WORKSHEET for Evidence-Based Review of Science for Veterinary CPCR

1. Basic Demographics

Worksheet author(s)

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[redacted]

2. Clinical question:

In dogs and cats in cardiac arrest (P), does the use of $EtCO_2$ (I), compared with clinical assessment (C), improve accuracy of diagnosis of a perfusing rhythm (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? NO

4. Search strategy (including electronic databases searched):

4a. Databases

-MEDLINE via PUBMED (Searched on 17 Apr 2011, no date limitations)

1. end tidal co2 cardiac arrest 10 hits (**Limits Activated:** Humans, Animals, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, English, MEDLINE, Veterinary Science)

2 arrest rhythm diagnosis 121 hits (**Limits Activated:** Humans, Animals, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, English, MEDLINE, Veterinary Science)

3. (end tidal co2[Title/Abstract]) and (rhythm[Title/Abstract]) 3 hits

4. cardiopulmonary resuscitation AND co2 OR carbon dioxide 9 hits (**Limits Activated:** Humans, Animals, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, English, MEDLINE, Veterinary Science)

-CAB (Searched 17 Apr 2011, no date limitations)

1. (cardiac arrest) AND (end tidal) 3 hits

2. (cardiac arrest) AND (rhythm) 58 hits

3. (cardiopulmonary resuscitation) AND (end tidal) 0 hits

4b. Other sources

-GOOGLE SCHOLAR (searched on 18 Apr 2011)

End tidal CO2 cardiac arrest veterinary 1060 hits (words appear in any order)

End tidal CO2 ECG rhythm diagnosis veterinary 285 hits

End tidal CO2 ECG rhythm diagnosis 1600 hits

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

Plunkett SJ, McMichael M. Cardiopulmonary resuscitation in small animal medicine: an update. J Vet Intern Med. 2008;22(1):9-25

Hand-checked references of ILCOR worksheet PEDS-005, which addresses this question in pediatrics.

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

Inclusion criteria for studies

- Clinical or experimental studies
- Peer-reviewed journal
- Animal studies or human studies
- Total of XXX studies selected

Exclusion criteria

- Review articles (aside from article listed in previous question)
- Short communications
- Letters to the editor
- Case reports/short case series
- Conference proceedings

5. Summary of evidence

Evidence Supporting Clinical Question

Good					Hofmiester et al, 2009 (A,C) dog/cat	
Fair			*Kolar et al, 2008 (A)humans*			
Poor			Kern et al, 1994 (A,D) dog Bhande et al, 1995 (A) dog *Chalak et al, 2011 (A,E) porcine*			
	1	**2**	**3**	**4**	**5**	**6**
Level of evidence (P)						

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint

B = Survival of event D = Intact neurological survival *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 C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival *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:

In recent years, the use of etCO2 as a tool to predict ROSC in humans has been studied extensively. In a paper by Kolar et al, 737 patients were prospectively studied in out-of-hospital cardiac arrest. End-tidal CO2 was monitored for the first 20 minutes of CPR and ROSC was the outcome. The authors found that an etCO2 <14.3 mmHg after 20 minutes of CPR accurately predicts death (provided a non-shockable rhythm is present). Furthermore, an etCO2 <11.3 mmHg after 20 minutes or 13.5 mmHg after 15 minutes was incompatible with ROSC. No person with etCO2 <10mmHg was successfully resuscitated. While this paper is not targeted towards veterinary medicine, the results are dramatic and consistent with the dozens of other studies evaluating etCO2 during human CPR.

In an experimental dog model of ventricular fibrillation arrest, Kern et al discovered that dogs who could not be successfully resuscitated had progressively decreasing etCO2 levels throughout the CPR attempt, and statistical significance between survivors and nonsurvivors was achieved at 14 minutes of CPR and an arbitrary value of ≥6 mmHg etCO2 was associated with ROSC. This paper also evaluated neurological outcome and followed the dogs for one week after the arrest episode. 6/15 dogs had ROSC following CPR, and 5 of them survived one week and were neurologically normal.

Behande et al reported a study using etCO2 to validate a colorimetric device for CO2 measurement. While ROSC or survival was not the objective of the initial study, the authors noted that there was a sharp increase in the etCO2 values at the onset of ROSC (from a mean of approximately 14 mmHg to 27 mmHg), and this was published as a separate paper cited here. All puppies used in the study were successfully resuscitated following an asphyxiation model of cardiac arrest.

A single veterinary article (Hofmeister et al) evaluated etCO2 levels as a prognostic indicator in dogs and cats undergoing CPR for naturally occurring cardiopulmonary arrest. In this paper, the arrest events occurred secondary to various causes, ranging from anesthetic-related arrest in otherwise healthy animals to cardiopulmonary arrest occurring as the terminal process of a critical systemic illness. In dogs, a statistically significant difference was found between etCO2 readings in survivors vs. nonsurvivors. The authors determined that 86% of dogs with etCO2 values maintained ≥ 15mmHg were successfully resuscitated, while 94% of the dogs with etCO2 values < 15mmHg achieved ROSC. In cats, similar trends were detected however statistical significance was not reached (p=0.08) potentially due to small sample size. The study showed that 90% of cats with etCO2 readings ≥20 mmHg were successfully resuscitated, while only 5/9 (55%) with etCO2 < 20 mmHg had ROSC.

Only one study was found (Chalak et al) that attempted to link etCO2 readings with physical examination parameters. The objective of this paper was to determine the etCO2 level that best correlated with the return of an audible heart rate, for purposes of minimizing interruption of chest compressions during CPR. The authors used 46 anesthetized piglets in an asphyxiation model of cardiac arrest. The piglets underwent CPR and continuous etCO2 monitoring was performed, auscultation was performed every 30 seconds. An etCO2 of 14 mmHg was the most sensitive cutoff (93%) with least false positives (specificity of 81%).

There is a paucity of studies evaluating CPR and end tidal CO2 monitoring in veterinary medicine. Much of the available data consists of experimental studies, which provide useful information, but are directed towards human cardiac arrest and CPR (ie the use of the asphyxiation model to simulate a newborn in the delivery room or the ventricular fibrillation models to simulate myocardial infarction). These models utilize anesthetized or sedated animals and a short duration of cardiac arrest. Very little information is known about

naturally occurring cardiac arrest and CPR in animals. Nonetheless, all of the studies analyzed have similar results- at the onset of cardiac arrest the etCO2 level drops presumably due to decreased cardiac output. As ROSC is obtained, the etCO2 values begin to rise again. Animals who are more likely to achieve ROSC may have higher etCO2 readings at the beginning of CPR, and maintain higher readings through the duration of the CPR attempt. Long term outcome of animals successfully resuscitated in this fashion are for the most part unknown.

7. Conclusion

Conclusion on science: There were no studies available that directly compared etCO2 readings to a specific physical exam finding in dogs and cats. A single LOE3 paper describing the correlation of etCO2 and palpable pulse in swine is the only paper found describing etCO2 and a physical exam finding in any animal species. End-tidal CO2 has been shown in numerous studies (LOE3-5) to be a good predictor of ROSC in dogs.
Treatment recommendation: End-tidal CO2 is a noninvasive method of obtaining information on cardiac output during CPR as well suggest likelihood of ROSC (providing that ventilation is constant during the CPR attempt). Values of ≥15 mmHg in the dog and ≥20 mmHg in the cat are correlated with ROSC. End-tidal CO2 monitors are easy to use and should be recommended in all CPR attempts. Further study is needed, especially in dogs and cats, to determine the correlation between etCO2 and specific clinical observations in dogs and cats.

8. Acknowledgement

None

9. Citation list

Behande MS, Karasic DG, Karasic RB. End-tidal carbon dioxide changes during cardiopulmonary resuscitation following experimental asphyxial cardiac arrest. *Am J Emerg* Med. 14(4); 349, 1996
Abstract
A study was undertaken to determine the pattern of end-tidal carbon dioxide (ETCO2) changes during asphyxia-induced cardiac arrest in a pediatric canine model. Eleven intubated, anesthetized, paralyzed dogs (mean age, 4.1 mo; mean weight, 5.5 kg) were used. Asphyxia was induced by clamping the endotracheal tube (ETT) and discontinuing ventilation. Cardiac arrest ensued a few minutes later, after which closed-chest cardiopulmonary resuscitation (CPR) and ventilation were initiated. The ETCO2 level was recorded at baseline and every minute during CPR. Mean baseline ETCO2 was 31.9 mm Hg. The initial ETCO2 immediately after unclamping the ETT (mean, 35 mm Hg) was higher than subsequent values (mean, 12.4 mm Hg; P < .001). There was a sudden increase in ETCO2 to a mean of 27.0 mm Hg at or just before return of spontaneous circulation (ROSC) in all 11 cases (P < .01). During CPR, ETCO2 levels were initially high, decreased to low levels, and increased again at ROSC. This pattern, not previously described, is different from that observed in animal and adult cardiac arrest caused by ventricular fibrillation, during which ETCO2 decreases to almost zero after the onset of arrest, begins to increase after the onset of effective CPR, and increases to normal levels at ROSC. In this model of asphyxial arrest, continued cardiac output prior to arrest allows continued delivery Of CO2 to the lungs, resulting in higher alveolar CO2; this, in turn, is reflected as increased ETCO2 once ventilation is resumed during CPR. Further study is needed to determine whether the pattern Of ETCO2 changes can be used prospectively to define the etiology of cardiac arrest.
Summary: One of the only papers describing etCO2 monitoring during cardiac arrest in dogs. This short manuscript appears to be a summary of another paper by the authors seeking to validate a colorimetric etCO2 monitor, as the study design and results are identical. All of the dogs were successfully resuscitated following a brief period (<10 minutes) of cardiac arrest. The authors do not state the funding source for this study in either paper reporting on these dogs.
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Chalak LF, Barber CA et al. End-Tidal CO2 detection of an audible heart rate during neonatal cardiopulmonary resuscitation after asystole in asphyxiated piglets. *Pediatr Res* 69 (5 part1), 401-405; 2011.

Abstract: Even brief interruption of cardiac compressions significantly reduces critical coronary perfusion pressure during cardiopulmonary resuscitation (CPR). End-tidal CO_2 ($ETCO_2$) monitoring may provide a continuous noninvasive method of assessing return of spontaneous circulation (ROSC) without stopping to auscultate for heart rate (HR). However, the $ETCO_2$ value that correlates with an audible HR is unknown. Our objective was to determine the threshold $ETCO_2$ that is associated with ROSC after asphyxia-induced asystole. Neonatal swine (n = 46) were progressively asphyxiated until asystole occurred. Resuscitation followed current neonatal guidelines with initial ventilation with 100% O_2 followed by cardiac compressions followed by epinephrine for continued asystole. HR was auscultated every 30 s, and $ETCO_2$ was continuously recorded. A receiver operator curve was generated using the calculated sensitivity and specificity for various $ETCO_2$ values, where a positive test was defined as the presence of HR >60 bpm by auscultation. An $ETCO_2$ cut-off value of 14 mm Hg is the most sensitive $ETCO_2$ value with the least false positives. When using $ETCO_2$ to guide uninterrupted CPR in this model of asphyxia-induced asystole, auscultative confirmation of return of an adequate HR should be performed when $ETCO_2$ >=14 mm Hg is achieved. Correlation during human neonatal CPR needs further investigation. **Summary**: a novel study attempting to link etCO2 to a physical examination parameter (auscultable heart rate of at least 60 beats/min). This appears to be the only current study linking etCO2 to a specific clinical parameter. ROSC was achieved in 42/46 piglets. The authors noted a large drop in etCO2 at the time of cardiac arrest, followed by a sudden increase when ROSC occurred. A research population of piglets was used, as well as a standardized induction of arrest and CPR protocol. Funding for the study was provided by the American Academy of Pediatrics Neonatal Resuscitation Program Research Grant.

Hofmeister EH, Brainard BM, et al. 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; 2009.
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.
Summary: One of very few veterinary-directed papers evaluating etCO2 (among other variables) during spontaneous cardiac arrest rather than an animal model of human cardiac arrest. Inclusion/exclusion criteria clearly defined, prospective observational design (no specific treatments administered). Dogs and cats who achieved ROSC had higher etCO2 readings during CPR, although statistical significance was not reached in cats (p=0.08).

Kolar M, Krizmarik M, et al. Partial pressure of end-tidal carbon dioxide successfully predicts cardiopulmonary resuscitation in the field: a prospective observational study. *Crit Care* 12(5) R115; 2008.
Abstract

INTRODUCTION: Prognosis in patients suffering out-of-hospital cardiac arrest is poor. Higher survival rates have been observed only in patients with ventricular fibrillation who were fortunate enough to have basic and advanced life support initiated soon after cardiac arrest. An ability to predict cardiac arrest outcomes would be useful for resuscitation. Changes in expired end-tidal carbon dioxide levels during cardiopulmonary resuscitation (CPR) may be a useful, noninvasive predictor of successful resuscitation and survival from cardiac arrest, and could help in determining when to cease CPR efforts. METHODS: This is a prospective, observational study of 737 cases of out-of-hospital cardiac arrest. The patients were intubated and measurements of end-tidal carbon dioxide taken. Data according to the Utstein criteria, demographic information, medical data, and partial pressure of end-tidal carbon dioxide (PetCO2) values were collected for each patient in cardiac arrest by the emergency physician. We hypothesized that an end-tidal carbon dioxide level of 1.9 kPa (14.3 mmHg) or more after 20 minutes of standard advanced cardiac life support would predict restoration of spontaneous circulation (ROSC). RESULTS: PetCO2 after 20 minutes of advanced life support averaged 0.92 +/- 0.29 kPa (6.9 +/- 2.2 mmHg) in patients who did not have ROSC and 4.36 +/- 1.11 kPa (32.8 +/- 9.1 mmHg) in those who did ($P < 0.001$). End-tidal carbon dioxide values of 1.9 kPa (14.3 mmHg) or less discriminated between the 402 patients with ROSC and 335 patients without. When a 20-minute end-tidal carbon dioxide value of 1.9 kPa (14.3 mmHg) or less was used as a screening test to predict ROSC, the sensitivity, specificity, positive predictive value, and negative predictive value were all 100%.

CONCLUSION: End-tidal carbon dioxide levels of more than 1.9 kPa (14.3 mmHg) after 20 minutes may be used to predict ROSC with accuracy. End-tidal carbon dioxide levels should be monitored during CPR and considered a useful prognostic value for determining the outcome of resuscitative efforts and when to cease CPR in the field. Summary: An outcome research study in humans evaluating the use of etCO2 as a predictor of ROSC in CPR attempts. The authors followed a large number of people with spontaneous cardiac arrest out of the hospital. A marked difference in etCO2 was noted between patients with ROSC versus not (33 mmHg vs 7 mmHg). This paper also determined a cut-off value of >14.3 mmHg etCO2 at 20 minutes of CPR could be used as a highly accurate predictor of ROSC (100% sensitivity, specificity, PPV and NPV).

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.

Summary: One of few articles to follow survivors of CPR, the authors tracked 5 dogs for a week after ROSC. Neurological function of these dogs was normal. EtCO2 proved to be a reliable indicator of ROSC after 14 minutes of CPR. The surviving dogs had consistent etCO2 levels for the duration of CPR, while dogs who did not have ROSC had a continuous decline in etCO2. The etCO2 cutoff of 6 mmHg was arbitrarily chosen.