Journal of Clinical Monitoring and Computing (2019) 33:843–851
https://doi.org/10.1007/s10877-018-0230-4

ORIGINAL RESEARCH

Identification of return of spontaneous circulation during cardiopulmonary resuscitation via pulse oximetry in a porcine animal cardiac arrest model

Chen Li[1] · Jun Xu[2] · Fei Han[3] · Joseph Walline[4] · Liangliang Zheng[2] · Yangyang Fu[2] · Huadong Zhu[2] · Yanfen Chai[1] · Xuezhong Yu[2]

Received: 3 June 2018 / Accepted: 26 November 2018 / Published online: 29 November 2018

Abstract

In this prospective study we investigated whether the pulse oximetry plethysmographic waveform (POP) could be used to identify return of spontaneous circulation (ROSC) during cardio-pulmonary resuscitation (CPR). Tweleve pigs (28 ± 2 kg) were randomly assigned to two groups: Group I (non-arrested with compressions) (n = 6); Group II (arrested with CPR and defibrillation) (n = 6). Hemodynamic parameters and POP were collected and analyzed. POP was analyzed using both a time domain method and a frequency domain method. In Group I, when compressions were carried out on subjects with a spontaneous circulation, a hybrid fluctuation or "envelope" phenomenon appeared in the time domain method and a "double" or "fusion" peak appeared in the frequency domain method. In Group II, after the period of ventricular fibrillation was induced, the POP waveform disappeared. With compressions, POP showed a regular compression wave. After defibrillation, ROSC, and continued compressions, a hybrid fluctuation or "envelope" phenomenon appeared in the time domain method and a "double" or "fusion" peak appeared in the frequency domain method, similar to Group I. Analysis of POP using the time and frequency domain methods could be used to identify ROSC during CPR.

Keywords Cardiac arrest · Cardiopulmonary resuscitation · Pulse oximetry plethysmographic waveform · Identification · Return of spontaneous circulation

Abbreviations

CCs	Chest compressions
CPR	Cardiopulmonary resuscitation
POP	The pulse oximetry plethysmographic waveform
ROSC	Return of spontaneous circulation
CA	Cardiac arrest
$P_{ET}CO_2$	Partial pressure of end-tidal carbon dioxide
VF	Ventricular fibrillation
HR	Heart rate
DAP	Diastolic arterial pressure
TDM	The time domain method
FDM	The frequency domain method

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10877-018-0230-4) contains supplementary material, which is available to authorized users.

✉ Jun Xu
xujunfree@126.com

[1] Emergency Department, Tianjin Medical University General Hospital, Tianjin, China

[2] Emergency Department, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, No.1 Shuaifuyuan Wangfujing, Dongcheng District, Beijing, China

[3] Institute of Life Monitoring, Mindray Corporation, Shenzhen, China

[4] Division of Emergency Medicine, Department of Surgery, Saint Louis University Hospital, Saint Louis, MO, USA

1 Introduction

High quality chest compressions (CCs) are critical during cardiopulmonary resuscitation (CPR) [1, 2]. The latest AHA CPR guidelines emphasize minimizing interruptions in compressions, for example by re-starting CCs immediately after a defibrillation shock [3, 4]. However, chest compressions might be detrimental to hemodynamics in the early post-ROSC stage [5]. Studies have shown that the mechanical force generated by CCs after ROSC in humans could lead to ventricular re-fibrillation [6, 7]. Therefore it is important to identify ROSC as early as possible during CPR in order

to halt CCs when they are no longer needed and may be harmful.

Until now, there have been no validated methods to guide physicians' decisions about how long to prolong CPR efforts. Pulse oximetry, which is noninvasive and convenient, is widely used in most clinical situations to monitor the oxygenation saturation of peripheral blood [8]. The operating principle of pulse oximetry is a light detector and a light source. The absorbance of the arterial blood varies with each beat, and this variance is transformed into an electrical signal which is then transferred from the detector as a waveform with each beat, i.e. the pulse oximetry plethysmographic waveform (POP) [9–11]. Since it directly reflects peripheral blood pulsations, the POP can be used as an early indicator of changes in circulation [9, 12, 13].

An earlier study showed that POP could reliably reflect the quality of CPR [14]. In clinical practice, we have noticed that POP changes when a patient in cardiac arrest achieves return of spontaneous circulation (ROSC). POP shows different characteristics when cardiac arrest (CA) appears or ROSC is achieved. In this prospective study we investigated whether the POP could be used to identify ROSC during CPR.

2 Methods

2.1 Animal preparation

This experimental protocol was approved by the Animal Care and Use Committee at Peking Union Medical College Hospital (2013S-512).

12 healthy 3-month-old male domestic swine [(28 ± 2)kg] were fasted overnight, and then anesthetized by 3% sodium pentobarbital (Merck, 719F034, Germany) 1 ml/kg by intramuscular injection followed by inhalational 4% isoflurane (ABBOTT, H20059911, USA) via a snout mask with 100% oxygen using an anesthesia apparatus (Veterinary Anesthesia Ventilator, Midmark Corporation, USA). Anesthesia was maintained with intravenous propofol (2 mg/(kg/h)) (Corden Pharma S.P.A., H20100645, Italy) after endotracheal intubation and mechanical ventilation initiation. The animals were anesthetized throughout the duration of the study until euthanasia. Volume control mode without PEEP was given (tidal volume = 8 ~ 10 ml/kg, Rate = 10/min) by mechanical ventilator (Esprit Ventilato, V1000, Germany). The tidal volume was adjusted to maintain a partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) of 35 ~ 45 mmHg.

The pigs were placed in specially-designed adjustable U-shaped fixation frames in a supine position to avoid tube dislocation or movement during CCs. A pulse oximetry sensor (T8, Mindray, Shenzhen, China) was fixed around the tails of the models to obtain the POP. The right femoral artery in each swine was cannulated with 4-Fr thermos-dilution PiCCO catheter (Pulsion Medical Systems AG, Munich, Germany) and connected to a monitor (T8, Mindray, Shenzhen, China) in order to continuously monitor each subject's arterial pressure. A central venous catheter was inserted into the left internal jugular vein in each animal to allow passage of an endocardial electrode catheter in order to induce ventricular fibrillation (VF) by 24V/50HZ alternating current lasting 1-s.

2.2 Experimental protocol

Twelve pigs (28 ± 2 kg) were randomly assigned to two groups: Group I (non-arrested with compressions) (n = 6); Group II (arrested with CPR and defibrillation) (n = 6) (Fig. 1). VF = ventricular fibrillation; CC = chest compressions in Group I; CC_1 = chest compressions after VF in Group II; DF = defibrillation; CC_2 = chest compressions after ROSC in Group II; SC = stop compression.

In Group I (n = 6), 30-min after animal preparation, CCs were performed on the animals for a total of five minutes. The rate and depth of CCs were controlled by a CPR machine (WISH-SL-FS-A, Wuhan, China). Hemodynamic parameters were collected at initiation and at the beginning of the second and sixth minutes.

In Group II (n = 6), VF was induced 30-min after animal preparation. After 3 min of untreated VF followed by 2 min of CCs with mechanical ventilation, animals were defibrillated at 100J biphasic. After ROSC was confirmed, CCs were re-started at the seventh minute and stopped at the twelfth minute. Hemodynamic parameters were collected at initiation and at the second, fourth, sixth, ninth and thirteenth minutes after VF. The standard of ROSC we used was: the return of a measurable pulse and blood pressure, an abrupt sustained increase in $P_{ET}CO_2$ (typically ≥ 40 mmHg), and the appearance of spontaneous arterial pressure waves on intra-arterial monitoring [15].

In both groups, mechanical ventilation was maintained, except during periods of untreated VF. All animals were

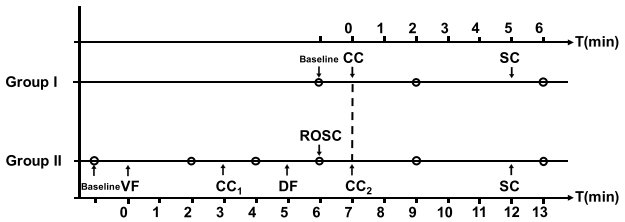

Fig. 1 Experimental Protocol. *Group I* non-arrested with chest compressions, *Group II* arrested with CPR and defibrillation, *ROSC* return of spontaneous circulation, *VF* ventricular fibrillation, *CC* chest compressions in Group I, CC_1 chest compressions after VF in Group II, *DF* defibrillation, CC_2 chest compressions after ROSC in Group II, *SC* stop compression

provided with CCs at a target rate of 110 CCs/min. They were transfused with normal saline at a rate of 10 ml/(kg/h) during the experimental protocol, and intravenously received propofol at a speed of 2 mg/(kg/h). 10 min after data collection, all the animals were euthanized with potassium chloride.

2.3 Outcome measurements

The following physical parameters were monitored: heart rate (HR), diastolic arterial pressure (DAP), and $P_{ET}CO_2$. Additionally, the POP was collected and analyzed for all animals.

2.4 POP acquisition and analysis

POP data was acquired by the T8 monitor and stored in Compact Flash cards. The data was analyzed on Mindray POP viewer V8.0 (Mindray Research Center for Monitoring and Life Support) using MATLAB software V7.10.0 (MathWorks, Natick, Massachusetts, USA).

POP was analyzed using both the time domain method (TDM) and the frequency domain method (FDM). TDM presenting dynamic signals on a time axis has a high correlation with the shape of the spontaneous pulse wave, and has the advantage of being a clear representation of the POP. The "envelope" feature reflects mixed signals of different frequency waveform in TDM. When there is motion interference, however, baseline drift and/or patient cardiac dysfunction, the waveform in TDM may be disrupted, in which case recognition based on the "envelope" feature may be affected (Fig. 2a). The waveform of the manual compression signal and the spontaneous circulation signal may have regular "envelope". Like two waveforms mixing, the peak of amplitude will change when two different frequency waveforms come across. Namely, the amplitude increases when the peaks appear at the same time and decreases when the trough comes across the peak. It could be seen that the mixing waveform shows regular increase and decrease in amplitude. This envelope characteristic thus can provide an effective feature point for the ROSC recognition in the CPR process. Applying the FDM can convert the signals into a figure with a frequency axis. The signals with different frequencies can be reflected at different locations on the frequency axis (Fig. 2b). The different frequencies of CCs and ROSC (spontaneous cardiac pulsations) can therefore be potentially seen by looking at both TDM and FDM.

The changes in POP were identified as present/absent by the investigators. There were two investigators analyzing the POP separately.

2.5 Statistical analysis

Statistical analysis was completed using SPSS (Version 20.0). Normality of the continuous variables was assessed using the Skewness-Kurtosis test. Normally distributed continuous variables were described as mean ± SD and compared by Student's T-test or repeated measurement analysis of variance. A two-tailed (two-sided) probability value of less than 0.05 was considered to be statistically significant.

3 Results

3.1 Physical parameters

There was no statistically significant difference in baseline physical parameters between Groups I and II ($p > 0.05$).

Within Group I, there was no statistical difference in HR among the different stages ($F = 0.78$, $p = 0.58$) (Fig. 3a). $P_{ET}CO_2$ ($F = 30.48$, $p < 0.01$) and DAP ($F = 9.31$, $p < 0.01$) were statistically different between the different stages (Fig. 3b, 2c), the differences of which came from comparing the baseline and CC stages, and the CC and SC stages.

In Group II, all physical parameters were descending statistically to a very low level after VF was induced ($p < 0.05$). Parameters were ascending to a stable level during CC_1 stage ($p < 0.05$). After defibrillation, HR, $P_{ET}CO_2$ and DAP were ascending between the CC_1 and DF stages ($p < 0.05$) (Fig. 3). During the DF, CC_2 and SC stages, HR was statistically different between the different stages ($F = 7.55$, $p < 0.05$), the difference of which came from the CC_2 and SC stages (Fig. 3a). DAP had a trend of ascending during the DF, CC_2 and SC stages, though no statistically significant difference existed ($F = 4.38$, $p = 0.0498$, the difference of which came from individual data) (Fig. 3b).

3.2 POP analysis

Both of the two investigators drew the same conclusion.

In Group I, at the baseline stage, POP showed a regular waveform in TDM and a single peak in FDM (Fig. 4a). POP showed a fluctuation hybrid or "envelope" phenomenon in TDM and a "double" or "fusion" peak of both pulse and CCs in FDM during the CC stage (Fig. 4b). POP resumed a regular waveform in TDM and a single peak waveform in FDM at the SC stage (Fig. 4c). The double or fusion peaks of pulse and compressions in FDM showed one of the peaks had a relatively fixed rate of 110 cc/m, matching the mechanical CCs, while the other peak matched the "drifting" frequency of a spontaneous pulse, as shown in Video 1 in Supplementary material. The waveform at the SC stage was no different

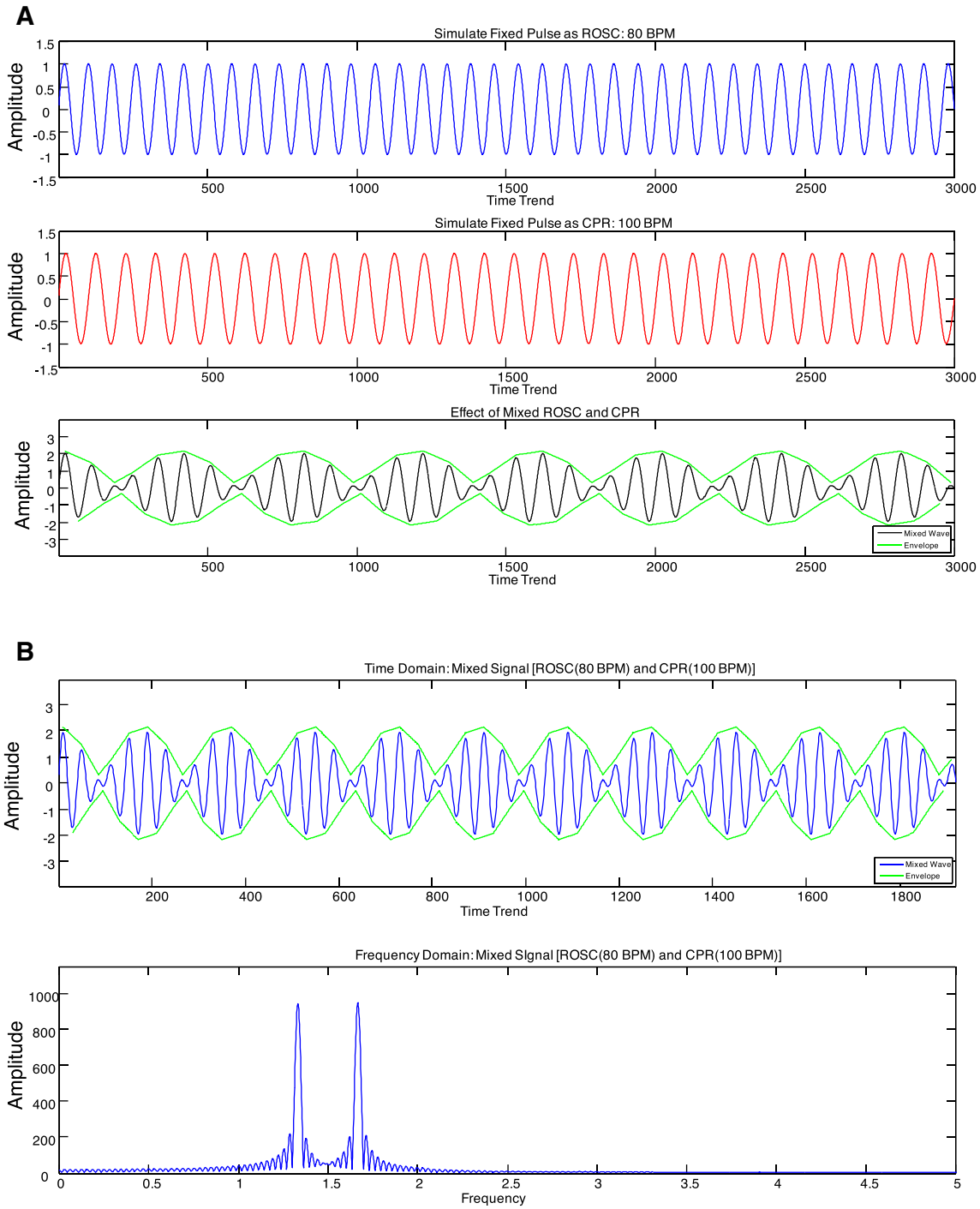

Fig. 2 POP in the time and frequency domain. **a** The waveform in the time domain and the envelope feature. **b** The waveform as seen in the frequency domain

than the waveform at the baseline stage morphologically. These wave transformations appeared in all 6 animals of Group I.

In Group II, at the baseline stage in all 6 animals, POP also showed a regular waveform in TDM and a single peak of pulse in FDM (Fig. 5a). At the VF stage, the regular waveform disappeared in TDM and a mixed and disorderly waveform appeared in FDM (Fig. 5b), this wave transformation appeared in all 6 animals. At the CC_1 stage, POP showed a regular compression wave in TDM and a single peak of compression in FDM in all 6 animals (Fig. 5c). At the DF stage in all 6 animals, POP showed a regular

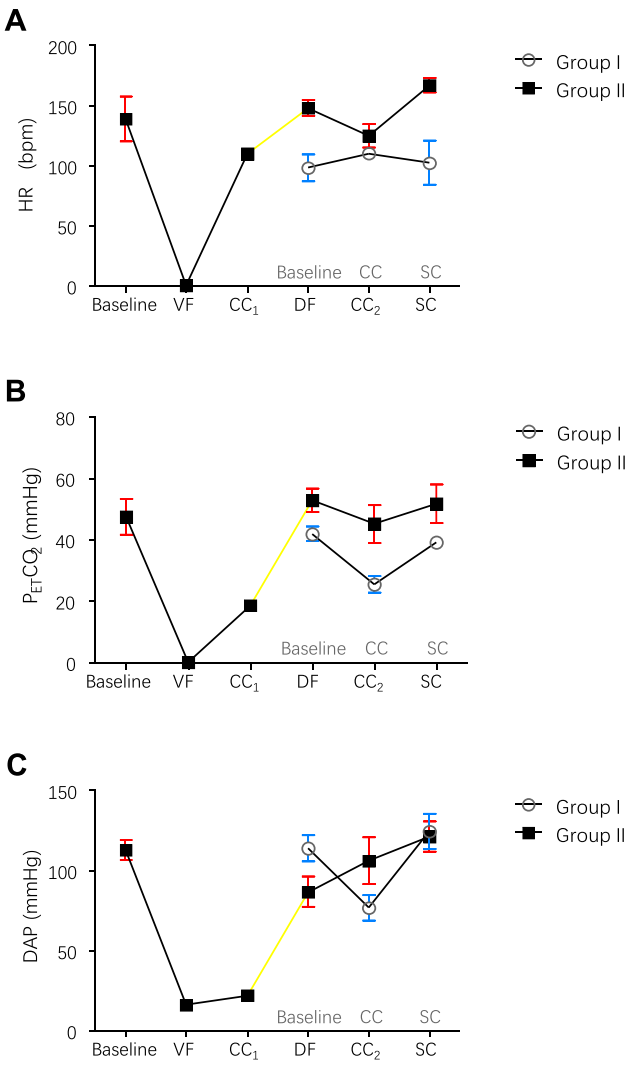

Fig. 3 Changing parameters in non-arrested animals with chest compressions compared to arrested animals with CPR. **a** HR changes in Group I and Group II; **b** $P_{ET}CO_2$ changes in Group I and Group II; **c** DAP changes in Group I and Group II. *Group I* non-arrested with chest compressions, *Group II* arrested with CPR and defibrillation, *HR* heart rate, $P_{ET}CO_2$ partial pressure of end-tidal carbon dioxide, *DAP* diastolic arterial pressure, *MAP* mean arterial pressure, *CPP* coronary perfusion pressure, *VF* cardiac arrest after ventricular fibrillation, *CC* chest compressions in Group I, CC_1 chest compressions after VF in Group II, *DF* return of spontaneous circulation (ROSC) after defibrillation, CC_2 chest compressions after ROSC in Group II, *SC* stop compression

compression wave in TDM and single peak of compression in FDM (Fig. 5d). At the CC_2 stage, POP showed either the fluctuation hybrid (appearing in all 6 animals) or "envelope" phenomenon (appearing in 5/6 animals) in TDM and "double" or "fusion" peaks in FDM (appearing in 5/6 animals) (Fig. 5e). Similarly to Group I, one of the double/fusion peaks in FDM had a relatively fixed rate of 110 cc/m, while the frequency of the other peak showed some drift as can be seen in Video 2 in Supplementary material. At the SC stage in all 6 animals, POP resumed a regular waveform in TDM and a single peak waveform in FDM (Fig. 5f). The waveform at the CC_1 (before ROSC) and the SC stages was no different compared to the waveform at the baseline stage morphologically. The waveform at the DF stage was similar to the baseline, CC_1 and SC stages, except the peak of red light was higher than the one for infrared light.

4 Discussion

CA is characterized by the absence of pulsatile flow, while ROSC marks the return of pulsatile flow. Using waveform analysis, POP can detect the dual-presence of a pulsatile flow waveform alongside the waveform of chest compressions as seen in the overlapping pulse waves in TDM and FDM. Additionally, POP can be used to monitor perfusion of the peripheral circulation during CPR and CA [16]. An earlier pilot study showed that POP has the potential to detect CA, and also to recognize ROSC during the peri-CPR period [17]. This current study showed a significant association between the transformation of POP and pathophysiologic changes following CA using the time and frequency domain waveform plotting methods.

The animals' POP demonstrates a stable peripheral circulatory state under normal physiological conditions. When the animals suffered CA, the regular POP waveform disappeared. In TDM, POP flat-lined, showing no evidence of pulsatile flow. While FDM showed a disorderly waveform coming from the external interference of residual pulsatile flow(s). The POP appeared to regain a regular waveform when chest compressions were performed.

When the animal subjects achieved ROSC after defibrillation, the POP returned to a regular waveform similar to their baseline, while other vital signs increased to a remarkably higher level (which is commonly seen in human patients after ROSC). The POP waveform showed a fluctuation hybrid or "envelope" phenomenon in TDM and "double" or "fusion" peaks in FDM when chest compressions were carried out, which also appeared under chest compressions in the non-arrest Group I. The double or fusion peaks were formed by the underlying fixed rate of chest compressions with the added presence of spontaneous pulses. When chest compressions were subsequently stopped, the POP returned to a regular (single) waveform. This transformation of POP could also be detected in the non-arrested animals with CPR (Group I).

If chest compressions continued after the post-ROSC period, the POP might show the "envelope" phenomenon in TDM and a two frequency spectrum separated out in FDM. The shape of the "envelope" depended on the frequency of spontaneous pulses and compressions. The greater the frequency deviation was, the narrower the envelope width was,

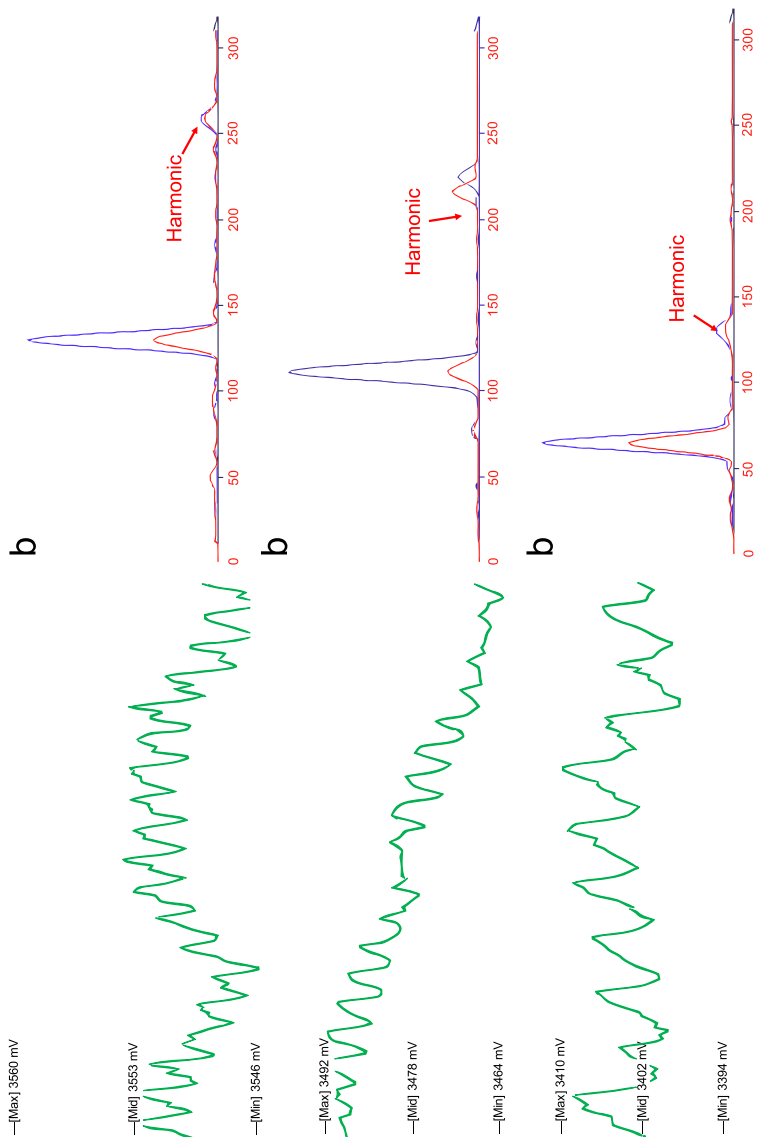

Fig. 4 Wave transformation in non-arrested animals with chest compressions. **A** Baseline, **B** Chest compressions, **C** Stop compressions; *a* Time domain method, *b* Frequency domain method. In all *b* figures, red lines stand for red light signals, while blue lines stand for infrared light signals. Harmonic: harmonic wave according to base frequency

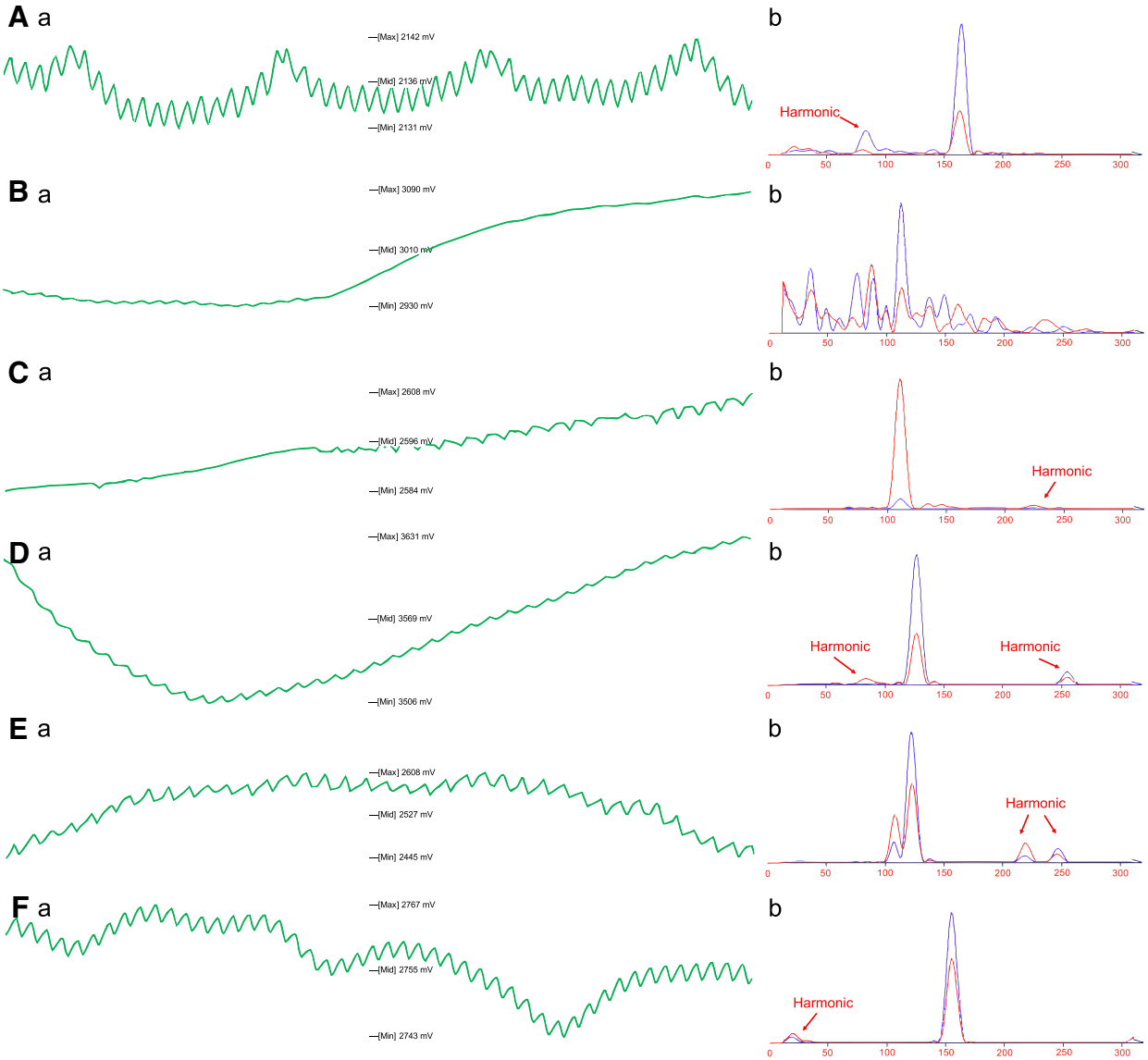

Fig. 5 Wave transformation in cardiac arrested animals with CPR. **A** Baseline, **B** Ventricular fibrillation, **C** Chest compressions after ventricular fibrillation, **D** ROSC after defibrillation, **E** Chest compressions after ROSC, **F** Stop compressions; *a* Time domain method, *b* Frequency domain method. In all *b* figures, red lines stand for red light signals, while blue lines stand for infrared light signals. *Harmonic* harmonic wave according to base frequency, *ROSC* return of spontaneous circulation

and vice versa. The "envelope" phenomenon might therefore be a characteristic change to detect ROSC during CPR.

When the spontaneous rhythm was different from the compressing frequency, there would logically be two peaks at different frequency points. When two identifiable peaks of different frequencies exist continuously for a period of time, it suggests that the patient has achieved ROSC during CPR.

Among other predictors of ROSC during resuscitation, $P_{ET}CO_2$ has been the most extensively studied to date since its detection relies on the presence of blood flow in the pulmonary circulation [18–20]. Studies have shown that $P_{ET}CO_2$ correlates with cardiac output and CPP in the cardiac arrest patient [18, 21]. In this study, $P_{ET}CO_2$ rose to a significantly higher level after the animals achieved ROSC in accordance with the CPR guidelines [22]. The cut-off value of $P_{ET}CO_2$ recommended to detect ROSC changed from 10 mmHg in 2010 to 20 mmHg in 2013 [23–26].

However, $P_{ET}CO_2$ has some limitations. Pathological dead spaces reduce $P_{ET}CO_2$ levels in patients with underlying lung disease [27]. During continuous ventilation, $P_{ET}CO_2$ levels are well-correlated with cardiac output during CPR, but transient changes can be seen when sodium bicarbonate is given [28]. Similarly, the correlation between $P_{ET}CO_2$ and CPP was affected by the administration of vasopressin during CPR

[29, 30]. Therefore, multi-parameter combination monitoring during CPR, such as using both POP and $P_{ET}CO_2$ together, may acquire better overall feedback on CPR quality. Finally, although $P_{ET}CO_2$ monitoring is recommended, SpO_2 monitoring is still more widely used, cheaper and can be used more widely for other clinical purposes.

4.1 Study limitations

The sample size of our study was small, which may have influenced the lack of statistical differences between the two groups. Second, our study was performed on animal models. The phenomena we observed were an indirect reflection of the real changes which occur in human beings.

5 Conclusion

Transformation of POP during the peri-CPR period likely can help detect changes in peripheral circulation. POP has the advantage of being non-invasive, real-time, widely-used, safe and economical. Analysis of POP using the time and frequency domain methods can be used to identify ROSC during CPR.

Author contributions CL conceived and designed the experiments, performed the experiments, analyzed the data and drafted the manuscript. JX conceived and designed the experiments, performed the experiments and finally approved the manuscript. FH analyzed the data. JW helped to draft the manuscript. LZ performed the experiments. YF performed the experiments. HZ, YC and XY helped to finally approve the manuscript. All authors read and approved the final manuscript.

Funding The study was funded by the National Health and Family Planning Commission of the People's Republic of China Special Research Fund (201502019) URL: http://www.moh.gov.cn/qjjys/s3577/201401/e9f3635e7acb47778225ccb729ffec62.shtml : Xuezhong Yu received this funding. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. All procedures performed in studies involving animals were in accordance with the ethical standards of the institution or practice at which the studies were conducted. This experimental protocol was approved by the Animal Care and Use Committee at Peking Union Medical College Hospital (2013S-512).

References

1. Edelson DP, Yuen TC, Mancini ME, Davis DP, Hunt EA, Miller JA, Abella BS. Hospital cardiac arrest resuscitation practice in the United States: a nationally representative survey. J Hosp Med. 2014;9(6):353–7. https://doi.org/10.1002/jhm.2174.
2. Cunningham LM, Mattu A, O'Connor RE, Brady WJ. Cardiopulmonary resuscitation for cardiac arrest: the importance of uninterrupted chest compressions in cardiac arrest resuscitation. Am J Emerg Med. 2012;30(8):1630–8. https://doi.org/10.1016/j.ajem.2012.02.015.
3. Neumar RW, Shuster M, Callaway CW, Gent LM, Atkins DL, Bhanji F, Brooks SC, de Caen AR, Donnino MW, Ferrer JM, Kleinman ME, Kronick SL, Lavonas EJ, Link MS, Mancini ME, Morrison LJ, O'Connor RE, Samson RA, Schexnayder SM, Singletary EM, Sinz EH, Travers AH, Wyckoff MH, Hazinski MF. Part 1: Executive Summary: 2015 American Heart Association Guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):315–67. https://doi.org/10.1161/CIR.0000000000000252.
4. Nolan JP, Soar J, Cariou A, Cronberg T, Moulaert VR, Deakin CD, Bottiger BW, Friberg H, Sunde K, Sandroni C. European Resuscitation Council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care. Intensive care Med. 2015. https://doi.org/10.1007/s00134-015-4051-3.
5. Xu J, Li C, Li Y, Walline J, Zheng L, Fu Y, Yao D, Zhu H, Liu X, Chai Y, Wang Z, Yu X. Influence of chest compressions on circulation during the peri-cardiac arrest period in porcine models. PLoS ONE. 2016;11(5):e0155212. https://doi.org/10.1371/journal.pone.0155212.
6. Osorio J, Dosdall DJ, Tabereaux PB, Robichaux RP Jr, Stephens S, Kerby JD, Stickney RE, Pogwizd S, Ideker RE. Effect of chest compressions on ventricular activation. Am J Cardiol. 2012;109(5):670–4. https://doi.org/10.1016/j.amjcard.2011.10.024.
7. Berdowski J, Tijssen JG, Koster RW. Chest compressions cause recurrence of ventricular fibrillation after the first successful conversion by defibrillation in out-of-hospital cardiac arrest. Circ Arrhythm Electrophysiol. 2010;3(1):72–8. https://doi.org/10.1161/CIRCEP.109.902114.
8. Bendjelid K. The pulse oximetry plethysmographic curve revisited. Curr Opin Crit Care. 2008;14(3):348–53. https://doi.org/10.1097/MCC.0b013e3282fb2dc9.
9. Arntz HR, Bossaert LL, Danchin N, Nikolaou NI. European Resuscitation Council Guidelines for Resuscitation 2010 Sect. 5. Initial management of acute coronary syndromes. Resuscitation. 2010;81(10):1353–63. https://doi.org/10.1016/j.resuscitation.2010.08.016.
10. Biarent D, Bingham R, Eich C, Lopez-Herce J, Maconochie I, Rodriguez-Nunez A, Rajka T, Zideman D. European Resuscitation Council Guidelines for Resuscitation 2010 Sect. 6. Paediatric life support. Resuscitation. 2010;81(10):1364–88. https://doi.org/10.1016/j.resuscitation.2010.08.012.
11. Richmond S, Wyllie J. European Resuscitation Council Guidelines for Resuscitation 2010 Sect. 7. Resuscitation of babies at birth. Resuscitation. 2010;81(10):1389–99. https://doi.org/10.1016/j.resuscitation.2010.08.018.
12. Reisner A, Shaltis PA, McCombie D, Asada HH. Utility of the photoplethysmogram in circulatory monitoring. Anesthesiology. 2008;108(5):950–8. https://doi.org/10.1097/ALN.0b013e31816c89e1.
13. Pizov R, Eden A, Bystritski D, Kalina E, Tamir A, Gelman S. Arterial and plethysmographic waveform analysis in anesthetized patients with hypovolemia. Anesthesiology. 2010;113(1):83–91. https://doi.org/10.1097/ALN.0b013e3181da839f.
14. Xu J, Li C, Zheng L, Han F, Li Y, Walline J, Fu Y, Yao D, Zhang X, Zhang H, Zhu H, Guo S, Wang Z, Yu X. Pulse oximetry: a non-invasive, novel marker for the quality of chest compressions in porcine models of cardiac arrest. PLoS ONE. 2015;10(10):e0139707. https://doi.org/10.1371/journal.pone.0139707.

15. Callaway CW, Donnino MW, Fink EL, Geocadin RG, Golan E, Kern KB, Leary M, Meurer WJ, Peberdy MA, Thompson TM, Zimmerman JL. Part 8: post-cardiac arrest care: 2015 American Heart Association Guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):465–82. https://doi.org/10.1161/CIR.0000000000000262.
16. Xu J, Zhu H, Wang Z, Yu X, Walline J. Why do not we use finger pulse oximeter plethysmograph waveform to monitor the effectiveness of cardiopulmonary resuscitation? Resuscitation. 2011;82(7):959. https://doi.org/10.1016/j.resuscitation.2011.03.030.
17. Li C, Xu J, Han F, Zheng L, Fu Y, Yao D, Zhang X, Zhu H, Guo S, Yu X. (2015) The role of pulse oximetry plethysmographic waveform monitoring as a marker of restoration of spontaneous circulation:a pilot study. Zhonghua wei zhong bing ji jiu yi xue 27 (3):203–08. https://doi.org/10.3760/cma.j.issn.2095-4352.2015.03.009.
18. Bullock A, Dodington JM, Donoghue AJ, Langhan ML. Capnography use during intubation and cardiopulmonary resuscitation in the pediatric emergency department. Pediatr Emerg Care. 2017;33(7):457–61. https://doi.org/10.1097/PEC.0000000000000813.
19. Kodali BS, Urman RD. Capnography during cardiopulmonary resuscitation: current evidence and future directions. J Emerg Trauma Shock. 2014;7(4):332–40. https://doi.org/10.4103/0974-2700.142778.
20. Scarth E, Cook T. Capnography during cardiopulmonary resuscitation. Resuscitation. 2012;83(7):789–90. https://doi.org/10.1016/j.resuscitation.2012.04.002.
21. Hsin T, Chun FW, Tao HL. Ultra-long cardiopulmonary resuscitation with thrombolytic therapy for a sudden cardiac arrest patient with pulmonary embolism. Am J Emerg Med. 2014. https://doi.org/10.1016/j.ajem.2014.04.035.
22. Link MS, Berkow LC, Kudenchuk PJ, Halperin HR, Hess EP, Moitra VK, Neumar RW, O'Neil BJ, Paxton JH, Silvers SM, White RD, Yannopoulos D, Donnino MW. Part 7: adult advanced cardiovascular life support: 2015 American Heart Association Guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132(18 Suppl 2):444–64. https://doi.org/10.1161/CIR.0000000000000261.
23. Ahrens T, Schallom L, Bettorf K, Ellner S, Hurt G, O'Mara V, Ludwig J, George W, Marino T, Shannon W. End-tidal carbon dioxide measurements as a prognostic indicator of outcome in cardiac arrest. Am J Crit Care. 2001;10(6):391–8.
24. Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, Deakin C, Koster RW, Wyllie J, Bottiger B, Group ERCGW. European Resuscitation Council Guidelines for Resuscitation 2010 Sect. 1. Executive summary. Resuscitation. 2010;81(10):1219–76. https://doi.org/10.1016/j.resuscitation.2010.08.021.
25. Meaney PA. Cardiopulmonary resuscitation quality: improving cardiac resuscitation outcomes both inside and outside the hospital: a consensus statement from the American Heart Association (vol 128, pg 417, 2013). Circulation. 2013;128(20):E408–8. doi:https://doi.org/10.1161/01.cir.0000437040.13277.4f.
26. Idris AH, Guffey D, Aufderheide TP, Brown S, Morrison LJ, Nichols P, Powell J, Daya M, Bigham BL, Atkins DL, Berg R, Davis D, Stiell I, Sopko G, Nichol G, Consortium RO. Relationship between chest compression rates and outcomes from cardiac arrest. Circulation. 2012;125(24):3004–12. https://doi.org/10.1161/Circulationaha.111.059535.
27. Donald MJ, Paterson B. End tidal carbon dioxide monitoring in prehospital and retrieval medicine: a review. Emerg Med J. 2006;23(9):728–30. https://doi.org/10.1136/emj.2006.037184.
28. Okamoto H, Hoka S, Kawasaki T, Okuyama T, Takahashi S. Changes in end-tidal carbon dioxide tension following sodium bicarbonate administration: correlation with cardiac output and haemoglobin concentration. Acta Anaesthesiol Scand. 1995;39(1):79–84.
29. Gonzalez ER, Ornato JP, Garnett AR, Levine RL, Young DS, Racht EM. Dose-dependent vasopressor response to epinephrine during CPR in human beings. Ann Emerg Med. 1989;18(9):920–6.
30. Cantineau JP, Merckx P, Lambert Y, Sorkine M, Bertrand C, Duvaldestin P. Effect of epinephrine on end-tidal carbon dioxide pressure during prehospital cardiopulmonary resuscitation. Am J Emerg Med. 1994;12(3):267–70.