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Evaluation of end-tidal carbon dioxide as a predictor of return of spontaneous circulation in dogs and cats undergoing cardiopulmonary resuscitation

Talli Hogen, DVM, DACVECC; Steven G. Cole, DVM, DACVECC, DACVIM (Cardiology); and Kenneth J. Drobatz, DVM, MSCE, DACVIM, DACVECC

Abstract

Objective – To determine whether the partial pressure of end-tidal carbon dioxide ($PetCO_2$) could predict return of spontaneous circulation (ROSC) in patients with cardiopulmonary arrest (CPA) undergoing CPR.
Design – Prospective observational study.
Setting – Two private specialty referral hospitals.
Animals – Thirty-five client-owned dogs and cats in CPA in which CPR was performed and pertinent data recorded on a purpose-made form.
Interventions – None.
Measurements and Main Results – $PetCO_2$ was recorded at 1-minute intervals during CPR. Hospital, animal, arrest, and outcome variables were also reported in the Utstein style where possible. Twelve animals (7 dogs and 5 cats) achieved ROSC; 4 of these (2 dogs and 2 cats) had sustained ROSC, of which 1 dog was discharged alive. Patients that achieved ROSC had significantly higher initial $PetCO_2$ ($P = 0.0083$), peak $PetCO_2$ ($P < 0.0001$), average $PetCO_2$ ($P < 0.0001$), and $\Delta PetCO_2$ (difference between last and first recorded $PetCO_2$; $P = 0.0004$) than patients not resuscitated. The $PetCO_2$ accurately discriminated between ROSC and failure to achieve ROSC at minutes 3, 4, 5, 6, 7, and 8 of CPR with area under the receiver operating characteristic curve of 0.926, 0.967, 0.938, 0.933, 0.956, and 1.00, respectively. The optimal cutoff $PetCO_2$ was 18 mm Hg (2.4 kPa), with a sensitivity of ≥80% and a specificity of ≥95% at minutes 3, 4, 5, 6, and 8, correctly classifying 91–100% of cases.
Conclusions – The results of this small study support previous recommendations to monitor $PetCO_2$ during CPR and suggest that $PetCO_2$ during CPR may be useful for determining the probability of ROSC. Absolute values and trends of $PetCO_2$ may assist clinicians and owners in making decisions for pets with CPA.

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Keywords: basic life support, BLS, capnometry, cardiopulmonary arrest, CPR, monitoring

Abbreviations

AUC	area under the receiver operating characteristic curve
CI	confidence interval
CPA	cardiopulmonary arrest
n-ROSC	not achieving return of spontaneous circulation
$PetCO_2$	partial pressure of end-tidal carbon dioxide
RECOVER	Reassessment Campaign on Veterinary Resuscitation
ROSC	return of spontaneous circulation

From the Advanced Critical Care, Emergency and Specialty Services Culver City, CA (Hogen, Cole); and the Matthew J. Ryan Veterinary Hospital University of Pennsylvania School of Veterinary Medicine, Philadelphia, PA (Drobatz).

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Address correspondence and reprint requests to
Dr. Talli Hogen, VCA West Los Angeles Animal Hospital, 1900 S. Sepulveda Blvd, Los Angeles, CA 90025, USA.
Email: tallihogen@gmail.com
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Introduction

The partial pressure of end-tidal carbon dioxide ($PetCO_2$) has long been used by physicians as a guideline for evaluating efficacy of chest compressions in CPR in people,[1] as well as for predicting outcome in patients with cardiopulmonary arrest (CPA). A $PetCO_2$ of 14.3 mm Hg (1.91 kPa) after 20 minutes of CPR discriminated between resuscitated patients and nonresuscitated patients with sensitivity, specificity, and positive and

negative predictive values of 100% in 1 human study.[2] The American Heart Association guidelines consider $PetCO_2$ to be one of the most important physiologic data points to monitor during CPR.[3]

Studies have also evaluated the use of $PetCO_2$ to predict resuscitation in small groups of dogs with experimentally induced CPA and have found that $PetCO_2$ has significant predictive value.[4,5] Prospective clinical studies evaluating variables associated with return of spontaneous circulation (ROSC) in veterinary CPR are rare.[6–8] Only 1 veterinary study has evaluated the use of $PetCO_2$ as an outcome variable in ROSC and detected a significant difference between mean highest $PetCO_2$ in dogs that did and did not achieve ROSC.[8] However, $PetCO_2$ monitoring was not mandatory for inclusion, and was monitored in a minority of the dogs and cats in the study. To the authors' knowledge, no clinical veterinary studies have been published to prospectively evaluate $PetCO_2$ as a primary outcome variable during CPR.

Many veterinarians use end-tidal carbon dioxide to guide their CPR efforts,[9] and the authors of the Reassessment Campaign on Veterinary Resuscitation (RECOVER) initiative recommend $PetCO_2$ monitoring during CPR. RECOVER graded the recommendation to use end-tidal carbon dioxide monitoring as an indicator of ROSC as supported by class I-A evidence,[10] while also identifying knowledge gaps in the use of $PetCO_2$ during CPR.[11] The ability to monitor the efficacy of chest compressions and to predict cardiac arrest outcomes would be useful to help determine when to change compression strategy or when to cease versus continue CPR. Outcome prediction would help to optimize use of resources while not abandoning resuscitative efforts too early.

The aim of this study was to investigate whether $PetCO_2$ could predict ROSC in patients with CPA undergoing CPR. We hypothesized that mean $PetCO_2$ would be higher in resuscitated than in nonresuscitated cats and dogs. Additionally, we hypothesized that the increase in the $PetCO_2$ value from beginning to end of CPR ($\Delta PetCO_2$) would be greater in resuscitated versus nonresuscitated patients. Finally, we hypothesized that at critical time points during CPR, $PetCO_2$ values could be used to accurately discriminate between patients that would achieve ROSC, and those not likely to be resuscitated.

Materials and Methods

Hospital settings

A prospective study was designed to collect data for 1 year (June 2015–May 2016) at 2 associated private referral hospitals, each with a 24-hour emergency service, 24-hour ICU, and multiple specialty services. All drugs described by the RECOVER initiative are stocked in dedicated "crash carts" in multiple areas of both hospitals, and a defibrillator is available in each ICU. Staff is trained in CPR basic and advanced life support with didactic lectures every 6–12 months, a yearly wet lab, and with hands-on experience under the supervision of lead technicians and trainers on a regular basis.

Data collection and definitions

A purpose-made data form was created for this study, filled out by an assistant standing by during CPR, and signed by the attending clinician, who also provided circumstantial and diagnostic information. The form was primarily designed to record the $PetCO_2$ at 1-minute intervals. Other prospectively collected information included time of arrest, time to start of compressions, time to intubation and ventilation, time ROSC was achieved or CPR was abandoned, and interventions (drugs, defibrillation, and IV fluids) administered.

For the purposes of this study, CPA was defined and confirmed by an attending clinician as unresponsive mentation and a lack of a detectable pulse or heartbeat. Patients with respiratory arrest only were not included in this study.

CPR was defined as resuscitation efforts that included chest compressions performed on a patient with CPA. The CPR protocol at the study hospitals during the time of data collection followed the algorithm recommended by the RECOVER initiative.[10] ROSC was defined as having evidence of spontaneous circulation lasting >30 seconds, identified with a palpable femoral pulse in the absence of chest compressions after a CPA event. Sustained ROSC was defined as ROSC lasting ≥20 minutes.

Blank data forms were kept in a box clipboard with the CPR crash cart, and an interval timer[a] was attached to the clipboard. The timer was preprogrammed to create a beeping sound every 60 seconds once turned on. The sound would continue for 5 seconds, and the highest $PetCO_2$ observed during that 5-second interval was recorded on the form next to the time of day (hour and minute) at 1-minute intervals. Because the data forms and requisite capnometers[b] were kept exclusively in the emergency room and ICU, and only emergency and ICU staff were instructed on study data collection, only CPR performed in the ICU was recorded for use in this study.

Other information was recorded based on the Utstein-style criteria for reporting of human CPR research.[12] The majority of the data collection for this study preceded the publication of the veterinary Utstein-style guidelines, but where possible the core and supplemental information recommended by these guidelines[13] was retrospectively collected and reported. Hospital variables reported included hospital location, hospital information and size metrics, persons assisting in CPR, and attending clinician. Patient variables recorded included age,

gender, species and breed, and patient identifiers (pet name, owner name, and hospital identification number). Arrest variables recorded included time and date of CPA (estimated based on owner history for unwitnessed events); location of CPA; presumed cause of CPA; heart rhythm at time of arrest if known; drugs and defibrillation doses, times, and routes of administration; times that chest compressions and ventilation were initiated; and time that CPR was stopped. Outcome variables recorded included heart rhythm postresuscitation if known, occurrence of any ROSC, occurrence of sustained ROSC, duration of ROSC if known, and reason for discontinuation of resuscitative efforts.

Subjects

All dogs and cats with in-hospital or out-of-hospital CPA, in which CPR was performed in the ICU between June 2015 and May 2016, were considered eligible for inclusion in this study. Patients were included if CPR was performed for any amount of time with ROSC, or for at least 5 minutes without ROSC; if a data form was completed during CPR; and if $PetCO_2$ monitoring and recording with a mainstream capnometer[a] were initiated within 5 minutes of starting CPR. Patients were excluded if $PetCO_2$ values were not recorded for more than 25% of the time monitored, if either cause of arrest and reason CPR was abandoned were not recorded, if time of arrest or time of CPR initiation were not recorded, or if patients were monitored with a different type of capnometer; these exclusions were determined prospectively. Similar to a previous prospective veterinary CPR study,[7] only the first CPA–CPR event for each animal was reported and included in the data analysis.

Statistical methods

Continuous variables were assessed for normality using the Shapiro–Wilk test. Nearly all the continuous variables were not normally distributed and hence median (range) for consistency were used to describe them. The Wilcoxon rank sum test or *t*-test was used to compare these variables between groups depending upon the data distribution. Categorical variables are described using proportion and percentages, and the chi-square test or Fisher's exact test (if any expected cell count was <5) was used to compare these variables. The trapezoid method was used to calculate the area under the receiver operating curve (AUC) and 95% confidence interval (CI) was calculated using the exact method. Ninety-five percent CIs for generated odds ratios were calculated using Woolf's method. Spearman's correlation test was used to assess the relationship between variables. A *P*-value <0.05 was considered significant for all comparisons. A computer software package[c] was used for all statistical evaluations.

Results

Hospital variables

During the year-long time frame of the study, Hospital A had an annual small animal caseload of approximately 12,200 cats and dogs with 2,500 hospital admissions and approximately 6,400 small animal emergency consultations per year. Hospital B had an annual small animal caseload of approximately 14,500 cats and dogs with 3,000 hospital admissions and approximately 6,700 emergency consultations per year. During this time period, approximately 240 animals at Hospital A and 130 animals at Hospital B showed computer entries indicating that CPR was performed.

Animal variables

Fifty-two dogs and cats experienced CPA and had CPR performed and captured with the purpose-made data form during the study period between June 2015 and May 2016. Hospital A collected 18 data forms and Hospital B collected 34. Of the 52 data forms collected, 17 were excluded for the following reasons: absence of $PetCO_2$ recording, or >25% of the $PetCO_2$ values missing (11); lack of CPA (patient sustained respiratory arrest only or had general resuscitation efforts without CPA (3); CPR monitoring lasting <5 minutes without ROSC (2); or lack of information on time of arrest and time to CPR initiation (1).

Therefore, 35 animals (28 dogs [80%] and 7 cats [20%]) were included. Of the dogs included, 15 (53.6%) were females (11 neutered and 4 intact) and 13 (46.4 %) were males (11 neutered and 2 intact). Of the cats included, 6 (85.7%) were males (5 neutered and 1 intact) and 1 (14.3%) was a neutered female.

The median age of dogs was 6.5 years (range, 0.50–15 y). The median age of cats was 8 years (range, 1–16 y). Five cats were domestic shorthair cats, 1 was a domestic longhair cat, and 1 was a Persian cat. The canine population consisted of 4 mixed breed dogs, 4 Chihuahuas or Chihuahua mix dogs, 3 Pomeranians or Pomeranian mix dogs, 2 Pit Bull Terriers, and 1 each of the following: American Bulldog, Border Collie, Boxer, Cavalier King Charles Spaniel, English Bulldog, Great Dane, German Shepherd mix, Husky, Jack Russell Terrier, Labrador Retriever, Llasa Apso, Miniature Pinscher, Pekingese, Silky Terrier, and Yorkshire Terrier. Animal weights were not consistently recorded.

Arrest variables

Overall, 12 animals (34.3%) achieved ROSC (7 dogs and 5 cats). Twenty-three animals (65.7%) did not achieve ROSC (21 dogs and 2 cats). ROSC was achieved in a significantly ($P = 0.033$) higher proportion of cats (71%) than dogs (25%). Cats were 7.5 times as likely to achieve

Table 1: Summary of animal and arrest variables in a group of cats and dogs experiencing cardiopulmonary arrest and undergoing CPR, divided by outcome and by species where appropriate

Animal/arrest variable	ROSC ($n = 12$)	n-ROSC ($n = 23$)
Species		
Cat (*n*)	5	2
Dog (*n*)	7	21
Location of arrest, total (dog and cat)		
In-hospital	11 (7D and 4C)	6 (6D)
Out-of-hospital	1 (1C)	17 (15D and 2C)
Cause of arrest, total (dog and cat)		
Trauma	2 (1D and 1C)	9 (8D and 1C)
Respiratory failure	3 (1D and 2C)	5 (5D)
Brain disease	0	2 (2D)
Metabolic disease	1 (1D)	1 (1D)
Multi-organ dysfunction syndrome	1 (1D)	1 (1D)
Heart failure	0	1 (1D)
Hemorrhage	1 (1D)	0
Non-hemorrhagic non-septic hypovolemia	1 (1D)	0
Unknown	3 (1D and 2C)	4 (3D and 1C)
Median duration of arrest before ROSC (ROSC group) or stopping CPR (n-ROSC group)	9 minutes	16 minutes

C, cat; D, dog; n, number; n-ROSC, not achieving return of spontaneous circulation; ROSC, return of spontaneous circulation.

ROSC compared to dogs (95% CI 1.2–47, $P = 0.0206$). Animal variables and arrest variables are summarized in Table 1.

Of the 35 patients included in the analysis, 17 experienced CPA while hospitalized in the ICU, whereas 18 sustained out-of-hospital arrest and were presented dead on arrival. Of the 12 dogs and cats with ROSC, 11 (91.7%) sustained in-hospital CPA. One cat with out-of-hospital arrest achieved ROSC an estimated 14 minutes after CPA and survived for 48 hours after ROSC until he was euthanized due to severity of illness. Of the 23 dogs and cats without successful resuscitation (not achieving-ROSC [n-ROSC]), 6 (26.1%) arrested in hospital and 17 (73.9%) arrested out of the hospital and were presented dead on arrival. ROSC was significantly ($P = 0.0002$) more common in patients with in-hospital versus out-of-hospital CPA (odds ratio: 31.0, 95% CI 3.0–1,417). No statistically significant association was detected ($P = 0.612$) between species and the location of arrest (in-hospital vs out-of-hospital arrest).

For animals that achieved ROSC, the median time interval from time of CPA (or estimated time of CPA for unwitnessed events) to ROSC was 9 minutes (range, 3–19 min). For animals not resuscitated, the median time interval from CPA to discontinuing CPR was 16 minutes (range, 5–29 min). The median time from CPA (estimated for unwitnessed events) to endotracheal intubation was significantly ($P = 0.0301$) longer for n-ROSC (4 min, range, 0–16 min) compared to ROSC patients (2 min, range 0–7 min). However, time from estimated or witnessed arrest to endotracheal intubation was not significantly associated with $PetCO_2$ at any time point from minute 1 to minute 8.

The suspected cause of CPA was retrospectively categorized according to the recently published veterinary Utstein-style guidelines.[13] Of the 35 patients included in the analysis, the suspected cause of death was trauma in 11 patients (9 n-ROSC, 2 ROSC), respiratory failure in 8 patients (5 n-ROSC and 3 ROSC), unknown causes in 7 patients (4 n-ROSC and 3 ROSC), brain disease in 2 patients (both n-ROSC), metabolic disease in 2 patients (1 n-ROSC and 1 ROSC), multiorgan dysfunction syndrome in 2 patients (1 n-ROSC and 1 ROSC), heart failure in 1 patient (n-ROSC), hemorrhage in 1 patient (ROSC), and nonhemorrhagic non-septic hypovolemia in 1 patient (ROSC).

At the time of arrest, 2 patients were undergoing general anesthesia. One patient was suspected to have died from respiratory causes, and 1 from hemorrhage. Both achieved ROSC at 12 and 6 minutes post-CPA, respectively, the latter of which was discharged alive from the hospital. All enrolled patients had basic life support, and none had open-chest CPR. Advanced life support measures were recorded in 33/35 enrolled patients, and in all of these, both epinephrine and atropine were administered. Doses of drugs and interventions administered during CPR were inconsistently recorded, although the hospitals generally observe doses recommended by the RECOVER guidelines.[10] The median number of epinephrine doses administered to patients was 1 in the ROSC group and 3 in the n-ROSC group. The median number of atropine doses administered to patients was 2 in both the ROSC and the n-ROSC groups. All 3 patients that received reversal drugs (naloxone and flumazenil) were successfully resuscitated. Two of these patients were anesthetized at the time of CPA. No patient that received external defibrillation ($n = 5$) or vasopressin ($n = 2$) was resuscitated. Six patients received an IV fluid bolus (4 ROSC and 2 n-ROSC). Lidocaine and mannitol were both administered during CPR to 1 trauma patient, which achieved ROSC.

Outcome variables

The duration of ROSC was known for 7/15 animals with ROSC. Of those, 3 had ROSC lasting <20 minutes (2 cats and 1 dog). Four animals had sustained ROSC (2 dogs and 2 cats); of these 4, 1 dog was discharged alive from

Table 2: Comparison of median (range) $PetCO_2$ variables in dogs and cats undergoing CPR that achieved ROSC and those that did not

Variable	ROSC	n-ROSC	*P*-Value
Initial $PetCO_2$	18 mm Hg; 2.4 kPa (4–42 mm Hg; 0.53–5.6 kPa)	6 mm Hg; 0.80 kPa (0–32 mm Hg; 0–4.3 kPa)	0.0083
Peak $PetCO_2$	30 mm Hg; 4.0 kPa (11–58 mm Hg; 1.5–7.7 kPa)	14 mm Hg; 1.9 kPa (0–32 mm Hg; 0–4.3 kPa)	<0.0001
$\Delta PetCO_2$	+8.5 mm Hg; 1.1 kPa (–6 to +16 mm Hg; –0.80 to +2.1 kPa)	–1.0 mm Hg; –0.13 kPa (–16 to +14 mm Hg; –2.1 to +1.9 kPa)	0.0004
Average $PetCO_2$	23.1 mm Hg; 3.08 kPa (6.25–45.3 mm Hg; 0.833–6.04 kPa)	6.69 mm Hg; 0.892 kPa (0–17.5 mm Hg; 0–2.33 kPa)	<0.0001

n-ROSC, not achieving return of spontaneous circulation; $PetCO_2$, partial pressure of end-tidal carbon dioxide; ROSC, return of spontaneous circulation.

the hospital, 1 dog and 1 cat were euthanized, and 1 dog arrested again 1.5 hours later.

In patients without ROSC, CPR was stopped at the request of the owner in 8 pets (5 due to poor prognosis, 1 due to economic considerations, and 2 due to both), and was stopped at the discretion of the attending clinician in 12 pets (4 because CPR was considered futile and 8 due to lack of response to CPR). CPR was discontinued in the other 3 pets for unknown reasons.

$PetCO_2$ and outcome

Initial, peak, and average $PetCO_2$ were all significantly greater in the ROSC group compared to the n-ROSC group (Table 2). While initial and final $PetCO_2$ were varied in both ROSC and n-ROSC groups, all patients that achieved ROSC had a final pre-ROSC $PetCO_2$ >10 mm Hg (1.3 kPa), whereas final values this high were only recorded in 4/23 n-ROSC patients (17.4%). Additionally, $\Delta PetCO_2$ (difference between last and first $PetCO_2$ measured) was significantly greater in ROSC compared to n-ROSC animals (Table 2). In other words, patients in the ROSC group showed increasing $PetCO_2$ from beginning to end of CPR, whereas patients in the n-ROSC group did not.

At each minute during CPR from minute 1 to minute 12, the mean $PetCO_2$ was significantly higher in patients with ROSC than n-ROSC (Table 3). Only the first 8 time points are reported due to the small number of patients with CPR that was monitored for >8 minutes ($n = 3$ in ROSC group and $n = 10$ in n-ROSC group).

$PetCO_2$ demonstrated excellent accuracy at discriminating between ROSC and n-ROSC at minutes 3, 4, 5, 6, 7, and 8, with AUC (95% CI) of 0.926 (0.819–1.00), 0.967 (0.914–1.00), 0.938 (0.845–1.00), 0.933 (0.796–1.00), 0.956 (0.858–1.00), and 1.00 (1.00–1.00), respectively (Figure 1). Minutes 1 and 2 of monitoring $PetCO_2$ also predicted ROSC with fair to good accuracy, with an AUC (95% CI) of 0.783 (0.612–0.954) and 0.814 (0.646–0.981), respectively. Again, time points after 8 minutes are not reported due to the small number of subjects in the ROSC group.

A cutoff $PetCO_2$ ≥18 mm Hg (2.4 kPa) at minutes 3–8 of $PetCO_2$ recording consistently performed well to predict ROSC, and it was the most accurate value at minutes 3, 4, 5, 6, and 8 (91–100% of cases correctly classified). Cutoff points of $PetCO_2$ ≥12 mm Hg (1.6 kPa) or ≥14 mm Hg (1.9 kPa) also performed with adequate accuracy (Table 4). As expected, a $PetCO_2$ cutoff of ≥18 mm Hg (2.4 kPa) was more specific but less sensitive for predicting ROSC than a $PetCO_2$ ≥12 mm Hg (1.6 kPa) or 14 mm Hg (1.9 kPa) in the time points available for comparison. A cutoff $PetCO_2$ ≥10 mm Hg (1.3 kPa) was at least 80.0% sensitive for predicting ROSC at every time point except for minute 1.

Discussion

As previously reported in the human and experimental animal literature, $PetCO_2$ was a strong predictor of ROSC in this small prospective study of dogs and cats with CPA. The initial, peak, average, and change in $PetCO_2$ were all statistically associated with ROSC. Moreover, $PetCO_2$ accurately discriminated between patients with ROSC and n-ROSC at minutes 3–8 of CPR monitoring, lending immediate clinical relevance to previous recommendations for monitoring these values during veterinary CPR.[10]

One clinical veterinary study evaluated $PetCO_2$ in a subpopulation of subjects during CPR and found that the mean highest recorded $PetCO_2$ during CPR was higher in dogs that were ultimately resuscitated than those that were not; no significant difference was found in cats. In that study, a $PetCO_2$ ≥15 mm Hg (2.0 kPa) had a sensitivity of 86% for ROSC in dogs; and a $PetCO_2$ ≥20 mm Hg (2.7 kPa) had a sensitivity of 90% for ROSC in cats.[8] Unfortunately, the present study had too few subjects to analyze the predictive value of $PetCO_2$ for dogs and cats separately.

The use of capnometry for monitoring human CPR was first described by the work of Dr. Zden Kalenda in 1978. That study illustrated that $PetCO_2$ tended to

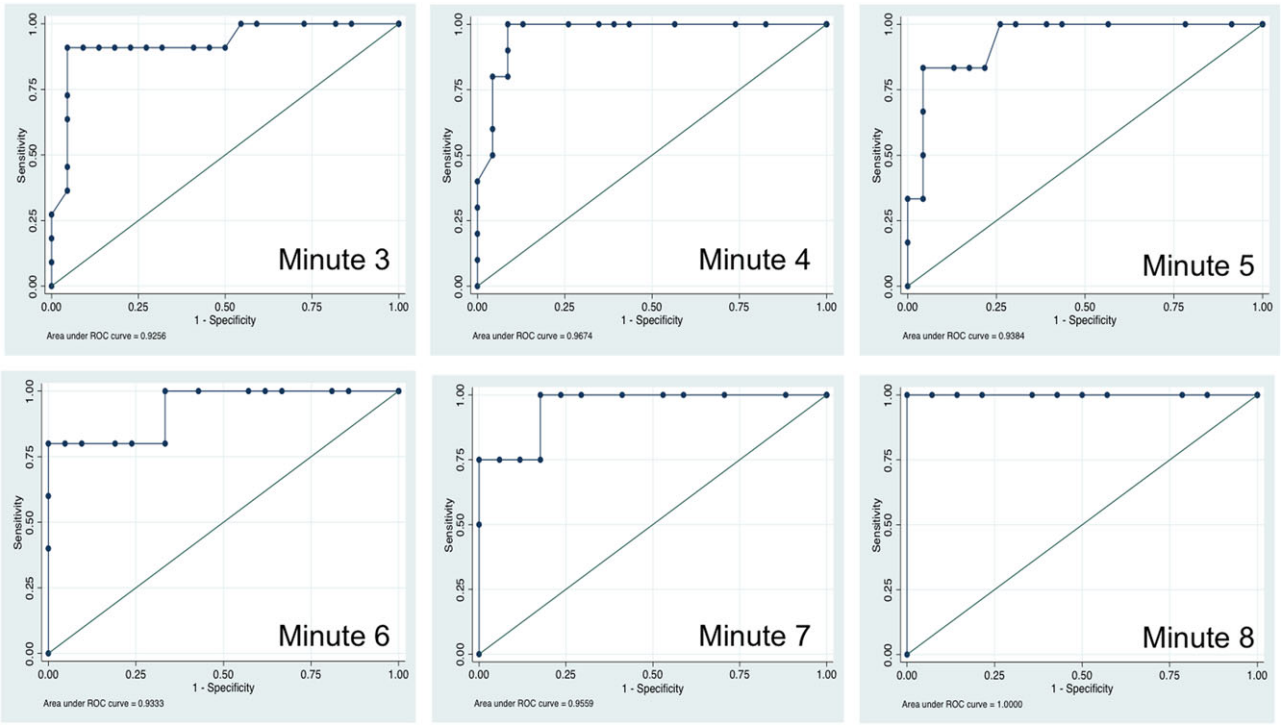

Figure 1: Receiver operating characteristic curves and associated AUC demonstrating sensitivity and specificity of $PetCO_2$ for predicting ROSC at various time points recorded during CPR in dogs and cats. AUC, area under the ROC curve; $PetCO_2$, partial pressure of end-tidal carbon dioxide; ROC, receiver operating characteristic; ROSC, return of spontaneous circulation.

decrease near the end of each chest compression cycle, appearing to correlate with compressor fatigue. When a new compressor was rotated in to perform chest compressions, the $PetCO_2$ consistently increased at the beginning of each cycle. Furthermore, $PetCO_2$ increased significantly concurrently with ROSC.[1]

Numerous experimental animal studies have also demonstrated an association between $PetCO_2$ and ROSC. Both induced asphyxial and ventricular fibrillation models of arrest have repeatedly demonstrated that $PetCO_2$ increases at the time of or just before ROSC and have discriminated between patients with and without ROSC.[5,14–16] Clinical studies have continued to validate this association and have demonstrated the predictive value of $PetCO_2$ in identifying patients likely to have successful resuscitation. In 2003, Grmec and Kupnik found that both initial and final $PetCO_2$ values were higher in adults with cardiac arrest that were successfully resuscitated than in those without ROSC, and that initial $PetCO_2$ could predict ROSC.[17] Another large prospective observational study showed that the average $PetCO_2$ was significantly higher in patients with ROSC than without ROSC.[18] Likewise, Kolar et al found that, in a similar cohort of adults, no patient with an initial, final, average, or maximum $PetCO_2$ value <10 mm Hg (1.3 kPa) could be resuscitated; and that a $PetCO_2$ ≥14.3 mm Hg (1.91 kPa) at 20 minutes of CPR predicted ROSC with a sensitivity and specificity of 100%.[2] Considering this information, a 2013 American Heart Association consensus statement on CPR quality advised that failure of $PetCO_2$ to exceed 10 mm Hg (1.3 kPa) strongly predicts unsuccessful resuscitation, and the expert panel recommended that rescuers titrate $PetCO_2$ to a goal value of >20 mm Hg (2.7 kPa) during CPR.[19] The findings of the current investigation agree with these prior studies, in that initial, average, and change in $PetCO_2$ were all strongly and significantly correlated with ROSC, and in finding that $PetCO_2$ cutoff values could be used to discriminate between survivors and nonsurvivors.

In the human hospital and prehospital settings, $PetCO_2$ is frequently used as an indicator of effectiveness of chest compressions and has been shown to correlate well with cardiac output and coronary perfusion pressure.[20,21] However, metabolism, circulation, and minute alveolar ventilation all influence its measurement, and all likely play roles in the mechanism by which $PetCO_2$ is linked with ROSC.[22] Therefore, it is likely that the measured value in patients with CPA is multifactorial and also represents ongoing tissue metabolism as well as ventilation parameters.[11] The role of tissue metabolism has been demonstrated by an interesting veterinary study, which showed higher median venous

Table 3: Median $PetCO_2$ in dogs and cats undergoing CPR with or without ROSC (with number of data points available for comparison) at minutes 1–8 of CPR monitoring

Time point in $PetCO_2$ monitoring	Median $PetCO_2$ ROSC	Median $PetCO_2$ n-ROSC	*P*-value
1 minute	19.9 mm Hg 2.65 kPa ($n = 11$)	8.87 mm Hg 1.18 kPa ($n = 23$)	0.0083
2 minutes	21.8 mm Hg 2.91 kPa (n = 10)	8.55 mm Hg 1.14 kPa ($n = 22$)	0.0049
3 minutes	25.4 mm Hg 3.39 kPa ($n = 11$)	7.64 mm Hg 1.02 kPa ($n = 22$)	0.0001
4 minutes	21.6 mm Hg 2.88 kPa ($n = 10$)	5.52 mm Hg 0.736 kPa ($n = 23$)	< 0.0001
5 minutes	22.7 mm Hg 3.03 kPa ($n = 6$)	5.91 mm Hg 0.788 kPa ($n = 23$)	0.0011
6 minutes	28.2 mm Hg 3.76 kPa ($n = 5$)	6.43 mm Hg 0.857 kPa ($n = 21$)	0.0030
7 minutes	23.8 mm Hg 3.17 kPa ($n = 4$)	6.35 mm Hg 0.847 kPa ($n = 17$)	0.0054
8 minutes	22.7 mm Hg 3.03 kPa ($n = 3$)	6.14 mm Hg 0.819 kPa ($n = 14$)	0.0079

n, number; n-ROSC, not achieving return of spontaneous circulation; $PetCO_2$, partial pressure of end-tidal carbon dioxide; ROSC, return of spontaneous circulation

carbon dioxide partial pressures (not to be confused with $PetCO_2$) during CPR than right after ROSC, although the difference did not reach statistical significance.[23] The role of ventilation in $PetCO_2$ during CPA has been demonstrated by studies of asphyxial cardiac arrest, in which $PetCO_2$ tends to be higher than in patients with other causes of cardiac arrest,[4,14] as well as by studies showing higher $PetCO_2$ in patients with all respiratory causes of death.[24] Unfortunately, our study was underpowered to evaluate patients with respiratory and asphyxial causes of arrest alone. Conversely, by including patients with all causes of arrest, our study supports the strength of the correlation between $PetCO_2$ and ROSC and validates the importance of its monitoring during CPR.

In the present study, a $PetCO_2$ ≥18 mm Hg (2.4 kPa) measured after minute 2 of CPR monitoring was the strongest discriminator between patients that were successfully resuscitated and those that were not. This value is similar to the values reported by Hofmeister et al to discriminate between ROSC and n-ROSC (≥15 mm Hg [2.0 kPa] in dogs and ≥20 mm Hg [2.7 kPa] in cats).[8] However, in the present study, lower values (12 mm Hg [1.6 kPa] and 14 mm Hg [1.9 kPa]) were also sensitive discriminators but performed with a slightly lower specificity than did 18 mm Hg (2.4 kPa). Similarly, a cutoff of ≥10 mm Hg (1.3 kPa) was at least 80% sensitive in predicting ROSC at every time point in recording CPR after minute 1. These results are within the range of $PetCO_2$ cutoff values described in the human studies above (10–20 mm Hg; 1.3–2.7 kPa). The small differences in numbers might be attributable to differing data collection techniques, species, population cross-section, and number of study subjects. Clinically, the use of a $PetCO_2$ cutoff of ≥10 mm Hg (1.3 kPa) to decide whether to continue CPR is likely warranted, rather than the higher value of 18 mm Hg (2.4 kPa), since avoidance of premature discontinuation of CPR may be more important than preventing CPR from being performed for longer than is necessary.

The 2 hospitals at which this study was conducted currently monitor $PetCO_2$ during CPR at the request of the attending clinician, using a portable capnometer stored in the crash cart. The capnometer generally used during CPR at these hospitals and used exclusively in this study is a self-contained highly portable mainstream continuous carbon dioxide monitoring device convenient for use in the emergency room setting. This specific capnometer has been validated for use in people in experimental settings[25] and in ventilated postoperative patients,[26] and found to correlate well with traditional $PetCO_2$ monitors in use. Unfortunately, missing capnometry data and malfunctioning capnometers were the most common reasons that clinicians at our hospitals cited for not enrolling patients in this study. While their ease of portability makes them a good choice for emergency room capnometry, the same quality led to monitors often being borrowed by other parts of the hospital, making them unavailable to the CPR team. Additionally, the capnometer typically suffered a short battery life and tubing components frequently clogged with airway secretions, both of which interfered with consistent $PetCO_2$ monitoring. Hospitals performing CPR frequently may consider dedicating capnometers to crash carts. Although sidestream capnometry values are slightly delayed and are affected by gas flow rates, they are also less prone to clogging with airway secretions. Therefore, they may be a better option for $PetCO_2$ monitoring in cases in which pulmonary infiltrates or pulmonary hemorrhage is expected.

In addition to mechanical problems, other reported limitations of capnometry during CPR include transient increases in $PetCO_2$ after administration of sodium bicarbonate, and decreases after administration of vasopressors including epinephrine.[22] Because no patient in our study received sodium bicarbonate, and almost every patient in our study received epinephrine, these medications were unlikely to affect our results.

Table 4: Sensitivity and specificity of selected $PetCO_2$ cutoff values for predicting ROSC in dogs and cats, organized by time point in CPR recording and listed with 95% confidence interval for associated ROC curve

Time in CPR		Cutoff: 10 mm Hg (1.3 kPa)	Cutoff: 11mm Hg (1.5 kPa)	Cutoff: 12 mm Hg (1.6 kPa)	Cutoff: 14 mm Hg (1.9 kPa)	Cutoff: 18 mm Hg (2.4 kPa)
Minute 3 (CI: 0.819–1.00)	Sens (%)	91	91	91	91	91
	Spec (%)	68	73	77	86	95
Minute 4 (CI: 0.914–1.00)	Sens (%)	100	100	90	80	80
	Spec (%)	87	91	91	91	96
Minute 5 (CI: 0.845–1.00)	Sens (%)	83	83	83	ND	83
	Spec (%)	78	83	87	ND	96
Minute 6 (CI: 0.796–1.00)	Sens (%)	ND	80	80	80	80
	Spec (%)	ND	76	81	90	100
Minute 7 (CI: 0.858–1.00)	Sens (%)	100	ND	75	ND	ND
	Spec (%)	82	ND	82	ND	ND
Minute 8 (CI: 1.00–1.00)	Sens (%)	ND	100	ND	100	100
	Spec (%)	ND	79	ND	86	100

CI, confidence interval; ND, no data for that time point; $PetCO_2$, partial pressure of end-tidal carbon dioxide; ROC, receiver operating characteristic; ROSC, return of spontaneous circulation; Sens, sensitivity; Spec, specificity.

The overall incidence of ROSC in this study (34.3%) was within range of previously reported incidences of ROSC. However, in this study 25% of dogs and 71.4% of cats achieved ROSC, compared to 13–60% of dogs and 15–57% of cats in previous veterinary studies.[6–8,27,28] Cats were much more likely to be successfully resuscitated than dogs, although the small number of cats in this study precluded the ability to statistically associate resuscitation with $PetCO_2$ in cats alone. While some veterinary studies have also reported a higher incidence of ROSC in cats than in dogs, none have previously reported a statistically significant difference in survival.[8,27,28] Because no association was found between species and location of CPA, a higher prevalence of feline in-hospital arrest (57%) than canine in-hospital arrest (46%) is thought unlikely to explain this phenomenon.

In the current study, as in previous ones, ROSC was more common in patients with in-hospital than out-of-hospital CPA.[7,8] The present study also found that time to intubation was significantly longer in patients that were not resuscitated than those that were, but time to intubation was not statistically correlated with $PetCO_2$. It is therefore unlikely that lower $PetCO_2$ values in n-ROSC patients could be explained by prolonged time to intubation alone, although it is logical that both prolonged time to intubation and decreased $PetCO_2$ are each independently associated with n-ROSC. Time to intubation may have been delayed in n-ROSC patients because these patients more commonly had out-of-hospital arrest.

While the prospective nature of the present study provides vital insight into the use of $PetCO_2$ monitoring in cats and dogs with CPA, multiple weaknesses were identified. Some weaknesses were related to data acquisition, and some to the challenges of reporting CPR data in general. The small number of study subjects, particularly in the ROSC group, may influence the statistical or clinical significance of the results. This is well demonstrated in the wide CIs in comparing likelihood of cat ROSC versus dog ROSC, or in comparing in-hospital versus out-of-hospital cardiac arrest. Additionally, while our study did not show an association between cause of death and ROSC, given the large number of disease categories and the small number of subjects, our study may have been inadequately powered to detect such an association.

Methods of including and excluding patients also likely introduced bias into the study population. Only CPR performed in the ICU was eligible for inclusion in the study, which may have eliminated a different population of patients arresting in other parts of the hospital, such as in the operating rooms. Most of the forms excluded from analysis were the result of incomplete $PetCO_2$ recording. It is possible that this biased our study population to CPR events with more people present, which allowed better recording or equipment troubleshooting. Two forms were excluded from analysis because CPR was short, and no ROSC occurred. These subjects could represent arrests in which CPR was considered futile, therefore excluding sicker patients from analysis.

Due to problems with availability and functionality of equipment, as well as limited human resources, many data points were also not recorded or available for review. In particular, while staff members are trained to ventilate CPA patients in a uniform manner according to RECOVER clinical guidelines at approximately 10 breaths per minute,[10] lack of consistent ventilation

rate reporting may limit interpretation of $PetCO_2$, which is known to be affected both by cardiac output and by ventilation.

As with many veterinary studies, patient outcomes were subject to owner decisions to stop CPR or to euthanize patients shortly after ROSC, confounding some outcome assessments. Clinicians, too, were not only able to discontinue CPR at their discretion, but were not blinded to capnometry vales, and therefore real-time $PetCO_2$ may have been influenced in their decision. The ability of the clinician to influence the results in this way may have been exacerbated by including patients in this study with CPR duration as short as 5 minutes. However, because median CPR duration was longer in the n-ROSC than in the ROSC patients, the effect of the $PetCO_2$ on clinician decision-making was thought to be minimal.

Because the maximum duration of CPA ultimately ending in ROSC in our study was 15 minutes, mandating that CPR be performed for a minimum of 15 minutes in all n-ROSC patients in future studies may help substantiate the association between $PetCO_2$ and ROSC. Standardization and recording of ventilatory rates would have also be ideal. Finally, a larger study adhering to prospectively determined veterinary Utstein-style guidelines would help validate the results of this and other veterinary and human studies on the association between ROSC and $PetCO_2$.

Conclusions

The findings of this investigation underscore the importance and clinical utility of monitoring $PetCO_2$ during CPR. Not only were median, maximum, and initial $PetCO_2$ values significantly higher in patients that were destined to be resuscitated than in those that were not, the values at each time point were also sensitive and specific for outcome. Thus, the results of this small study strongly support previous recommendations to monitor $PetCO_2$ during CPR in dogs and cats. The data also suggest that clinicians may be able to use these measurements in real time to offer a credible prognosis to owners of pets with CPA, and to better delegate the often-limited resources of the emergency room or ICU.

Footnotes

[a] Gymboss Classic Interval Timer, St. Clair, MI.
[b] EMMA Mainstream Capnometer, Masimo, Danderyd, Sweden.
[c] Stata 14.0 for MAC, Stata Corporation, College Station, TX.

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