RESUSCITATION 179 (2022) 225–232

Available online at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Contribution of chest compressions to end-tidal carbon dioxide levels generated during out-of-hospital cardiopulmonary resuscitation

Jose Julio Gutiérrez[a], *Camilo Leonardo Sandoval*[b], *Mikel Leturiondo*[a], *James Knox Russell*[c], *Koldo Redondo*[a], *Mohamud Ramzan Daya*[c], *Sofía Ruiz de Gauna*[a,*]

Abstract

Aim: Characterise how changes in chest compression depth and rate affect variations in end-tidal CO_2 ($ETCO_2$) during manual cardiopulmonary resuscitation (CPR) in out-of-hospital cardiac arrest (OHCA).

Methods: Retrospective analysis of adult OHCA monitor-defibrillator recordings having concurrent capnogram, compression depth, transthoracic impedance and ECG, and with atleast 1,000 compressions. Within each patient, during no spontaneous circulation, nearby segments with changes in chest compression depth and rate were identified. Average $ETCO_2$ within each segment was standardised to compensate for ventilation rate variability. Contributions of relative variations in depth and rate to relative variations in standardised $ETCO_2$ were characterised using linear and non-linear models. Normalisation between paired segments removed intra and inter-patient variation and made coefficients of the model independent of the scale of measurement and therefore directly comparable.

Results: A total of 394 pairs of segments from 221 patients were analysed (33% female, median (IQR) age 66 (55–74) years). Chest compression depth and rate were 50.4 (43.2–57.0) mm and 111.1 (106.5–116.1) compressions per minute. $ETCO_2$ before and after standardization was 32.1 (23.0–41.4) mmHg and 28.5 (19.4–38.7) mmHg. Linear model coefficient of determination was 0.89. Variation in compression depth mainly explained $ETCO_2$ variation (coefficient 0.95, 95% confidence interval (CI): 0.93–0.98) while changes in compression rate did not (coefficient 0.04, 95% CI: 0.01–0.07). Non-linear trend analysis confirmed the results.

Conclusion: This study quantified the relative importance of chest compression characteristics in terms of their impact on CO_2 production during CPR. With ventilation rate standardised, variation in chest compression depth explained variations in $ETCO_2$ better than variation in chest compression rate.

Keywords: Cardiopulmonary resuscitation (CPR), Chest compression quality, Chest compression depth, Chest compression rate, Ventilation rate, End-tidal CO_2, Out-of-hospital cardiac arrest (OHCA), Advanced life support (ALS)

Introduction

Waveform capnography analysis can help in assessing a patient's condition during cardiopulmonary resuscitation (CPR). It reflects the evolution of the partial pressure of carbon dioxide in the exhaled air, whose value at the end of expiration is called end-tidal CO_2 ($ETCO_2$). $ETCO_2$ reflects cardiac output, organ perfusion and pulmonary blood flow potentially providing a non-invasive measurement of the patient's response to resuscitation efforts.[1–3] Current resuscitation guidelines promote waveform capnography to help to confirm correct advanced airway placement, to detect restoration of spontaneous circulation (ROSC) early, to assist with termination of resuscitation and for real-time monitoring of CPR quality.[4,5] During CPR,

Abbreviations: CPR, Cardiopulmonary resuscitation, ETCO2, End-tidal carbon dioxide, OHCA, Out-of-hospital cardiac arrest, ROSC, Return of spontaneous circulation, ALS, Advanced life support

* Corresponding author.
E-mail address: sofia.ruizdegauna@ehu.eus (S. Ruiz de Gauna).

https://doi.org/10.1016/j.resuscitation.2022.07.009
Received 21 April 2022; Received in Revised form 23 June 2022; Accepted 5 July 2022

0300-9572/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

ventilations and compressions influence CO_2 extraction and generation, respectively; therefore, ventilation rate, and chest compression depth and rate, among others, affect $ETCO_2$.[6–11] The optimal values to objectively guide CPR based on $ETCO_2$ remain unknown. Quantifying interactions among CPR components and $ETCO_2$ levels and trends may help to better understand CPR quality in terms of patients' responses,[12,13] avoid hyperventilation[14] and optimize chest compressions during resuscitation.[15–17]

Linear regression models for describing the relationship between $ETCO_2$ and ventilation rate, chest compression depth and chest compression rate have been proposed, under the assumption of additive effects and similar dependency between $ETCO_2$ and the variables under study.[18–20] Correlations have been reported in terms of absolute $ETCO_2$ increments (i.e. in mmHg),[18,19] or in terms of $ETCO_2$ relative changes.[20] Conversely, animal studies have shown a non-linear relationship between ventilation rate and $ETCO_2$.[21,22] Two retrospective observational studies conducted by our research group with out-of-hospital cardiac arrest (OHCA) data supported those findings through a mathematical model explaining in isolation the effect of ventilation rate on $ETCO_2$.[23,24] Furthermore, we suggested that variability of ventilation rate obscures measurement of the underlying patient response thereby precluding reliable interpretation of $ETCO_2$ during resuscitation. We hypothesized that standardizing the measured values to a common reference ventilation rate would enhance clinical usefulness of $ETCO_2$ during resuscitation.[25]

Continuing that line of study, our next aim has been to determine how much of the measured $ETCO_2$ is related to the characteristics of chest compressions. We sought to establish a quantitative relationship between $ETCO_2$ and compression depth and rate, through retrospective analysis of adult OHCA episodes. To eliminate ventilation rate as a confounder, measured $ETCO_2$ values were standardised according to a model we defined in an earlier study.[24] Other confounders, such as the specific metabolism of each patient, were controlled for by carefully defining the inclusion criteria and by studying how relative changes of the explanatory variables affected $ETCO_2$ changes.

Materials and methods

Data collection

The data set derives from adult OHCA episodes attended by Tualatin Valley Fire & Rescue (TVF&R), an ALS fire first response Emergency Medical Services (EMS) agency (Tigard, Oregon, USA), from 2006 through 2017. The database is a part of the Portland Resuscitation Outcomes Consortium Epidemiological Cardiac Arrest Registry, approved by the Institutional Review Board (IRB00001736) of the Oregon Health & Science University (OHSU). Patient personal information is not included in the records. Heartstart MRx monitor-defibrillators (Philips Healthcare, USA), used to record the episodes, were equipped with capnography monitors, using sidestream sampling (Microstream™, Oridion Systems Ltd., Israel) and with chest compression monitors (Q-CPR™technology).[26] The database included only episodes with chest compressions and concurrent ventilations provided manually. Episodes with concurrent capnogram, compression depth, electrocardiography (ECG), and transthoracic impedance signals were extracted. Only episodes corresponding to patients receiving at least 1,000 chest compressions were included in the study.

Segment pair selection

The purpose of the study was to quantify the influence of relative variations of compression depth and rate on relative variations of $ETCO_2$. Thus, the model we were looking for would explain how changes in the independent variables affect changes in the dependent variable. For that purpose, we sought to locate pairs of nearby segments within patients, characterise each segment in terms of ventilation rate, compression depth and rate, and $ETCO_2$, and normalise these measures so that we could characterise changes. Normalisation within patients, comparing each second segment to the corresponding first segment, was necessary for several reasons: first, to remove variation among patients; second, to isolate the results from the influence of the evolution of patient's metabolism, and third, to make coefficients of our model independent of the scale of measurement and therefore directly comparable.

Three biomedical experts (JJG, ML, CLS) used a custom-made Matlab (Mathworks, USA) graphical tool for displaying signals and for annotation. The graphical tool included automatic pre-annotation of compression pauses, compression and ventilation instances, and $ETCO_2$. We anticipated that the segment pairs would generally appear separated by compression pauses, where the dynamics of chest compression delivery usually changes. A maximum of 1-min separation between segments in a pair was permitted to minimise changes in metabolic activity. Absence of spontaneous circulation was confirmed by ECG inspection and by the ROSC annotations of ALS providers. In case of doubt between a perfusing rhythm or pulseless electrical activity, we used the transthoracic impedance signal for discrimination.[27] Within each segment, we required a reliable capnogram showing stability (low variability) in the duration of ventilations and $ETCO_2$ per ventilation, and a reliable compression depth signal with low variability in compression depth and rate. Thus, annotations were representative of each segment. The three reviewers jointly annotated 100 cases, agreeing upon criteria. Fig. 1 illustrates the annotation of a pair of segments. The remaining cases were each annotated by an individual reviewer. Finally, all uncertainties were reviewed jointly, and discrepancies resolved by consensus.

Annotated $ETCO_2$ values were made independent of ventilation rate. For that purpose, we referred measured $ETCO_2$ values to a common reference ventilation rate using the standardization equation: [24]

$$ETs_i = ET_i \cdot \frac{1 - k^{vr_s}}{1 - k^{vr_i}}, \quad (1)$$

where:

- ETs_i : ET_i value standardised to vr_s (mmHg).
- ET_i: ETCO2 value associated to the *i*-segment (mmHg).
- vr_i: ventilation rate of the i-segment (in ventilations per minute, vpm).
- vr_s: reference ventilation rate for standardisation (vpm).
- k: CO_2 concentration decay coefficient.

We used a decay coefficient $k = 0.91$ and a reference ventilation rate $vr_s = 10$ vpm in Eq. 1, according to our previous study.[24] The value for the decay coefficient yielded the best model fit with low dispersion among patients. The reference ventilation rate is the target currently recommended by the guidelines. As illustrated in Fig. 1, each pair of segments was characterised by the relative change in $ETCO_2$ (measured and standardised), chest compression depth

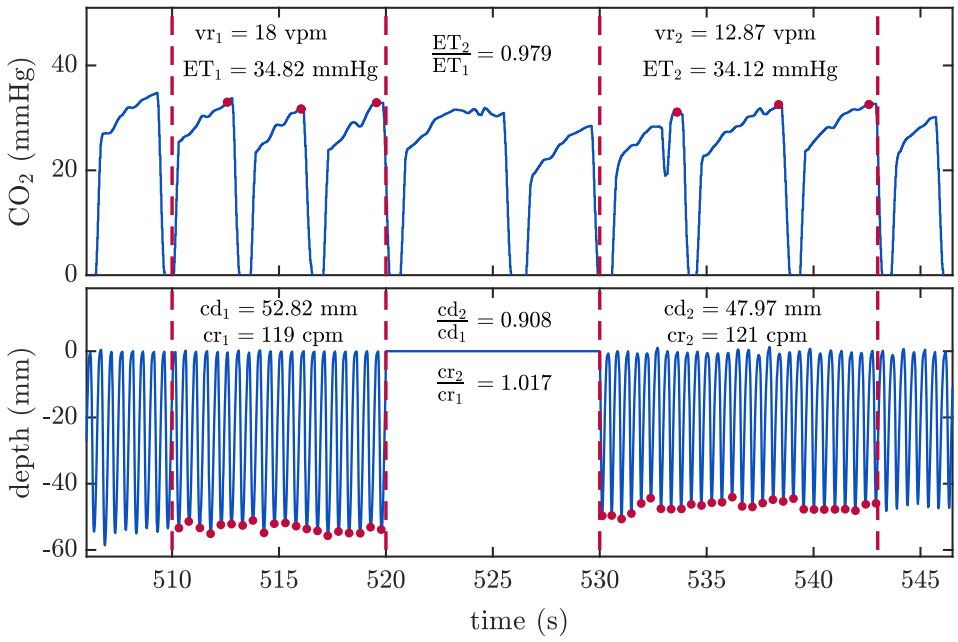

Fig. 1 – Example of paired segments. Annotated values within each segment and corresponding ratios are shown: $ETCO_2$ (ET_1, ET_2), average chest compression depth (cd_1, cd_2), chest compression rate (cr_1, cr_2) and ventilation rate (vr_1, vr_2).

and chest compression rate from the first to the second segment, expressed as ratios.

Statistical analysis

The contributions of changes in depth and rate to changes in standardised $ETCO_2$ were characterised according to the model:

$$\frac{ETs_2}{ETs_1} = a \cdot \frac{cd_2}{cd_1} + b \cdot \frac{cr_2}{cr_1} \quad (2)$$

Model variables are scale-free ratios making magnitude comparison of model coefficients meaningful. The model was fitted using the bi-square method for robustness, with a confidence level of 95%. This method minimises a weighted sum of the squared residuals, finding a curve that fits the bulk of the data using the least-squares approach and, simultaneously, minimising the effect of outliers.[28] Coefficients of determination were used to evaluate the goodness of fit and linear associations among metrics. Trends with compression depth and rate ratios were assessed with Jonckheere-Terpstra tests[29] conditioned on statistically significant differences from Kruskal–Wallis ANOVA.[30] We considered p (from ANOVA) and p_{trend} (from tests for trend) values below 0.05 to be statistically significant. Values were reported as median (interquartile range, IQR).

Results

The database contained 1,036 patient episodes. Of these, 502 had concurrent required signals and at least 1,000 chest compressions. Total analysed capnogram duration was 12,898 min. Pairs of segments meeting the inclusion criteria were identified in 221 patients, whose characteristics are reported in Table 1. For this cohort of patients, the median age was 66 (55–74) years and 33% were female. Patients were intubated with endotracheal tube (47%) or had their airway managed with a supraglottic King LT-D device (45%). Airway type was unknown for 8% of the patients. Initial EMS rhythm was asystole in 46% of the episodes, shockable in 30%, and pulseless electrical activity in 24%. ROSC was achieved in the field in 34% of the patients. Death occurred in the field in 32% of the episodes, in the Emergency Department (ED) in 45% and after hospital admission in 19%; 4% of the patients survived to hospital discharge. Note that this low survival rate reflects outcomes only in these extended cases (with at least 1,000 chest compressions).

Table 1 – Patient characteristics, disposition and advanced airway type for the annotated episodes (n = 221). ROSC refers to any ROSC event.

Characteristic	Observed value
Age (y), median (IQR)	66 (55–74)
Sex, n (%)	
Female	74 (33)
Male	147 (67)
Advanced airway type, n (%)	
Endotracheal tube (ETT)	103 (47)
Supraglottic King LT-D (SGA)	100 (45)
Unknown	18 (8)
Initial rythm, n (%)	
Shockable (VF/VT)	66 (30)
Pulseless electrical activity	54 (24)
Asystole	101 (46)
Return of Spontaneous Circulation (ROSC), n (%)	76 (34)
Disposition, n (%)	
Died in field	71 (32)
Died in emergency department	100 (45)
Died after hospital admission	41 (19)
Discharged alive	9 (4)

A total of 394 pairs of segments were included in the study. Median separation between segments within a pair was 42.3 (37.6–46.4) s. Mean coefficient of variability of the per compression and per ventilation measures within each segment were 0.054, 0.034, 0.028, and 0.141 for compression depth, compression rate, $ETCO_2$, and ventilation rate, respectively. These results confirm the required stability of the measures within each segment. Table 2 shows the distributions of annotated values and ratios between segments in each pair. Median measured $ETCO_2$, ET, was 32.1 (23.0–41.4) mmHg. $ETCO_2$ after standardization to 10 vpm, ETs, was 28.5 (19.4–38.7) mmHg. Ventilation rate was 8.3 (7.0–11.0) vpm. Compression rate was 111.1 (106.5–116.1) cpm. Compression depth was 50.4 (43.2–57.0) mm.

Table 2 – Distributions of annotated values for all segments and for ratios between paired segments. Notice the effect of standardization of measured $ETCO_2$ values to a common reference ventilation rate of 10 vpm. ET: measured $ETCO_2$; ETs: $ETCO_2$ standardised to 10 vpm; cd: chest compression depth; cr: chest compression rate; vr: ventilation rate.

	Measured value, median (IQR)	Ratio, median (IQR)
ET (mmHg)	32.1 (23.0–41.4)	1.01 (0.90–1.14)
ETs (mmHg)	28.5 (19.4–38.7)	0.99 (0.87–1.13)
cd (mm)	50.4 (43.2–57.0)	1.01 (0.89–1.16)
cr (cpm)	111.1 (106.5–116.1)	1.01 (0.95–1.06)
vr (vpm)	8.3 (7.0–11.0)	–

After fitting of the linear model, the coefficient *a* for explaining the effect of varying compression depth was 0.95 (95% CI: 0.93–0.98). The coefficient *b* for explaining the effect of varying compression rate was 0.04 (95% CI: 0.01–0.07). Coefficient of determination of the combined model was $R^2 = 0.89$. We conducted several sensitivity analyses for testing the consistency of our model. Results were essentially the same for ventilation rates in the range 5–15 vpm (321 pairs); whether only one or both compression metrics within the paired segments were adherent with guidelines (depth: 5–6 cm; rate: 100–120 cpm, 142 pairs); and for segments from ROSC patients (128 pairs).

Fig. 2 shows the relations between ratios of standardised $ETCO_2$ and ratios of chest compression depth (top) and rate (bottom). The coefficient of determination for linear correlation for standardised $ETCO_2$ and compression depth was $R^2 = 0.89$ (panel a). This coefficient lowered to $R^2 = 0.49$ without $ETCO_2$ standardization for ven-

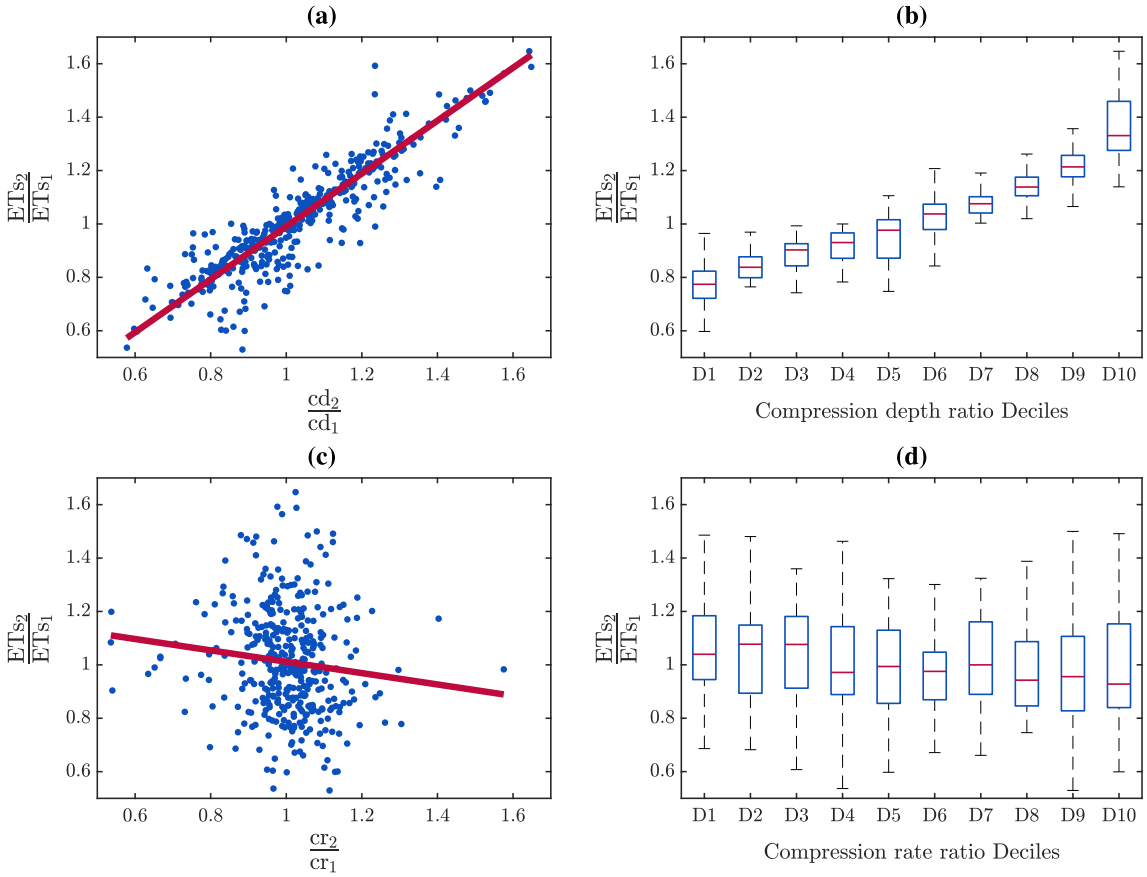

Fig. 2 – Relations of standardised $ETCO_2$ ratios with compression depth ratios (a, b), and with compression rate ratios (c,d). Left panels show scatter plots and linear regressions; right panels show boxplots versus deciles. Coefficients of determinations and trend significance for compression depth: (a) $R^2 = 0.89$, (b) $p_{trend} < 0.001$; for compression rate: (c) $R^2 = 0.02$ (d) $p_{trend} = 0.32$. Jonckheere-Terpstra trend analysis assesses whether these differences are in order with the independent variable, here compression depth and rate deciles.

tilation rate. Panel b shows distributions by deciles, avoiding assumption of linearity. Dependence relations were highly significant (ANOVA: $p < 0.001$). The trend of $ETCO_2$ with depth was significant ($p_{trend} < 0.001$). For chest compression rate, the coefficient of determination was $R^2 = 0.02$ (panel c). No trend of $ETCO_2$ with compression rate was observed ($p_{trend} = 0.33$ for standardised $ETCO_2$ (panel d) and $p_{trend} = 0.32$ for measured $ETCO_2$), showing no sensitivity to the distribution of the independent variable. Variation in compression depth was the factor of greatest significance and best explained the variations in standardised $ETCO_2$. Influence of compression rate changes was not significant.

Fig. 3 illustrates the potential clinical usefulness of our findings. Fig. 3(a) and (b) correspond to a ROSC and a non-ROSC patient, respectively. Top panels depict measured (blue) and standardised (red) $ETCO_2$, and the contribution of compression to $ETCO_2$ modelled with Eq. 2 (green). Bottom panels show the ventilation rate (blue) and the compression depth (red). Note the differences between measured and standardised $ETCO_2$ prior to ROSC: from minute 9 onwards, the rise in the standardised value was 6.1 mmHg per minute, whereas the measured value increased 3.2 mmHg per minute. This was coincident with ventilation rate increasing substantially from 5.3 to 9.7 vpm. Note also that the standardised values remained very close to the contribution of compressions until minute 9, separating from it as ROSC was approached. However, in the non-ROSC patient, both remained close together along the intervention. In this case, there were also differences between measured and standardised $ETCO_2$ caused by varying ventilation rate.

Discussion

The widespread use of waveform capnography as a promising indicator of patient haemodynamic response during resuscitation requires critical analysis to ensure its correct interpretation. The influence of individual CPR components must be understood and quantified, preferably separately, since they contribute very differently to CO_2 concentration. Ventilations allow extraction of CO_2 while chest compressions contribute to CO_2 generation by facilitating forward blood flow. Accordingly, we demonstrated an exponential decrease of $ETCO_2$ with increasing ventilation rate in line with previous observations in animal experiments, and proposed a model to compensate $ETCO_2$ changes related to ventilation rate variability.[24] In the present study, we took a step forward in this multifactorial approach and quantified the influence of compression depth and rate on $ETCO_2$. For that purpose, $ETCO_2$ was firstly made independent of ventilation rate using our standardization model.[24] Then, normalisation of measurements between segments of each pair eliminated the problem of variation among patients. Our model based on ratios also made it possible to make variables independent of the scale of measurement, therefore magnitude of their coefficients provides more robust information.

Our study supports quantifying the contributions of chest compression rate and depth to support of critical blood flow by assessing their relative impacts on $ETCO_2$. Over the years, efforts to find optimal values for the compression components have resulted in weak recommendations and low quality evidence.[31] One possible reason for this is the large number of influencing variables which, if not adequately quantifiable, may have confounded the results. Determining how depth and rate of chest compressions influence $ETCO_2$ could help to provide more evidence to reconsider treatment recommendations. Our work proposes a new framework for quantifying CPR quality based on $ETCO_2$.

Our results showed that compression depth is a good linear predictor of $ETCO_2$ variations, while compression rate explains little of this variation. Fig. 2.a and Fig. 2.b show that standardised $ETCO_2$ ratio increases monotonically with depth ratio, while there is no such pattern with rate ratio. The limited influence of compression rate was in line with the study by Sheak et al.[19] Other authors reported an ambiguous association between compression rate and $ETCO_2$.[20] In the study by Murphy et al. compression rate was 101 (75.9, 179) cpm. While median rate was within recommendations, variability was large. Conversely, in the study by Sheak et al. compression rate was 110.3 (102.5, 117.7) cpm, consistent with our results, with much less dispersion. In our narrow range of variation we found no influence of compression rate on $ETCO_2$. Lack of adherence to guidelines recommendations, resulting in a high compression rate variability, may explain this divergence.

Trends of ventilation rate and $ETCO_2$ are opposite. Increasing ventilation rate reduces the time for alveolar gas exchange and lowers CO_2 concentration, corresponding to an exponential decay model.[23] This complicates the correct interpretation of a multivariable model in which ventilation rate is one of the explanatory factors.[19,20] By compensating for ventilation rate variability through standardization to 10 vpm, the anticipated influence of compression depth on $ETCO_2$ was highlighted, showing tight relationship ($R^2 = 0.89$ for standardised values in contrast to $R^2 = 0.49$ without standardization). According to our model there is an association between compression depth and $ETCO_2$ trends of 0.95. Our model remained consistent after removing too high and too low ventilation rates because of their deleterious haemodynamic effects.[32,33] The model was also consistent for segments adherent with guidelines and for ROSC patients. The previous studies by Sheak et al. and Murphy et al. reported an increase in $ETCO_2$ of 1.4 mmHg and 4% for every 10 mm increase in compression depth, respectively. Both models included ventilation rate as independent variable without considering its non-linear relationship with $ETCO_2$ or its influence as a confounding factor. This explains the notable differences with respect to our results. As an example, an increase in compression depth from 40 to 60 mm would increase $ETCO_2$ by 2.8 mmHg (Sheak), by 8% (Murphy) or by 42.5% according to our model.

This study illustrates that, within practical values, controlling chest compression depth could have more importance than controlling chest compression rate, the latter being much easier to asess and control even without a real-time CPR monitor, simply by relying on a metronome.[34–36] Our study emphasizes the value of monitoring chest compression depth, and thus the value of CPR monitors.[37].

The results of our study can have other direct clinical applications since we now know how to remove the influence of ventilation rate on $ETCO_2$ and to quantify how much it is affected by chest compressions. From Fig. 3 we concluded: first, strong differences between measured and standardised $ETCO_2$ reflect poor control of ventilation rate. Second, current evidence suggests that an increase in $ETCO_2$ could be predictive of ROSC.[38] This was much better reflected in the standardised values than in the measured values. Our hypothesis is therefore that standardization would strongly highlight the occurrence of ROSC. In addition, standardisation could flatten apparent increasing trends in measured $ETCO_2$ that could yield false suspicions of ROSC.

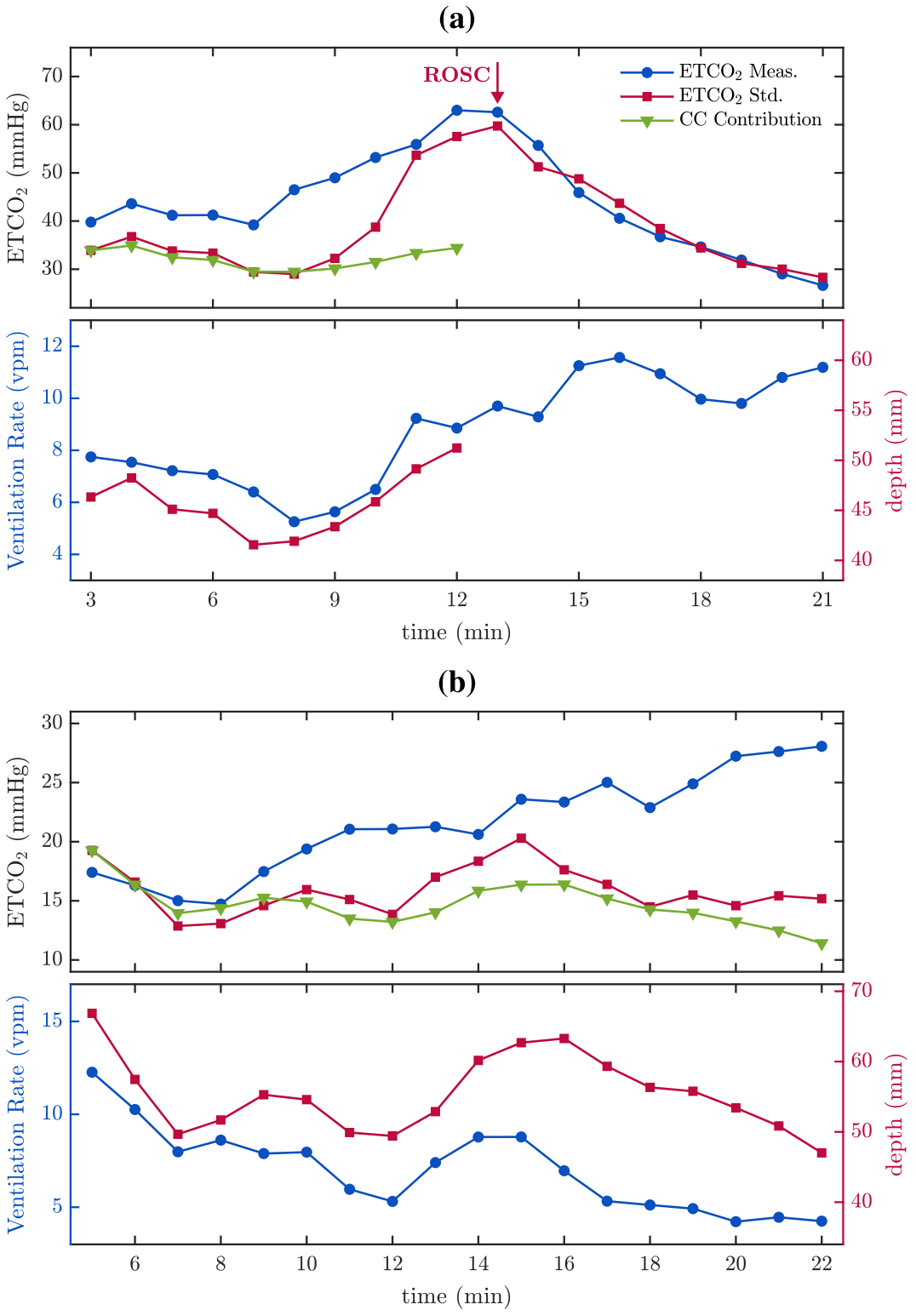

Fig. 3 – Comparison of measured and standardised $ETCO_2$ evolution in a ROSC patient (a) and a non-ROSC patient (b) from our dataset. Values were averaged for every minute. Top panels: measured $ETCO_2$ (blue line); $ETCO_2$ standardised to 10 vpm (red); $ETCO_2$ generated by chest compressions estimated by our model (green). Bottom panels allow assessing the influence of ventilation rate and compression depth in the observed $ETCO_2$ differences. Notice the pre-ROSC increasing difference in standardised $ETCO_2$ with respect to compression contribution. This is not observed in the non-ROSC patient. CC: chest compressions.

When standardised $ETCO_2$ begins to differentiate from the expected contribution from compressions, this suggests there is other source of ETCO2. In Fig. 3 (a), this highlights the improved circulation attending ROSC. Conversely, when the difference between both levels remains low, this could be a confirmation of absence of ROSC (Fig. 3 (b)). In summary, we believe that the estimation of the contribution of chest compressions to $ETCO_2$ is a promising additional metric to advance ROSC detection. Our ongoing research is focused on testing the validity of this hypothesis.

Limitations

We analysed recordings from a single ALS EMS agency database. Chest compression depth and especially compression rate generally adhered with recommendations, since real-time CPR feedback was available. Q-CPR technology also provided feedback on complete chest recoil but we did not include this factor in our study. In previous studies with episodes from the same ALS agency, leaning was rare and recoil was well-sustained despite the long resuscitation efforts.[39,30] Consequently, results derived from our model may not generalise to other scenarios with more variability in CPR performance and absence of real-time feedback. We had no information about tidal volume and the timing of drug administration, both of which could be important confounding factors for the interpretation of $ETCO_2$ evolution. Finally, we imposed strict criteria for the inclusion of episodes and segments to control the variables under study. This was inherently necessary for our methodology but may have an impact on the generalisability of the results.

Conclusions

This study quantified the influence of chest compressions on $ETCO_2$ levels observed during manual CPR. We applied a novel methodology for standardising $ETCO_2$ to compensate for the influence of variation in ventilation rate on measurements. Variation in chest compression depth was the factor of greatest impact and best explained the variations in standardised $ETCO_2$. Influence of chest compression rate changes was not significant. Our model also allows for estimating the contribution of chest compressions to $ETCO_2$ in isolation. Our findings could help to better understand $ETCO_2$ as an indicator of CPR quality.

CRediT authorship contribution statement

Jose Julio Gutiérrez: Conceptualization, Data curation, Methodology, Formal analysis, Investigation, Software, Validation, Writing – review & editing. **Camilo Leonardo Sandoval:** Data curation, Methodology, Software, Validation, Writing – review & editing. **Mikel Leturiondo:** Data curation, Software, Validation, Visualization, Writing – review & editing. **James Knox Russell:** Resources, Data curation, Formal analysis, Methodology, Validation, Writing – review & editing. **Koldo Redondo:** Formal analysis, Validation. **Mohamud Ramzan Daya:** Resources, Writing – review & editing, Supervision. **Sofía Ruiz de Gauna:** Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This study was funded by the grant RTI2018-094396-B-I00 by MCIN/AEI/10.13039/501100011033 and by ERDF A way of making Europe. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

We would like to thank Dr. Jesus M. Ruiz for his helpful advice in the conceptualization of this study and to the staff of TVF&R and their dedication to supporting research in emergency medicine.

Author details

[a]*Group of Signal and Communications, University of the Basque Country (UPV/EHU), Bilbao, Bizkaia, Spain*[b]*Unidades Tecnológicas de Santander, Bucaramanga, Colombia* [c]*Center for Policy and Research in Emergency Medicine (CPR-EM), Oregon Health & Science University, Portland, OR, USA*

REFERENCES

1. Sandroni C, De Santis P, D'Arrigo S. Capnography during cardiac arrest. Resuscitation 2018;132:73–7.
2. Hamrick JL, Hamrick JT, Lee JK, Lee BH, Koehler RC, Shaffner DH. Efficacy of chest compressions directed by end-tidal CO2 feedback in a pediatric resuscitation model of basic life support. J Am Heart Assoc 2014;3:e000450.
3. Aminiahidashti H, Shafiee S, Kiasari AZ, Sazgar M. Applications of end-tidal carbon dioxide (ETCO2) monitoring in emergency department; a narrative review. Emergency 2018;6:e5.
4. Soar J, Böttiger BW, Carli P, et al. European Resuscitation Council guidelines 2021: adult advanced life support. Resuscitation 2021;161:115–51.
5. Panchal AR, Bartos JA, Cabañas JG, et al. Part 3: adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2020;142:S366–468.
6. González R, Pascual L, Sava A, Tolón S, Urbano J, López-Herce J. Ventilation during cardiopulmonary resuscitation in children: a survey on clinical practice. World J Clin Pediatr 2017;13:544–50.
7. Ristagno G, Tang W, Chang YT, et al. The quality of chest compressions during cardiopulmonary resuscitation overrides importance of timing of defibrillation. Chest 2007;132:70–5.
8. McDannold R, Bobrow BJ, Chikani V, Silver A, Spaite DW, Vadeboncoeur T. Quantification of ventilation volumes produced by compressions during emergency department cardiopulmonary resuscitation. Am J Emerg Med 2018;36:1640–4.
9. Vickers NJ. Animal communication: when i'm calling you, will you answer too? Curr Biol 2017;27:R713–5.
10. Sutton R, French B, Meaney P, et al. American Heart Association's Get With The Guidelines Resuscitation Investigators. Physiologic monitoring of CPR quality during adult cardiac arrest: a propensity-matched cohort study. Resuscitation 2016;106:76–82.

11. Paiva EF, Paxton JH, O'Neil BJ. The use of end-tidal carbon dioxide (ETCO2) measurement to guide management of cardiac arrest: a systematic review. Resuscitation 2018;123:1–7.
12. McAlister O, Guldenring D, Finlay DD, et al. CPR Guideline Chest Compression Depths May Exceed Requirements for Optimal Physiological Response. Computing in Cardiology Conference (CinC). IEEE; 2018. p. 1–4.
13. Eftestøl T, Stokka SE, Kvaløy JT, et al. A Probabilistic Function to Model the Relationship between Quality of Chest Compressions and the Physiological Response for Patients in Cardiac Arrest. 2020 Computing in Cardiology Conference (CinC). IEEE; 2020. p. 1–4.
14. Neth MR, Idris A, McMullan J, Benoit JL, Daya MR. A review of ventilation in adult out-of-hospital cardiac arrest. JACEP Open 2020;1:190–201.
15. Buléon C, Parienti JJ, Morilland-Lecoq E, et al. Impacts of chest compression cycle length and real-time feedback with a CPRmeter on chest compression quality in out-of-hospital cardiac arrest: study protocol for a multicenter randomized controlled factorial plan trial. Trials 2020;21:1–12.
16. Stiell IG, Brown SP, Christenson J, et al. What is the role of chest compression depth during out-of-hospital cardiac arrest resuscitation? Crit Care Med 2012;40:1192.
17. Segal N, Metzger AK, Moore JC, et al. Correlation of end tidal carbon dioxide, amplitude spectrum area, and coronary perfusion pressure in a porcine model of cardiac arrest. Physiol Rep 2017;5:e13401.
18. Ruiz JM, Ruiz de Gauna S, González-Otero DM, et al. Relationship between EtCO2 and quality-parameters during cardiopulmonary resuscitation. 2016 Computing in Cardiology Conference (CinC). IEEE; 2016. p. 957–60.
19. Sheak KR, Wiebe DJ, Leary M, et al. Quantitative relationship between end-tidal carbon dioxide and CPR quality during both in-hospital and out-of-hospital cardiac arrest. Resuscitation 2015;89:149–54.
20. Murphy RA, Bobrow BJ, Spaite DW, Hu C, McDannold R, Vadeboncoeur TF. Association between prehospital CPR quality and end-tidal carbon dioxide levels in out-of-hospital cardiac arrest. Prehosp Emerg Care 2016;20:369–77.
21. Gazmuri RJ, Ayoub IM, Radhakrishnan J, Motl J, Upadhyaya MP. Clinically plausible hyperventilation does not exert adverse hemodynamic effects during CPR but markedly reduces end-tidal PCO 2. Resuscitation 2012;83:259–64.
22. Lamoureux L, Radhakrishnan J, Gazmuri RJ. A rat model of ventricular fibrillation and resuscitation by conventional closed-chest technique. J Vis Exp 2015;98:52413.
23. Gutiérrez JJ, Ruiz JM, Ruiz de Gauna S, et al. Modeling the impact of ventilations on the capnogram in out-of-hospital cardiac arrest. PLoS One 2020;15:e0228395.
24. Ruiz de Gauna S, Gutiérrez JJ, Ruiz J, et al. The impact of ventilation rate on end-tidal carbon dioxide level during manual cardiopulmonary resuscitation. Resuscitation 2020;156:215–22.
25. Noordergraaf GG, De Vormer AA. ETCO2 values during CPR: Your ventilation tempo matters. Resuscitation 2020;156:260–2.
26. Hostler D, Everson-Stewart S, Rea TD, et al. Effect of real-time feedback during cardiopulmonary resuscitation outside hospital: prospective, cluster-randomised trial. Bmj 2011;342:d512.
27. Ruiz JM, Ruiz de Gauna S, González-Otero DM, et al. Circulation assessment by automated external defibrillators during cardiopulmonary resuscitation. Resuscitation 2018;128:158–63.
28. Huber PJ, Ronchetti EM. Robust statistics. John Wiley & Sons; 2009.
29. Cardillo G. Jonckheere-Terpstra test: A nonparametric test for trend; 2008. https://github.com/dnafinder/jttrend
30. Russell JK, González-Otero DM, Leturiondo M, Ruiz de Gauna S, Ruiz JM, Daya MR. Chest stiffness dynamics in extended continuous compressions cardiopulmonary resuscitation. Resuscitation 2021;162:198–204.
31. Considine J, Gazmuri RJ, Perkins GD, et al. Chest compression components (rate, depth, chest wall recoil and leaning): a scoping review. Resuscitation 2020;146:188–202.
32. Aufderheide TP, Lurie KG. Death by hyperventilation: a common and life-threatening problem during cardiopulmonary resuscitation. Crit Care Med 2004;32:S345–51.
33. Gupta N, Kamlin CO, Cheung M, Stewart M, Patel N. Improving diagnostic accuracy in the transport of infants with suspected duct-dependent congenital heart disease. J Paediatr Child Health 2014;50:64–70.
34. Kern KB, Stickney RE, Gallison L, Smith RE. Metronome improves compression and ventilation rates during CPR on a manikin in a randomized trial. Resuscitation 2010;81:206–10.
35. Hafner JW, Jou AC, Wang H, Bleess BB, Tham SK. Death before disco: the effectiveness of a musical metronome in layperson cardiopulmonary resuscitation training. J Emerg Med 2015;48:43–52.
36. Scott G, Barron T, Gardett I, et al. Can a software-based metronome tool enhance compression rate in a realistic 911 call scenario without adversely impacting compression depth for dispatcher-assisted CPR? Prehosp Disaster Med 2018;33:399–405.
37. Meaney PA, Bobrow BJ, Mancini ME, et al. Cardiopulmonary resuscitation quality: improving cardiac resuscitation outcomes both inside and outside the hospital: a consensus statement from the American Heart Association. Circulation 2013;128:417–35.
38. Pokorná M, Nečas E, Kratochvíl J, Skřipsky' R, Andrlík M, Franěk O. A sudden increase in partial pressure end-tidal carbon dioxide (PETCO2) at the moment of return of spontaneous circulation. J Emerg Med 2010;38:614–21.
39. Russell JK, González-Otero DM, Ruiz de Gauna S, Daya M, Ruiz J. Can chest compression release rate or recoil velocity identify rescuer leaning in out-of-hospital cardiopulmonary resuscitation? Resuscitation 2018;130:133–7.