

**End-tidal carbon dioxide output in manual cardiopulmonary resuscitation vs. active compression-decompression device during prehospital quality-controlled resuscitation, a case-series study.**

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## ABSTRACT

**Background** Active compression-decompression (ACD) devices have enhanced end-tidal carbon dioxide (ETCO<sub>2</sub>) output in experimental cardiopulmonary resuscitation (CPR) studies. However, the results among out-of-hospital cardiac arrest (OHCA) patients have shown inconsistent outcomes and earlier studies lack quality-control of CPR attempts. We compared manual CPR to ACD-CPR by measuring ETCO<sub>2</sub> output using an audio-visual feedback defibrillator to ensure continuous high-quality resuscitation attempt.

**Methods** Ten witnessed OHCAs were resuscitated rotating a two minute cycle with manual CPR and a two minute cycle of ACD-CPR. Patients were intubated and ventilation rate was held constant during CPR. The CPR quality parameters and ETCO<sub>2</sub> values were collected continuously with the defibrillator. The differences in ETCO<sub>2</sub> output between manual CPR and ACD-CPR were analysed using linear mixed-model, where ETCO<sub>2</sub> output produced by summary of two minute cycles was included as dependent variable, patient as random factor and method as fixed effect. These comparisons were made within each OHCA case to minimise confounding factors between the cases.

**Results** Mean length of the CPR episodes was 37 (SD=8) minutes. Mean compression depth was 76 (SD=1.3) mm vs 71 (SD=1.0) mm and mean compression rate was 100 (SD=6.7)<sup>min<sup>-1</sup></sup> vs 105 (SD=4.9)<sup>min<sup>-1</sup></sup> between ACD-CPR and manual CPR, respectively. For the ETCO<sub>2</sub> output, interaction between the method and the patient was significant ( $p<0.001$ ). The ETCO<sub>2</sub> output was higher with manual CPR in six out of ten cases.

**Conclusions** This study suggests that quality-controlled ACD-CPR is not superior to quality-controlled manual CPR when ETCO<sub>2</sub> is used as a quantitative measure of CPR effectiveness.

<b>What is already known on this subject?</b>
<ul style="list-style-type: none"> <li>Active compression-decompression (ACD) devices have improved venous return and cardiac output during cardiopulmonary resuscitation (CPR) in experimental studies.</li> </ul>
<ul style="list-style-type: none"> <li>Earlier clinical reports comparing ACD-CPR and manual CPR have been controversial and completely lack the quality control measurements of CPR attempts.</li> </ul>
<b>What this study adds?</b>
<ul style="list-style-type: none"> <li>Our experimental study presents a novel approach to the evaluation of an active compression-decompression (ACD) device vs. manual CPR by applying continuous quality measurement of both CPR methods in the prehospital setting.</li> </ul>
<ul style="list-style-type: none"> <li>This study suggests that when using ETCO<sub>2</sub> as an indicator of CPR performance, quality controlled ACD-CPR is not superior to quality controlled manual CPR under the guidance of real-time audio-visual feedback system defibrillator in the prehospital setting.</li> </ul>

## INTRODUCTION

Novel resuscitation guidelines emphasise high quality cardiopulmonary resuscitation (CPR): chest compression rate should be at least  $100^{-1\text{min}}$ , chest compression depth should be at least 5cm and external defibrillation should be delivered as early as possible.[1] End-tidal carbon dioxide (ETCO<sub>2</sub>) reflects cardiac output during low-flow states.[2, 3] Thus ETCO<sub>2</sub> is a surrogate for CPR performance and has been shown to predict return of spontaneous circulation (ROSC) and survival.[4]

Active compression-decompression (ACD) devices have enhanced negative intrathoracic pressure and improved venous return and myocardial perfusion during CPR, thus one would expect improved resuscitation outcomes.[5] However, reported clinical results have been controversial and they completely lack quality control of the resuscitation attempts; the current conclusion is that there is neither harm nor benefit from using an ACD device.[6]

A more recent approach to improve resuscitation quality is the use of real-time audio-visual feedback system defibrillators that provide continuous guidance for a proper performance of CPR by measuring chest compression rate, depth, duty-cycle and no-flow time during the resuscitation attempt.[7-8] The quality of chest compressions is measured with a sensor attached to the patient's chest and automatic guidance prompts the CPR provider directly for optimal performance to match goals that are set in the resuscitation guidelines.

There is a constant need of an independent quality analysis of the healthcare industry produced equipment like the ACD device in the clinical setting. Using ETCO<sub>2</sub> as an indicator, the aim of this study was to evaluate whether ACD-CPR provides better overall resuscitation quality than manual CPR when both methods are provided alternating in two minute cycles during the on-going resuscitation attempt under the guidance of an audio-visual feedback system defibrillator in the prehospital setting.

## **METHODS**

### **Study objective**

The purpose of the present study was to assess whether quality-controlled ACD-CPR provides better overall resuscitation quality compared to quality-controlled manual CPR by using the ETCO<sub>2</sub> as a surrogate marker.

This observational self-controlled case-series study was carried out in the anaesthetist staffed Pirkanmaa Helicopter Emergency Medical Service (HEMS) unit, Tampere University Hospital, Finland.

### **Organisation**

The anaesthetist staffed HEMS serves approximately 600,000 inhabitants in the Pirkanmaa area and the surrounding area in Finland. In addition to the HEMS, the Emergency Medical Service (EMS) system includes first responding units (FRU) and basic life support (BLS) units staffed with firemen-emergency medical technicians (EMT), and paramedic staffed advanced life support (ALS) units. An FRU and the nearest BLS or ALS unit with the HEMS unit are always dispatched to high-risk medical emergencies such as sudden cardiac arrest.

### **Study design**

The study core data comprised of ten adult OHCA patients' continuous ETCO<sub>2</sub> measurements during CPR attempt. Data were collected during seven months, 9/2013 to 3/2014. Adult patients not suffering from trauma or hypothermia were enrolled to the study if the HEMS crew decided to continue resuscitative

efforts on scene for at least five minutes after securing the airway by endotracheal tube to ensure adequate collection of every single ventilation associated ETCO<sub>2</sub> data. All patients were treated according to the European Resuscitation Council (ERC) resuscitation guidelines.[9] On arrival at the scene, the HEMS crew attached a real-time audio-visual feedback defibrillator (Zoll® X Series™, Real CPR Help™, ZOLL Medical Corporation, USA) to the patient's chest during on-going resuscitation and the defibrillator's compression quality sensor was placed in the midsternal position on the patient's chest. HEMS physician performed an endotracheal intubation and the defibrillator's continuous sidestream CO<sub>2</sub> recording connector was attached to the endotracheal tube. The first ACD-CPR cycle started as soon as the previous 2 minute cycle of CPR was finished and the measurements started as soon as all parameter sensors were ready. Thereafter patients were resuscitated a two-minute cycle with standard manual CPR followed by a two-minute cycle of ACD-CPR with continuous guidance from the audio-visual feedback defibrillator. These cycles rotated as long as resuscitation was attempted. The person delivering chest compressions was changed with every two-minute cycle during rhythm analysis according to the resuscitation guidelines. A manual lightweight ACD-CPR device (Ambu CardioPump, Ambu International Inc. Copenhagen, Denmark) consisting of a silicone rubber suction cup and a plastic handle containing a force gauge and a metronome, was placed over the defibrillator's compression quality sensor to perform ACD-CPR cycles, Figure 1. To assure the seal of the ACD device, the outer insulator layer of the wires from the compression quality sensor crossing under the suction cup had been removed prior the resuscitation attempt and the thin wires were under adhesive tape when crossing the suction cup. The sensor itself fitted inside the rubber suction cup without touching the cup. Compressions and decompressions were performed with a 50 % duty cycle at the rate of 100 min<sup>-1</sup> in accordance with the ERC guidelines. HEMS paramedics were responsible in delivering the ACD-CPR cycles during the resuscitation attempts. The feedback device remained attached to the patient's chest during all cycles. The ventilation rate was maintained constant manually during the cycles. The beat-by-beat CPR quality data with measurements of every single chest compression depth, rate and duty cycle, and every single ventilation associated ETCO<sub>2</sub> values were recorded continuously with the defibrillator during the resuscitation attempt. Data were analysed using dedicated quality analysis software

(RescueNet Code Review™, ZOLL Medical Corporation, USA). One of the authors (PS) compared the ETCO<sub>2</sub> values with the capnography curve data to ensure correct analysis of every single ventilation associated ETCO<sub>2</sub> value during the entire resuscitation attempt. The differences in ETCO<sub>2</sub> output produced by summary of two minutes manual CPR cycles and by two minutes ACD-CPR cycles were compared in each individual patient separately to minimise confounding factors between the cases.

## **Statistics**

The study was designed based on preliminary results of a pilot study of a continuous response variable from matched pairs of both CPR methods in four study subjects. A pair consisted of measurements on both methods within a same subject patient. Pilot study data indicated that the difference in the response of matched pairs was normally distributed with a standard deviation of 0.35 and the true difference in the mean response of matched pairs was 0.7kPa. This led to the conclusion that we needed to study 4 pairs of subjects to be able to reject the null hypothesis, at power 0.8 and the Type I error 0.05.

The statistical analysis was performed using SPSS software (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Data are presented as numbers or as means and standard deviations (SD) as indicated. In linear mixed-model the ETCO<sub>2</sub> output produced by summary of two minutes cycles was included as dependent variable. The model included patient as random factor, method as fixed effect and patient\*method interaction effect. All comparisons were two-tailed, and a p-value <0.05 was considered statistically significant.

## **Ethics**

This study was carried out in the physician staffed Pirkanmaa Helicopter Emergency Medical Service (HEMS) unit, Tampere University Hospital, Finland, (Clin Trials: NCT 00951704). The Regional Ethics Committee of Pirkanmaa Health District approved the study and waived the need for informed consent as both CPR methods were considered as standard of care (R08116).

## RESULTS

EMS attempted CPR in 194 OHCA cases during the study period. The HEMS unit was on scene in 108 cases and terminated the resuscitative efforts by consultation before reaching the scene in 86 cases. Twelve adult OHCA patients met the inclusion criteria during the study period. One patient suffering from submersion was excluded from the study because of insufficient attachment of ACD-CPR device on the patient's chest and one patient was excluded from the study due to data loss.

Table 1. Patient characteristics and the differences in end-tidal carbon dioxide values between manual CPR and active compression-decompression CPR with data point measurements.

Patient	Age, (years)	Gender	First rhythm	ETCO <sub>2</sub> (kPa)			ETCO <sub>2</sub> (kPa)		
				ACD-CPR			Manual CPR		
				data points (n)	mean <sup>†</sup>	SD	data points (n)	mean <sup>†</sup>	SD
1	85	female	VF	32	2.30	0.4	40	3.45	0.2
2	68	male	ASY	50	3.47	0.6	41	3.07	0.1
3	83	male	PEA	56	4.61	0.7	64	4.63	0.5
4	92	male	ASY	44	4.37	0.5	53	4.76	1.0
5	59	male	VF	54	4.76	1.1	50	4.39	0.7
6	68	male	PEA	31	4.02	0.5	43	3.78	0.5
7*	68	male	PEA	65	3.77	0.2	70	4.08	0.4
8	75	male	PEA	35	4.92	0.6	31	5.05	0.5
9	76	female	PEA	65	2.21	0.3	74	1.88	0.4
10	71	male	PEA	66	4.30	0.7	62	4.44	0.9

ACD-CPR indicates active compression-decompression cardiopulmonary resuscitation; ASY, asystole; CPR, cardiopulmonary resuscitation; ETCO<sub>2</sub>, in end-tidal carbon dioxide; PEA, pulseless electrical activity; SD, standard deviation; VF, ventricular fibrillation. \*Return of spontaneous circulation achieved † The mean value of single ventilation associated ETCO<sub>2</sub>

Patient characteristics and the differences in ETCO<sub>2</sub> output between manual CPR and ACD-CPR are presented in Table 1. All cardiac arrests were witnessed. The mean age was 75 (SD=10) years. The mean length of the CPR episode was 37 (SD=8) minutes and the mean delay to arrival of the HEMS crew from the onset of cardiac arrest was 17 (SD=8) minutes. One patient achieved ROSC. In linear mixed-model analysis

the interaction between the method (fixed effect) and the patient (random factor) was significant ( $p < 0.001$ ), resulting significant difference in  $\text{ETCO}_2$  output between manual CPR and ACD-CPR within every patient. In six out of ten cases the  $\text{ETCO}_2$  output was higher with manual CPR and in four cases ACD-CPR showed higher  $\text{ETCO}_2$  values, as shown in Figure 2. The quality measurements of resuscitation attempts with manual CPR versus ACD-CPR are presented in Table 2. All parameters showed rescuers performing good-quality CPR during both ACD-CPR and manual CPR. Ventilation rate was maintained constant during the individual resuscitation attempts within both resuscitation methods.

Table 2. Resuscitation quality measurements during cardiopulmonary resuscitation attempts.

	Depth (mm) Mean (SD)	Rate (cpm) Mean (SD)	No flow time (%) Mean (SD)	Ventilations (vpm) Mean (SD)
ACD-CPR	76 (1.3)	100 (6.7)	8 (10.4)	11 (2.9)
Manual CPR	71 (1.0)	105 (4.9)	1 (4.6)	11 (2.6)

ACD-CPR indicates active compression-decompression cardiopulmonary resuscitation; cpm, compressions per minute, CPR, cardiopulmonary resuscitation;  $\text{ETCO}_2$ , end-tidal carbon dioxide; no flow time, the ratio between all pauses between the compressions; SD, standard deviation; vpm, ventilations per minute.

## DISCUSSION

In this observational self-controlled case-series study, we compared manual CPR with ACD-CPR to evaluate the differences in  $\text{ETCO}_2$  production during quality-controlled resuscitation using a defibrillator with audio-visual feedback and continuous every single ventilation associated sidestream  $\text{CO}_2$  recording with capnography. In our study, a novel approach to the evaluation of the ACD device vs. manual CPR was the application of continuous measurement of quality parameters within both CPR methods. Typical confounding factors that affect the interpretation of CPR attempts such as age, gender, previous medical history, the cause of the cardiac arrest, primary rhythm, location of the arrest and the time delay of beginning the CPR attempt were minimised by comparing both methods in each individual patient separately, and by controlling the quality of chest compressions and ventilation rate to ensure they would



not have an impact to the ETCO<sub>2</sub> production. According to our results, quality-controlled ACD-CPR is not superior to quality-controlled manual CPR.

Previously, ACD-CPR has been shown to enhance aortic systolic pressure and myocardial perfusion pressure and increase myocardial and cerebral blood flow compared to manual CPR in experimental animal and human studies.[5, 10] Thus one might expect ACD-CPR to create higher EtCO<sub>2</sub> output compared to manual CPR. Despite its promising effects in these studies, ACD-CPR has failed to demonstrate any superiority in prehospital patient care.[6] Regarding the use of ETCO<sub>2</sub> values as a surrogate for CPR produced cardiac output, an earlier study by Mauer et al. found no difference in ETCO<sub>2</sub> values between the ACD patient group and the manual CPR patient group in OHCA.[11] However, these ETCO<sub>2</sub> readings were recorded only in every two minutes. Plaisance et al. reported an improvement with ACD group versus manual CPR on hospital discharge,[12] whereas other studies did not show statistically significant differences in ROSC, hospital admission, survival or neurological prognosis.[13-15] The importance of evaluating the ETCO<sub>2</sub> values by analysing capnography curves was described recently.[16] Chest compressions generate minimal tidal volumes during the resuscitation attempt and plain capnometry will monitor these numerical values as part of the ETCO<sub>2</sub>. In our study, we analysed every single ventilation associated ETCO<sub>2</sub> data and beat-by-beat chest compressions with associated capnography curves to exclude values that were not associated with a ventilation assisted ETCO<sub>2</sub>. Variations in chest compression depth and ventilation rate also alternate ETCO<sub>2</sub> values during the resuscitation attempt,[17] and therefore quality parameters are essential when comparing two CPR methods. In our study, the ventilation rate was maintained constant during the resuscitation attempt as ETCO<sub>2</sub> values were compared between the two CPR methods in every patient separately.

It is currently acknowledged that delay in the commencement of CPR and insufficient chest compressions have detrimental effects on the patient's arterial and perfusion pressures.[18] A multicentre case series study reported in 2005 that prehospital personnel with advanced cardiac life support training and regular retraining failed to deliver CPR according to guidelines during OHCA by not delivering chest compressions

half of the time and compressing too shallow most of the time.[19] Regarding the earlier studies in which manual CPR without quality feedback were compared to ACD-CPR, it should be taken into consideration that the ACD device itself is a feedback device as it has a gauge in the handle for the measurement of both sufficient compression depth and upward force and nowadays also a metronome to ensure an appropriate compression rate. More encouraging results with earlier ACD-CPR studies might have resulted from the active chest lift stopping the rescuer from leaning on the chest during the recoil phase that would have an undesirable effect on coronary and cerebral perfusion pressures by impeding venous return and decreasing mean arterial pressure.[18] However, performing ACD-CPR requires 25 per cent more effort than manual CPR and thus may be more difficult to perform over sustained periods of time.[20] Multicentre studies have reported that the ACD device demanded a longer period of training and rescuer fatigue was a common problem.[12, 13] These studies demonstrate the utmost importance of regularly changing the person providing CPR to avoid fatigue during the resuscitation attempt and to provide continuous high quality CPR. Parameters for high quality CPR such as chest compression depth, compression rate, duty cycle of 50 %, minimal no-flow time and full recoil of the chest during the decompression phase are easily monitored with the real-time audio-visual feedback defibrillator during resuscitation.

### **Study strengths and limitations**

The strength of this study is that we handled the confounding factors between the cases by analysing the differences in  $\text{ETCO}_2$  between manual CPR and ACD-CPR separately with every patient and present a study measuring the quality parameters of chest compressions when comparing these two resuscitation methods. The data was recorded by compression-to-compression and from every single ventilation during the entire resuscitation attempt to ensure the quality of measurements. The ventilation rate was maintained constant during the resuscitation attempt and every single ventilation associated  $\text{ETCO}_2$  values were recorded continuously and data were evaluated with capnography during the analysis of the data. Changing the CPR method during the resuscitation attempt did not affect the quality as indicated in the CPR quality parameter recordings.

On the other hand there are some limitations in this study. First, the total number of patients was small. However, the study was conducted after a pilot study that provided us the power calculations described in the methods section. Secondly, the minute ventilation of the patient was not controlled due to manual ventilation during the resuscitation attempt as mechanical ventilation during CPR is regarded as contraindicated. Third, all but one patient died on the scene which may have an impact to the ETCO<sub>2</sub> values recorded. Fourth, in the study design, patients were not randomised by the first attempted CPR method, but the measurements started with either ACD-CPR or with manual CPR cycle depending on when all the parameter sensors were ready. This could have affected the results and caution should be exercised in the interpretation and extrapolation of the data.

## **Conclusions**

According to our results, quality-controlled ACD-CPR does not provide better overall resuscitation quality compared to quality-controlled manual CPR when using ETCO<sub>2</sub> as a surrogate for CPR performance.

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## **Competing interests**

The authors declare that they have no competing interests.

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## **Authors' contributions**

All authors certify that they have participated sufficiently in the work including participation in the concept, design, analysis, writing, or revision of the manuscript. IV, AK and SH planned the study design. All authors collected the patient data. PS analysed and interpreted the patient data. PS and HH performed the statistical tests. PS was a major contributor in writing the manuscript. AY made the revision of the manuscript. All authors read and approved the final manuscript. Furthermore each author certifies that this material has not been submitted to or published in any other publication before.

## **Ethics approval**

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### **Legends for the figures**

Figure 1. Resuscitation with active compression-decompression device and the audio-visual feedback defibrillator.

Figure 2. The mean values of end-tidal carbon dioxide between active compression-decompression and manual cardiopulmonary resuscitation.

