonary Cerebral Resuscitation: Techniques. Steven Marks,Sarah Haldane,Jennifer Campbell
Compendium October 2004;26(10):780-790: 8 relevant references

AHA CPR guidelines 36 relevant references

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

Inclusion criteria:
Randomized controlled studies
Veterinary or Human data
Peer reviewed journals
Related to monitoring in cardiopulmonary resuscitation

Exclusion criteria
Review articles: 2
Non target species studies without controls: 31
Abstract only/ Full article not accessible: 54
Unknown journal: 2
Monitoring system not routinely available in veterinary medicine::3
Model used does not simulate cardiac arrest or is inappropriate: 2
Monitoring was instituted after CPCR: 1
Repeated: 3

4d. Number of articles/sources meeting criteria for further review: 6
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-One relevant non target species study: (Gazmuri, von Planta, et.al. 1989)
-Four relevant experimental studies in the target species: (Kern , Sanders et.al. 1989)), (Blumenthal, Voorhees 1997), (Bhende, Karasic et.al. 1995), (Angelos, DeBehnke, et.al 1992)
-One observational study in the target species: (Hofmeister, Brainard, et.al. 2009)

5. Summary of evidence

Evidence Supporting Clinical Question

Good			Angelos 1992; A		Hofmeister 2009; AC	
Fair						
Poor			Kern 1989; A. Blumenthal 1997; A. Bhende 1995; A.			*Gazmuri 1989; A*
	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						
	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						
	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:

Many monitoring techniques have been used in the treatment of cardiopulmonary arrest (CPA) to try and determine effectiveness of therapy and likelihood of a positive outcome. Evidence in support of this approach is derived from animal (dog and pig) models using ventricular fibrillation (VF) or asphyxiation (ASP) to induce CPA and observational studies. Randomized controlled clinical trials are lacking.

Only one veterinary study is available that provides information on prognostic indicators for CPA in dogs and cats undergoing non-experimental arrests (Hofmeister et.al. 2009). The authors found that the mean highest recorded ETCO2 was significantly higher in dogs that were successfully resuscitated than those that were not, this difference was not found in cats. In dogs, 94% of the non-successful cases had an ETCO2 of <15 mm Hg, whereas 86% with values ≥15 mmHg had return of spontaneous circulation (ROSC). 90% of cats with an ETCO2 of ≥ 20 mm Hg had ROSC, while only 55% of those with values <20 mmHg did. Kern et. al. (1989) used an experimental VF dog model to evaluate ETCO2 as a prognostic guide for resuscitation as well with a 1 week follow up period. Six of fifteen dogs had ROSC and 5 of these survived and were neurologically normal during the 1week follow up period. There was a significant decline in ETCO2 values over time during CPR in the non-resuscitated group while values remained constant in the resuscitated group during this period. An arbitrarily chosen ETCO2 value of ≥ 6 mmHg was found to have a positive predictive value of 75% and values < 6 mmHg had a negative predictive value of 80%. ETCO2 was also significantly correlated (r= .306) to measured coronary perfusion pressure (CoPP) (which was found to be a good predictor of outcome). The differences in ETCO2 in this study only became evident at the 14 min time point and were not significantly different at the 2, 7 and 12 minute time points. A pediatric dog model of CPA using ASP evaluated the correlation between ETCO2 and a colormetric CO2 detector (Bhende et.al. 1995). The authors found a mean ETCO2 of 12.37 +/- 3.54 mmHg during resuscitation and a sudden increase to 27 +/- 7.22 at or just prior to ROSC, all 11 puppies had ROSC; however investigating ETCO2 levels was not the primary goal of this study, but rather to investigate a color-change ETCO2 monitor. A porcine model of CPA induced by VF showed significantly higher ETCO2 and PaCO2 values in resuscitated animals (14/23) with ETCO2 values exceeding pre arrest levels (Gazmuri et.al. 1989). Changes in ETCO2 and PaCO2 were parallel and both correlated with CoPP. Blumenthal et. al (1997) measured airway CO2 and PaCo2 changes in dogs with experimental CPA by VF. They took measurements at different compression forces and reported CO2 and CO2 excretion (CO2Ex) based on a given equation. Respiration variables were held constant so that CO2Ex would be determined only by production and delivery to the lungs. Airway CO2 decreased from baseline during CPA and altering the force of compression could change the airway CO2 in the same direction. CO2 excretion during CPR was lower than during non-arrest periods. CO2Ex was significantly correlated with cardiac output during CPR (r =0.62)

Experimental research in dogs by Angelos et. al. (1992) used three different techniques of resuscitation (standard external CPR with advanced life support, closed chest cardiopulmonary bypass and open chest CPR) to evaluate arterial pH and CO2. All animals developed a respiratory alkalosis after induction of VF. Eventual survivors from all groups (16/24) were noted to have a significantly lower pH and higher PaCO2 and base deficits during CPA. All three variables were significantly correlated to coronary artery perfusion pressure.

These studies clearly indicate that there is a fall in ETCO2 during CPA and suggest when a higher level of ETCO2 during CPR is obtained, that the likelihood of ROSC and survival increase. A sudden marked increase in ETCO2, which may surpass the pre arrest level, is indicative of ROSC. There is minimal clinical data on dogs and even less in cats however, it appears that reaching ETCO2 levels of at least 15 mmHg in dogs and 20 mmHg in cats is indicative or ROSC during CPR. Although an increase in PaCO2 and decrease in arterial pH

were significant findings in CPA survivors in one study arterial blood sampling is not commonly available in the clinical setting. The time and skill necessary to set up and use ETCO2 monitors is minimal while arterial sampling is time consuming and includes the risk of hemorrhage. Given the paucity of data and possible complications arterial sampling is not recommended as a routine monitoring technique in clinical veterinary CPR.

7. Conclusion

Consensus on Science:
Evidence from one prospective observational study in dogs (LOE 5) and supportive evidence from one other study in this species (LOE 3) document that ETCO2 monitoring has prognostic significance in regards to ROSC. Two other experimental studies in dogs (LOE 3) and one in pigs (LOE 6) have demonstrated an increase in ETCO2 once ROSC was achieved. Evidence from two of these studies (LOE 3-6) have shown ETCO2 values correlate with CoPP. One randomized experimental study in dogs (LOE 3) provides evidence that lower arterial pH and higher PaCO2 and base deficits occur during CPA. All three variables were significantly correlated to coronary artery perfusion pressure. In addition, several of these studies (LOE 3-6) demonstrated that an increase in ETCO2 may predict resuscitation outcome.

Treatment Recommendations:
End-tidal CO2 does provide valuable physiologic feedback during CPCR and, when ventilation is held constant, may provide evidence or ROSC and survivability. ETCO2 monitoring should be used in all CPCR attempts; an ETCO2 of at least 15mmHg in dogs and 20 mmHg in cats is indicative of ROSC.
If an arterial catheter is already in place and blood sampling is easily possible then monitoring trends in pH, PaCO2, and base deficit may be helpful guides of CoPP and the quality of CPR being provided.

8. Acknowledgement

None

9. Citation list

Angelos, M.G., D.J. DeBehnke, J.E. Leasure. (1992). "Arterial pH and carbon dioxide tension as indicators of tissue perfusion during cardiac arrest in a canine model." Critical care medicine 20 (9): 1302-08.
Abstract
BACKGROUND AND METHODS:
Previous studies have shown that Paco2 and end-tidal CO2 reflect coronary artery perfusion pressures during cardiac arrest. We investigated the relationship of coronary artery perfusion pressure to central arterial pH and Paco2 values during resuscitation from cardiac arrest in a canine model. Twenty-four mongrel dogs were block randomized to three different resuscitation groups after induction of ventricular fibrillation and cardiac arrest: a) standard cardiopulmonary resuscitation (CPR) and advanced life support (n = 8); b) cardiopulmonary bypass (n = 8); or c) open-chest CPR (n = 8). Central arterial blood gases and perfusion pressures were monitored during cardiac arrest and during resuscitation.
RESULTS:
Prearrest blood gases and hemodynamic values were similar between groups. Sixteen dogs from all three groups were successfully resuscitated. Survivors had significantly higher coronary artery perfusion pressure (p = .03), Paco2 (p = .015), and lower pH (p = .01) values than nonsurvivors. There was no correlation of pH and Paco2 during mechanical external CPR. However, after institution of the different resuscitation techniques, pH and Paco2 each showed a statistically significant correlation (r2 = .50 and .33, respectively) with coronary artery perfusion pressure.
CONCLUSIONS:
Central arterial pH and Paco2 monitoring during cardiac arrest may reflect the adequacy of tissue perfusion during resuscitation and may predict resuscitation outcome from ventricular fibrillation.

LOE 3 good quality, supportive, funding: Emergency Medicine Foundation/Carl Jelenko Research Award and the Kettering Medical Center Research Fund.
Summary: The importance of arterial blood gas sampling in CPA is controversial. It used to be the gold standard but studies have shown discrepancies between arterial and venous pH and PCO2. Took 24 mixed breed dogs and induced CPA via coronary artery occlusion and then ventricular fibrillation. There was no resuscitation for the first 4 minutes, 4-12 min consisted of chest compression with a ACD, at 12 min one of the 3 resuscitation techniques were implemented. Initial defibrillation attempts were first made at 14 min and followed a given protocol if not successful. All animals were accounted for. pH, PaO2, PaCO2, MAP, HR, CoPP and temp were measured, ROSC was clearly defined. Do not state what happened to the animals at the end of the study.

Bhende, M.S., D.G. Karasic, J.J. Menegazzi. (1995). "Evaluation of an end-tidal CO2 detector during cardiopulmonary resuscitation in a canine model for pediatric cardiac arrest." Pediatric emergency care 11(6): 365-68.
Abstract
Our objective was to evaluate a colorimetric end-tidal CO2 detector in a canine model for pediatric cardiac arrest. In a prospective unblinded study, cardiac arrest was induced in 11 anesthetized and paralyzed puppies, weighing 5.0 to 6.1 kg, by clamping the endotracheal tube (ETT) and discontinuing mechanical ventilation. During cardiopulmonary resuscitation (CPR), the detector and the capnometer were connected between the ETT and ventilator tubing. Color shades on the detector ranged from 1 (purple) to 6 (yellow) corresponding to increasing concentrations of CO2. End-tidal CO2 concentrations as indicated by detector color and capnometric reading were monitored and recorded throughout the study. The results showed that there was a significant correlation between the detector color score and capnometric readings ($P < 0.001$). A sudden rise in end-tidal CO2 indicated by both the capnometer and the detector occurred at return of spontaneous circulation (ROSC) in seven or < 1 minute before ROSC in four animals. This association was significant ($P = 0.0009$). We conclude that these results demonstrate that, in a canine model for pediatric cardiac arrest, the detector readings correlate with capnometry during CPR and indicate ROSC.
LOE 3, poor, supportive, funding: not mentioned.
Summary: They wanted to compare a portable ETCO2 detector with a capnometer. 11 4-5 month old puppies, breed not mentioned, weighed between 5-6.1 kg. Pancuronium was given while under halothane anesthesia for an unknown reason. Implemented asphyxiation by obstructing the endotracheal tube. They used a CPR protocol from another concurrently timed study, the protocol is not given in this paper. All puppies were accounted for and ROSC was clearly defined. Capnograph readings were every minute. Other variables were measured pre arrest, unclear if measured during/after arrest as not stated or reported. Do not state what happened to the animals at the end of the study.

Blumenthal, S. R., W.D. Voorhees. (1997) "The relationship between airway carbon dioxide excretion and cardiac output during cardiopulmonary resuscitation." Resuscitation 35(2):135-43.
Abstract
Currently, there are no practical means of prospectively determining cardiopulmonary resuscitation (CPR) adequacy in the field. Airway CO2 excretion can be noninvasively and stably measured under changing environmental conditions. We investigated the relationships between the volume of airway CO2 excreted (CO2EX) during CPR to regional blood flow (RBF) and survival. A total of 21 dogs were randomly divided into four CO2EX groups (< 5, 5-6, > 6-7 and > 7 ml CO2/min per kg), anesthetized, instrumented and ventilated with an in-line infrared airway CO2 sensor. Anesthesia was reduced and baseline measurements made. Ventricular fibrillation (VF) was initiated and resuscitation withheld for 3 min, followed by 17 min of CPR. Compression force alone was adjusted to maintain predetermined CO2EX. Animals were resuscitated, monitored for 2 h and observed for an additional 22 h. RBF was determined at baseline, 16 min post-VF and 60 min post-resuscitation. Mean CO2EX during CPR was significantly higher in survivors than nonsurvivors. The probability of survival increased as CO2EX increased. The highest CO2EX group had the highest rate of survival (86%), but did not always have significantly higher cardiac output (CO), myocardial or cerebral blood flows (MBF, CBF) than the lowest CO2EX group with a 0% survival rate. These data suggest survival is tracked better by CO2EX

than by CO, MBF or CBF. Therefore, CO2EX appears to provide a practical reliable noninvasive method of determining CPR efficacy in the field.
LOE 3, poor, supportive, funding: American Heart Association, Indiana Affiliate and the David Ross Foundation.
Summary: Wanted to identify a parameter that would indicate the metabolic state and dynamic state of the cardiovascular system in CPA that could also be used in the field. CO2 excretion is the complement of O2 consumption (which cannot be measured easily in the field). 13 mixed breed dogs. Used a weight based nomogram to set tidal volume. Ventricullar fibrillation was used to induce CPA and CPR was immediately started. An ACD was used at different randomly chosen compression forces, these forces are not reported. When the airway PCO2 was stable cardiac output measures were made. After 4 measurements the animal was defibrillated and resuscitated. There is no report of outcome of resucitation, if any dog did not survive. ROSC is not clearly defined. Do not state what happened to the animals at the end of the study.

Gazmuri, R.J., M. von Planta, M.H.Weil, E.C. Rackow. (1989) "Arterial PCO2 as an indicator of systemic perfusion during cardiopulmonary resuscitation." Crit Care Med 17(3):237-40.
Abstract
End-tidal PCO2 (PetCO2) is a quantitative indicator of pulmonary blood flow generated by precordial compression and therefore predicts resuscitability during CPR. A striking increase in PetCO2 follows return of spontaneous circulation. Since PaCO2 is closely related to alveolar PCO2 (PACO2) and therefore PetCO2, we hypothesized that PaCO2 may itself serve as an indicator of the blood flow generated during CPR. In a porcine model of cardiac arrest, PaCO2 during precordial compression was highly correlated with PetCO2 (r = .89), cardiac output (r = .72), and coronary perfusion pressure (CPP) (r = .74). In 14 successfully resuscitated animals, PaCO2, PetCO2, and CPP during precordial compression were significantly higher than in nine nonresuscitated animals. After restoration of spontaneous circulation, there was a marked increase in PaCO2 to levels exceeding control values, which corresponded to the sharp increase in PetCO2 that is characteristic of successful resuscitation. We therefore confirm that both PetCO2 and PaCO2 correspond to the pulmonary blood flow and therefore cardiac output which is generated by precordial compression during CPR. Moreover, both serve as prognosticators of cardiac resuscitability and early indicators that spontaneous circulation has been restored.
LOE 6, poor, supportive, funding: American Heart Association, the National Institutes of Health and the Laerdal Foundation of Oslo. Dr. vo Planta is supported by a grant from the Swiss National Science Foundation.
Summary: Investigated whether PaCO2 could be an indicator of blood flow generated in CPR. They used 23 minature pigs and induced CPA with ventricular fibrillation. As part of another study, sodium bicarbonate, sodium carbonate or sodium chloride was given but there is no mention of how this was chosen and if randomly assigned. All other treatments during CPR had the same protocol. All animals are accounted for. 14 pigs had ROSC but they do not define what that is although they use unsuccessful defibrillation (after the first attempt) as an indication to continue to countershock at 30 s interval up to 3 times. Changes in PaCO2 and ETCO2 were altered transiently by buffers. No mention on what happened to the animals at the end of the study.

Hofmeister, Erik H Brainard, Benjamin M Egger, Christine M Kang, Sangwook. (2009) "Prognostic indicators for dogs and cats with cardiopulmonary arrest treated by cardiopulmonary cerebral resuscitation at a university teaching hospital." J Am Vet Med Assoc 235(1):50-7.
Abstract
OBJECTIVE:
To determine the association among signalment, health status, other clinical variables, and treatments and events during cardiopulmonary cerebral resuscitation (CPCR) with the return of spontaneous circulation (ROSC) for animals with cardiopulmonary arrest (CPA) in a veterinary teaching hospital.
DESIGN:
Cross-sectional study.
ANIMALS:

161 dogs and 43 cats with CPA.
PROCEDURES:
Data were gathered during a 60-month period on animals that had CPA and underwent CPCR. Logistic regression was used to evaluate effects of multiple predictors for ROSC.
RESULTS:
56 (35%) dogs and 19 (44%) cats had successful CPCR. Twelve (6%) animals (9 dogs and 3 cats) were discharged from the hospital. Successfully resuscitated dogs were significantly more likely to have been treated with mannitol, lidocaine, fluids, dopamine, corticosteroids, or vasopressin; had CPA while anesthetized; received chest compressions while positioned in lateral recumbency; and had a suspected cause of CPA other than hemorrhage or anemia, shock, hypoxemia, multiple organ dysfunction syndrome, cerebral trauma, malignant arrhythmia, or an anaphylactoid reaction and were less likely to have been treated with multiple doses of epinephrine, had a longer duration of CPA, or had multiple disease conditions, compared with findings in dogs that were not successfully resuscitated. Successfully resuscitated cats were significantly more likely to have had more people participate in CPCR and less likely to have had shock as the suspected cause of CPA, compared with findings in cats that were not successfully resuscitated.
CONCLUSIONS AND CLINICAL RELEVANCE:
The prognosis was grave for animals with CPA, except for those that had CPA while anesthetized.
LOE 5, good, supportive, funding: none listed.
Summary: Prospectively collected clinical cases that had clearly defined inclusion criteria. No specific interventions were instituted as part of the study. Data collected was based on a questionnaire answered during the CPCR event by the person running the code or their assistant (nurse). Changes in available monitors (ETCO2) and staffing (CC service) that occurred during the data collection period were noted. All animals were accounted for.

Kern, K.B.,, A.B. Sanders, W.D.Voorhees, C.F. Babbs, W.A. Tacker, G.A. Ewy. (1989) “Changes in expired end-tidal carbon dioxide during cardiopulmonary resuscitation in dogs: a prognostic guide for resuscitation efforts.” J Am Coll Cardiol 13(5):1184-9.
Abstract
Expired end-tidal carbon dioxide (PCO2) measurements made during cardiopulmonary resuscitation have correlated with cardiac output and coronary perfusion pressure when wide ranges of blood flow are included. The utility of such measurements for predicting resuscitation outcome during the low flow state associated with closed chest cardiopulmonary resuscitation remains uncertain. Expired end-tidal PCO2 and coronary perfusion pressures were measured in 15 mongrel dogs undergoing 15 min of closed chest cardiopulmonary resuscitation after a 3 min period of untreated ventricular fibrillation. In six successfully resuscitated dogs, the mean expired end-tidal PCO2 was significantly higher than that in nine nonresuscitated dogs only after 14 min of cardiopulmonary resuscitation (6.2 +/- 1.2 versus 3.4 +/- 0.8 mm Hg; p less than 0.05). No differences in expired end-tidal PCO2 values were found at 2, 7 or 12 min of cardiopulmonary resuscitation. A significant decline in end-tidal PCO2 levels during the resuscitation effort was seen in the nonresuscitated group (from 6.3 +/- 0.8 to 3.4 +/- 0.8 mm Hg; p less than 0.05); the successfully resuscitated group had constant PCO2 levels throughout the 15 min of cardiac arrest (from 6.8 +/- 1.1 to 6.2 +/- 1.2 mm Hg). Changes in expired PCO2 levels during cardiopulmonary resuscitation may be a useful noninvasive predictor of successful resuscitation and survival from cardiac arrest.
LOE 3, poor, supportive, fundingAmerican Heart Association, Flinn Foundation, and the National Heart, Lung, and Blood Institute.
Summary: Examined changes in ETCO2 and its prognostic usefulness in dogs during CPR. Fifteen mixed breed dogs. CPA was induced with ventricular fibrillation while under light general anesthesia. Protocol follwoed was clearly defined and was the same for all dogs. ROSC was clearly defined. Surviving animals were monitored for up to 7 days after. At that point any alive dog was euthanized- do not say how. Six dogs were resuscitated and five survived the 7 day period, they do not say what happened to the sixth dog.