CPR Guideline Chest Compression Depths May Exceed Requirements for Optimal Physiological Response

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Abstract

The following analyses evaluate the association between chest compression (CC) depth, systolic blood pressure (SBP) and end-tidal carbon dioxide ($ETCO_2$) with their target cut-offs during cardiopulmonary resuscitation (CPR).

A twelve-animal porcine study dataset was retrospectively analyzed to assess associations between CC depth, SBP and $ETCO_2$. Manual CCs were applied for 7 two-minute episodes, at CC depths between 10mm-55mm. A rolling 15s analysis window was applied to the continuous signals. Mean peak values were calculated for each window. Correlation analysis was applied to assess strength of association. Optimal CC depth to achieve physiological targets was determined via cut-off analysis.

A total of 672 observations for each variable were available for analysis. Pearson correlations (95% confidence interval; p-value) between CC depth and both SBP and $ETCO_2$ were 0.84 (0.82, 0.86; $p < 0.001$) and 0.75 (0.71, 0.78; $p < 0.001$) respectively. Optimal CC depth cut-off (sensitivity, specificity) to achieve SBP $\geq$ 100mmHg and $ETCO_2 \geq$ 10mmHg was 33 mm (98.29%, 88.94%) and 20 mm (95.08%, 78.30%) respectively.

A reasonable relationship between CC depth and physiological response was observed. Optimal SBP and $ETCO_2$ cut-offs were achieved significantly below guideline depths. Furthermore, cut-off analysis suggests a disparity between CC depth and physiological targets.

1. Introduction

Cardiac arrest is a leading cause of premature death worldwide. To increase survival rates early defibrillation and effective cardiopulmonary resuscitation (CPR) are crucial. American Heart Association (AHA) and European Resuscitation Council (ERC) basic life support guidelines consider chest compressions (CCs) at a rate of 100 to 120 CCs min^{-1} and a depth of 50 to 60 mm to be effective, amongst an adult population [1], [2].

Guideline CC depth between 50 to 60 mm has been proven to marginally increase survival to hospital admission, compared to previous guideline depths of 40 to 50 mm [3], [4]. While associated survival improves with deeper CCs so does the risk of causing injury to the patient [5]. It has been reported that CPR performance is poor for both professional and lay rescuers over several revisions of the basic life support guidelines [6], [7]. The low incidence of CC depth meeting the minimum guideline depth of 50 mm may be due to the target not being suitable for the entire adult population or early onset of fatigue [8], [9].

Research into patient response as an indicator of CPR quality is in its infancy with few physiological endpoints and cut-offs established. Advanced life support guidelines do suggest an alternative indicator of measuring CC quality. Observing a patient $EtCO_2$ response of < 10 mmHg is associated with mortality and efforts to improve CPR quality should be made. Supporting evidence suggests continuous CCs between 100 and 120 compressions min^{-1} maintains ideal blood pressure [10]. Friess *et al.* investigated the use of SBP as an indicator of CPR quality and used a physiological cut-off of 100 mmHg [11].

2. Methods

The purpose of this analysis is to determine the optimal CC depth cut-off to achieve $EtCO_2 \geq$ 10 mmHg and SBP $\geq$ 100 mmHg. To this retrospective analysis was conducted on a porcine dataset. The dataset included continuous time-series data for CC depth, $EtCO_2$ and SBP.

2.1. Study Design

All experiments were performed in accordance with the Home Office Guidance on the Operation of the Animals (Scientific Procedures) Act 1986 (UK).

Twelve (12) adult pigs, aged approximately 9 to 10 weeks and weighing between 30 to 35 kg, were enrolled in the study. Ventricular fibrillation (VF) was induced electrically, and the animals were left untreated for 3 minutes. During the untreated period animals were ventilated at an approximate rate of 12 ventilations min^{-1}.

Each animal had 7 episodes of continuous CCs applied at a rate of 110 compressions min^{-1}. The initial 4 episodes of CPR were applied to achieve an $EtCO_2$ response of < 15 mmHg. The remaining 3 episodes targeted an $EtCO_2$ response of ≥ 15 mmHg. There was a rest period of at least 10-seconds between CC episodes to simulate an automatic external defibrillator electrocardiogram analysis period.

2.2. Signal Data

A HeartStart Mrx (Philips, USA) coupled with Q-CPR technology (Laerdal Medical, Norway) was used to capture CC depth data. Depth signal data was captured at a sample frequency of 50 Hz and a resolution of 0.01 mm per least significant bit (LSB).

Physiological signals were captured using a Datex-Ohmeda S/3 Anesthesia Monitor (GE Healthcare, USA) using VitalSignsCapture [12]. Side-stream capnograph was used to measure $EtCO_2$ at a sampling frequency of 25 Hz. Arterial blood pressure (BP) was captured from the carotid artery and sampled at a rate of 100 Hz. Outputs from the anesthesia were recorded in physical units and did not require scaling prior processing.

2.3. Data Processing

An annotation review was conducted on each of the signals, by study personnel, to identify the beginning of each CPR episode. Episodes were segmented into 15-second epochs. An analysis widow was applied to each epoch to determine the amplitude of the signal.

Local minima were identified in the CC depth using a peak detection algorithm. The absolute value of the mean of the local minima within a CC depth epoch represented the mean CC depth for that 15-second period.

Capnograph and BP signals were analyzed by peak envelope. The mean upper envelope in the capnograph and BP signals were taken as the representative values of $EtCO_2$ and SBP for a given epoch respectively. The mean lower envelope represented the DBP for a given epoch.

Additional processing of the capnograph signal was conducted. A rolling, non-overlapping analysis widow was applied to the signal starting at the point of VF induction. Each window had a fixed duration of 12-seconds which terminated after 180-seconds of signal had been processed. The amplitude of the capnogram was calculated for each analysis window.

2.4. Data Analyses

Data was audited by independent review prior to analysis. R for statistical computing version 3.5.1 was used for all analyses.

Between-subject, within-subject and Pearson correlation analyses were applied to each combination of CC depth, $EtCO_2$ and SBP [13], [14].

Cutoff analyses were applied to the data to determine the probabilistic CC depth cutoffs for $EtCO_2 \geq 10$ mmHg and peak BP ≥ 100 mmHg. Depth cutoffs increased in increments of 1 mm and accuracy, sensitivity, specificity and Youden index were calculated for each CC depth cutoff. Cutoffs which are associated with maximum accuracy and maximum Youden index were reported.

The decay of $EtCO_2$ post VF induction was characterized by applying a log-log regression model to $EtCO_2$ and time data.

3. Results

A total of 672 observations (12 animals x 7 episodes x 8 analysis windows) of $EtCO_2$ and SBP were processed. There were 13 missing observation for CC depth due to the administration of shallow CCs.

There were non-significant, between-subject correlations observed for all combinations of CC depth, $EtCO_2$ and SBP (Table 1).

Strong within-subject correlations were observed for all combinations of the study endpoints; $EtCO_2$ and CC depth (0.83), $EtCO_2$ and SBP (0.86) and SBP and CC depth (0.89). Additionally, lower, yet strong Pearson correlations were observed between all combinations of study endpoints. Further details of all correlation analyses are listed in Table 1.

The maximum accuracy cut-off for CC depth to predict $EtCO_2 \geq 10$ mmHg was 20 mm. This provided an accuracy of 89.68% (sensitivity = 0.95; specificity = 0.78; Youden index = 0.73). The optimal depth cut-off to classify SBP ≥ 100 mmHg was 33 mm with an accuracy of 92.26% (sensitivity = 0.98; specificity = 0.89; Youden Index = 0.87).

Adjusting this analysis in favor of maximum Youden index the optimal cut-off for $EtCO_2 \geq 10$ mmHg increases to 21 mm with an accuracy of 87.86% (sensitivity = 0.90; specificity = 0.84; Youden index = 0.74). There was no change to the depth-cut off after adjusting for maximum Youden index.

The deterioration of $EtCO_2$ post VF induction resembled characteristics indicative of exponential decay. Data obtained for each 12-second analysis window during the untreated duration of VF were not considered to be normally distributed (Figure 1). The median value for each

Table 1 Pearson, between-subject and within-subject correlation analyses for each combination of $EtCO_2$ (n = 672, SBP (n = 672) and CC depth (n = 659).

Covariates	r	95% CI	p-value
Between-Subjects			
$EtCO_2$ and Depth	-0.28	(-0.77, 0.43)	0.386
SBP and Depth	-0.22	(-0.75, 0.48)	0.491
SBP and $EtCO_2$	0.35	(-0.35, 0.80)	0.258
Within-Subjects			
$EtCO_2$ and Depth	0.83	(0.80, 0.85)	< 0.001
SBP and Depth	0.89	(0.87, 0.91)	< 0.001
SBP and $EtCO_2$	0.86	(0.84, 0.88)	< 0.001
Pearson			
$EtCO_2$ and Depth	0.75	(0.71, 0.78)	< 0.001
SBP and Depth	0.84	(0.82, 0.86)	< 0.001
SBP and $EtCO_2$	0.80	(0.78, 0.83)	< 0.001

timepoint was applied to a regression model to trend the decay. A log-log model was trained after applying a natural log transform to both $EtCO_2$ and time data. This provides the following model satisfied in terms of $EtCO_2$ (y) as a response of time (x):

$$y = e^{-0.71.log_e(x) + 5.45}$$

The coefficient of determination for the model (R^2) was 0.996, suggesting the model is a good fit for the data.

4. Discussion

The analysis conducted could not identify a relationship between animals which received higher CC depths and

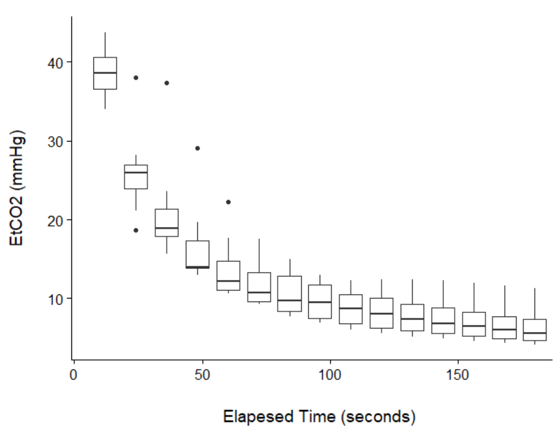

Figure 1 Boxplot series displaying the exponential decay of $EtCO_2$ as function of time, after induction of VF. (N = 144; 12 observations per time point x 12 timepoints)

those which produced higher $EtCO_2$ or SBP responses. This may be consequential to the damage which occurred to one animal’s thorax or that each animal received the same treatment.

The Pearson correlation analysis suggests there is a moderate relationship between CC depth and $EtCO_2$ (0.75). Comparisons of CC depth and SBP show a stronger relationship (0.84). Comparing the Pearson and within-subject correlation analyses, however, suggests there is a considerable improvement between the covariates when fitting for each animal individually. With variability amongst such a small and homogenous sample of animals, it would be interesting to see the variation on a random sample of the human population.

The binary outcome for $EtCO_2 \geq 10$ mmHg was predicted accurately using a CC depth cut-off of 20mm; Accuracy (89.68%) and Youden index (0.73). Similarly, binary outcome for SBP was accurately predicted with a depth cut-off of 33 mm; Accuracy (92.26%) and Youden index (0.87).

Depths required to meet the physiological targets however, are considerably lower than the current guideline recommended depths of 50 to 60 mm. It is also worth noting that depths required to achieve the defined physiological cut-offs were also not in agreeance. This reflects the conclusion of Steill et al, that an increase in CC depths is associated with better patient outcomes, however, the optimal depth of CC is still unknown [9].

One animal suffered extensive thoracic trauma as a result of receiving CC depths in excess of 45 mm. Complications due to this treatment included bleeding into the thorax, bleeding into the pericardial sac, bruised myocardium, bullae on the lungs and most severely ruptured atria. This highlights that a balanced approach to delivering safe and efficacious CC depth targets is required. This study demonstrated depths greater than 45 mm were acceptable for 11 of the 12 enrolled animals, however, one displayed irreversible damage as a result of this treatment. At what point are the CC depth targets considered safe for use on the human population? Can damage such as that observed during this study be avoided if patient response is monitored during CPR instead of sternum displacement?

Upon visual inspection of the synchronized signals, it is apparent that $EtCO_2$ is a slow response variable, which does not reflect sudden changes in applied CC depth (Figure 2). This is especially evident when VF is induced or there is a cessation of CCs, as decay period in the capnogram may be observed. However, SBP appears to respond instantaneously to changes in applied CC depth.

5. Limitations

The investigation was a retrospective analysis of a previously obtained dataset. The objective of the original study did not match the objective of this post hoc analysis.

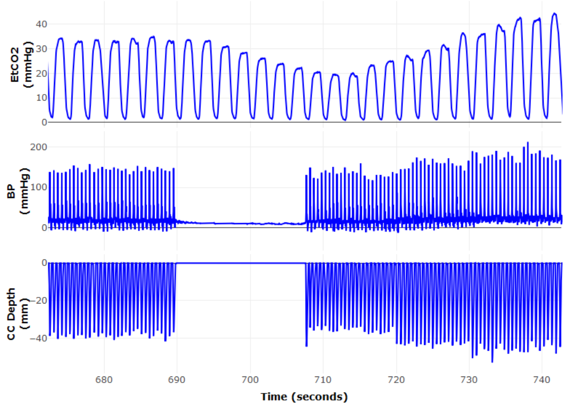

Figure 2 Representative time series plots of $EtCO_2$, BP and CC depth demonstrating the slow response of EtCO2 to sudden changes in CC depth

Treatment was not randomized during the study. Depth of CC increased with each episode which may have an indirect impact on physiological response of the animal. As observed as part of the analysis, $EtCO_2$ had a decay artefact and requires a considerable amount of time to baseline, perhaps the 10-second interval between CC episodes would need extended to accommodate this.

6. Conclusions

This investigation provides encouraging preliminary results indicating that CC depths recommended by AHA and ERC guidelines may be excessive. As this is a retrospective analysis further research is required to establish the relationship between animals for CC depth and the physiological endpoints.

Conflicts of Interest

Olibhéar McAlister, Hannah Torney, Ben McCartney, Laura Davis and Adam Harvey are employees of HeartSine Technologies Ltd. Paul Crawford is a consultant veterinary anesthetist contracted by HeartSine Technologies Ltd.

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