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Review

Pointless Yoyo-Perfusion Mode in CPR: Potential Solutions!

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Abstract: Cardiac arrest (CA) is a hemostatic state only reversible via dynamics intracardiac action potentials implementing hemorheological-biochemical reactions of adequate blood volumes (BV). Undeniably exclusive electrophysiological processes that began since intrauterine life remain compromised by cardiopulmonary resuscitation (CPR). Failure of CPR to adapt these hemostatic-electrophysiological conditions as well as human cardiotorsal anatomy, and thoracic biomechanics results in a staggering number of CA mortalities worldwide. Except for mechanical circulatory support (MCS), CPR induces a pointless back-and-forth mode of perfusion that worsens the stalled metabolism. Since the heart and respiratory pump, the main generators of endothelial shear stress (ESS) that control organs microcirculation, thereby metabolism, no longer function. Accordingly, we propose ESS-induced meditators as a potential solution in CA, mechanically with pulsatile MCSs providing rapid circulatory flow restoration (CFR), regardless of return of spontaneous circulation (ROSC). And manually with a novel technique of cardiac massage inducing snaping atrial wall shear stress with adequate BV, promoting a less-traumatic ROSC. Our goal is to evaluate the therapeutic proposal through an in-depth analysis that could change the fierce strain in evolving current CPR doctrine, thus improving the dismal outcomes of CA victims.

Keywords: cardiac arrest (CA); cardiopulmonary resuscitation (CPR); circulatory flow resuscitation (CFR); microcirculation; endothelial dysfunction; endothelial shear stress (ESS); mechanical circulatory support (MCS)

1. Introduction

Cardiac arrest (CA) still claims a staggering number of lives annually, causing widespread disabilities over six decades of CPR employment [1,2].

Current CPR modalities may combine mid-sternal chest compressions (manually, mechanically); automated external defibrillators (AEDs), ventilation and invasive procedures like drug injection, implantable cardioverter defibrillators (IDC), extracorporeal membrane oxygenation (ECMO) or E-CPR, and cardiopulmonary bypass (CPB) [3–11].

Despite progress in CPR, out-of-hospital CA (OHCA) still results in a 30-day brain injury-free survival of approximately 2% [12–14].

Apart from E-CPR, which is still a work in progress, none of CPR modalities can achieve a single metabolic process before return of spontaneous circulation (ROSC).

Difficulties encountered in achieving ROSC with CPR can be attributed to the pathophysiological challenges posed by the CA state, summarized in (Figure 1).

As is known, ROSC occurs due to intracardiac action potentials requiring at least ≥ 15 mmHg coronary perfusion pressure, provided by adequate blood volumes (BV) dynamics, electrolytes, neurohumoral factors, and wall shear stresses [15]. Meanwhile, the arrested heart be-comes almost empty due to massive shifts of BV to low-pressure zones increasing the hepatosplanchnic venous capacitance. Also, the heart will be pulled even further away from the sternum by the cardiotorsal gravitational effect in the supine position. In addition, vigorous mid-sternal chest compressions,

disregarding the cylindrical ribcage biomechanics, especially ribs' orientations and axis of their movements, cause frequent CPR-related trauma [16].
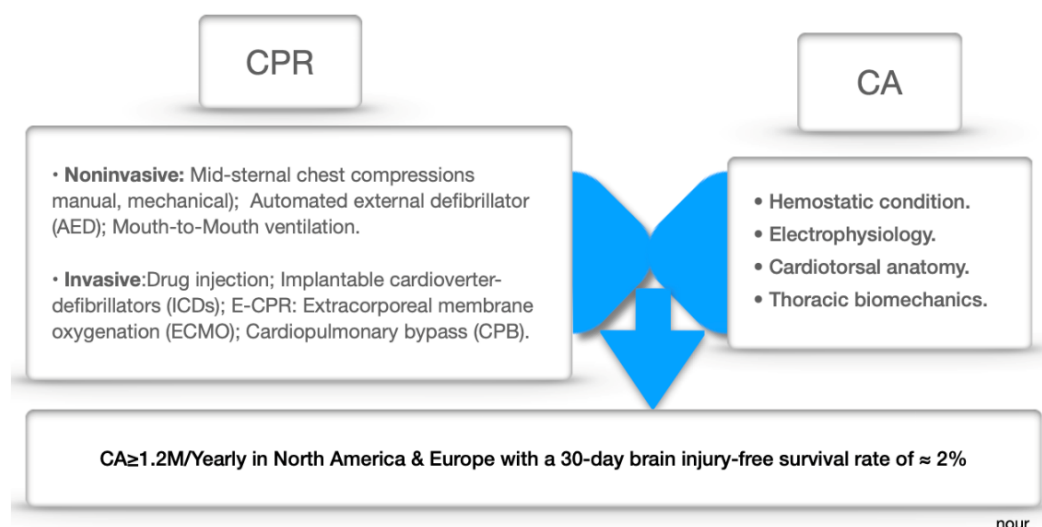

Figure 1. Schema demonstrating outcomes of cardiopulmonary resuscitation (CPR) collision with the pathophysiological conditions of cardiac arrest (CA).

Ultimately, performing CPR in a hemostatic condition induces a back-and-forth ineffective perfusion momentum.

As a result, most CPR survivors succumbing to multiorgan failure shortly due to inadequate organs perfusion during the procedure [17–20].

Such shortcomings of CPR represent a significant burden for global health authorities, requiring a thorough analysis of the entire structure of CA.

In-Depth Glance at CA

Literally, CA defines an abrupt discontinuity of organs perfusion following sudden asystole of the systemic ventricle, whether fibrillated, dysfunctional by cardiac-extracardiac events (e.g., myocardial injury, asphyxia), or knocked-out (e.g., Zwaardemaker-Libbrecht effect) [21–26].

This means that regardless of cardiac conditions, we must restore organs perfusion and metabolism as quickly as possible before irreversible cellular damage occurs [27]

Since salvage of cellular metabolism, either with rapid ROSC or E-CPR, depends on microcirculations controlled by endothelial shear stress (ESS)-induced mediators [28]

Therefore, in this study we present novel techniques implementing rational mobilizations of the massive stagnant BV, inducing physiological pulse-pressure, thus ESS across the aorta.

These include proven methods employing invasive as well as noninvasive pulsatile mechanical circulatory support (MCS), tested in beatless-heart and CA neonatal piglets, respectively [29–33]. In addition, a novel chest compression technique inducing an intracardiac hemorheological effect with adequate BV promoting less traumatic ROSC has recently been used in two drownings [34,35].

Our aim is to corroborate ESS as a potentially effective method to significantly improve the dismal outcomes of CA.

2. Results

Novel Concept

ESS-mediated endothelial functions are mainly generated by the cardiopulmonary pump through the closed pressurized hydraulic left and right heart-circuits. Under the hydrostatic state of

CA, the human body (Soma) becomes like a container composed of an inner sphere (A) containing stagnant amounts of fluids (blood, air,) surrounded by a barrier sphere (B) of endothelium (vascular, alveolar), overlapped by an outer sphere (C) of covering layers e.g., muscles, ribcage… (Somarheology theory) [29,30]. Therefore, creating a shear momentum across (A) inducing ESS at (B) can be achieved by direct intraluminal stimuli or indirect extraluminal impacts on (C) with pulsatile MCS.

STUDIES

To address factors compromising rapid ROSC as well as ESS suppression by conventional E-CPR during CA. Details are available in the corresponding references of each study.

1- A noninvasive MCS composed of multi-layer Vest and Corset driven by a low-pressure alternating pulsatile generator. Functionally, the device depicted in (Figure 2), can induce extracorporeal pulsatile impacts on several covering C-zones, circulating a massive amount of stagnant BV in regular rhythm. As detailed in references [29,30], prototypes were used in refractory CA models (≥20min). Results showed significant hemodynamics improvement, presented in (Figure 3), with near-physiological AP (systolic AP ≥100mmHg) and improved cerebral perfusion manifested by recovered carotid artery echo-doppler. In addition, a laser flowmeter (Perimed PeriScan PIM 3 System) measurements from the tip of the tongue showed significant improvements in microcirculation. There were increased urine output and global vasodilation compensated with IV fluids (1–2 L). The TUNEL test showed inferior apoptotic cells in the treated animal with an obvious dilation of the intracardiac coronary bed (Figure 4).
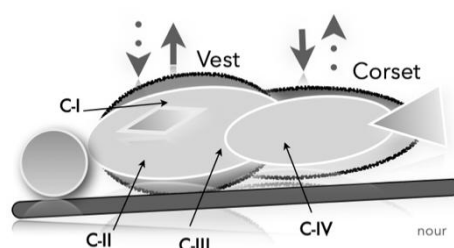

Figure 2. Diagram representing the mechanism of the CFR device alternating pulsations between Corset and Vest on several covering zones (C): Mediastinal (C-I), Parenchyma (C-II), Diaphragm C-III, and hepatosplanchnic (C-IV) compartments.
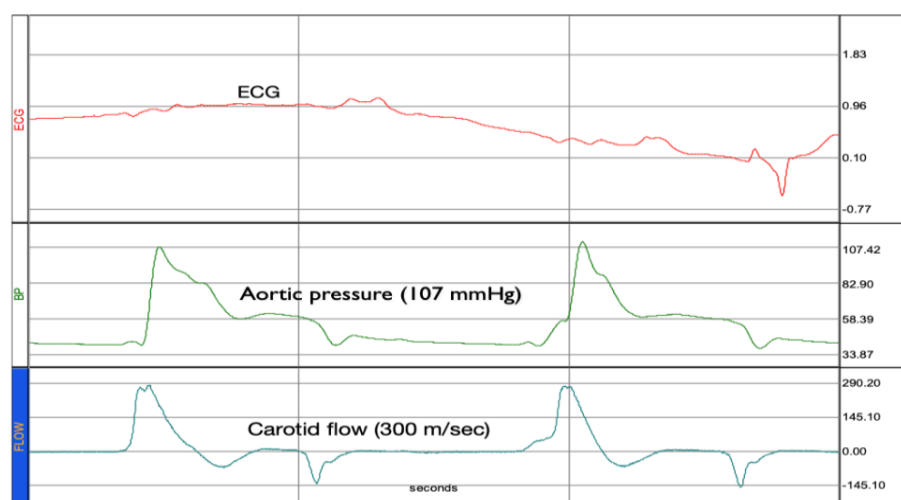

Figure 3. Hemodynamic data obtained in refractory CA model (≥30min) with noninvasive MCS, showing near-physiological AP (middles line) and carotid artery flow (lower line), without return of heartbeats (upper line).
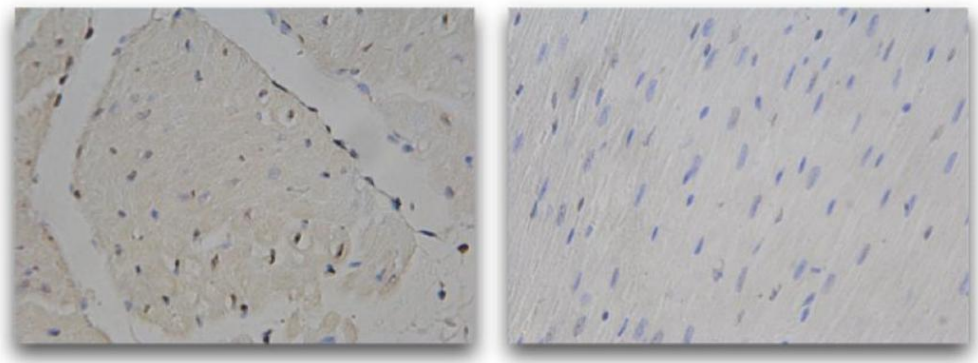
Figure 4. TUNEL test (X400). Left image showing few myocardial apoptotic cells with dilated coronary bed in same treated animal model (CA with asphyxia ≥30min). Right image shows myocardial apoptosis in animal model treated with conventional CPR after 8 min of CA and kept alive for 6H.

2- Invasive MCS (pulsatile Tube) tested as pulsatile CPB versus conventional CPB in beatless-heart model [31–33]. Fourteen neonatal piglets were divided into three groups: Group I (Gr-I, n=6) underwent pulsatile CPB at 100 bpm. Group II (Gr-II, n=6) underwent non-pulsatile CPB, with all subjects in these groups exposed to normothermic CPB for 120 minutes. A third sham group (n=2) technically managed like the other groups but without CPB. Hemodynamic, biochemical and histopathological data were collected and compared between groups. These include post-sternotomy insertion of right atrium, left atrium, left internal mammary and intra-infundibular catheters, for RAP, LAP, AP and PAP measurements, respectively. Cardiac output (CO) measured with transit time probe temporary placed around the PA (Transonic System Inc. Flowmeter). Cardiac index (CI), systemic vascular resistance index (SVRI) and pulmonary vascular resistance index (PVRI) were calculated according to the following formulae: SVRI= (mean AP-RAP)/CI X 79.9; PVRI= (mean PA-LAP)/CI X 79.9; CI=CO/Weight. Endothelial function and vasorelaxation (induced by acetylcholine and nitroprusside) were assessed in segments collected from the pulmonary artery (PA), carotid artery (CA), femoral artery (FA), and renal artery (RA) in all groups. Apoptosis was evaluated using the TUNEL test on myocardial and pulmonary tissue samples collected from all groups. Data collection points included: before CPB (T0), at the start of CPB (T1), one hour after CPB (T2), and at the end of CPB (T3). Results: As shown in (Figure 5), the device induced near-physiological AP (≥80mmHg) with a mean pulse-pressure of 46±7.55 mmHg in Gr-I versus 1.6±0.54 mmHg in the steady-flow Gr-II (P<0.05). SVRI was 1.372±0.35 versus 3.140±0.344 dynes.s.cm^{-5}/m^2 in Gr-I versus Gr-II, respectively. PVRI was 0.3±0.06 versus 0.85±0.05 dynes.s.cm^{-5}/m^2 in Gr-I versus Gr-II, respectively (P<0.05). Unlike Gr-II, acetylcholine reactivity test showed significant endothelial function restoration of endothelial function almost closer to sham in Gr-I as presented in (Figure 6) and (Table 1). The TUNEL test presented (Figure 7) revealed myocardial apoptotic cells in Gr-II and none in Gr-I as well as Sham. Hemolysis were higher and lactic acid were lower in Gr-I versus Gr-II (p≤0.05).

Table 1. Acetylcholine endothelial reactivity test.

Arterial segments	Sham	Pulsatile CPB	Control	Acetylcholine
Carotid	40±24.4	39.4±27.6	32.3±22.03	
Femoral	40±26.7	39.3±15.6	30.6±14.2	%
Pulmonary	78±37.5	72.2±25.9	39.3±16.6	
Renal	67±28.9	26±17.7	5.3±8.7	

Endothelial dependent vascular relaxation Acetylcholine Test in 3 groups of newborn piglets, underwent pulsatile and conventional cardiopulmonary bypass (CPB) and Sham. P<0.01, ANOVA test.
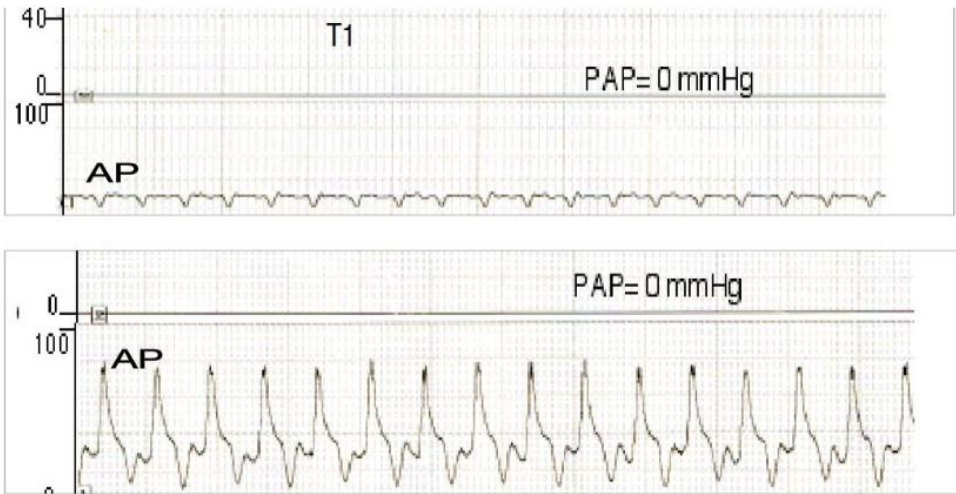
Figure 5. Hemodynamic data of conventional (upper panel) versus pulsatile (lower panel) cardiopulmonary bypass (CBP). AP: Aortic pressure. PAP: Pulmonary artery pressure was 0 mmHg as the heart was fully discharged and taken over by CPB in both groups.
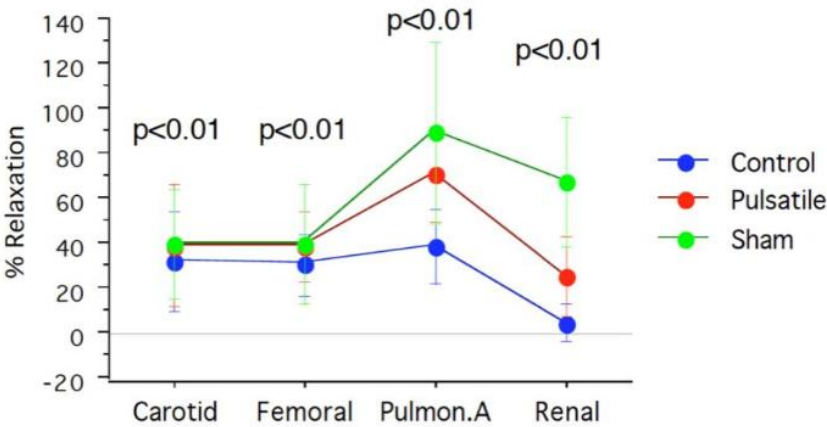

Figure 6. Acetylcholine endothelial reactivity test, showing restored endothelial function in the pulsatile group, versus sham and control groups. P<0.01 (ANOVA test).

Figure 7. TUNEL test, showing myocardial apoptotic cells in the control group (right image) versus pulsatile group (left image).

3- Novel technique of chest compressions through the 5th intercostal space while placing the victim in the left lateral decubitus position to bypass the sternal barrier, with wrapped abdomen and raised legs. In short, refill-recoil-rebound the chest (3R /CPR), within the axis of the cylindrical ribcage will create a sudden intracardiac water hammer-like mechanism with an adequate BV

hemorheological-biochemical effect promoting less-traumatic ROCS. The technique was recently used successfully by a skilled lifeguard instructor as a last-chance intervention in two drownings incidents after failed CPR. ROSC occurred instantly with the refill maneuver in one victim, and several times with recoil-rebound chest compressions in another victim despite CA ≥ 25 minutes with ultimately severely depleted myocardial oxygen reserves and alcoholemia [34,35].

3. Discussion

Results demonstrated the feasibility and potential advantages of rapid CFR-inducing ESS in significantly improving hemodynamics, microcirculation, regardless of heartbeats.

Notably, rapid CFR-inducing ESS, either with the lifeguard's Heimlich maneuver or with the cardiac surgeons' CPB, induces ROSC in ≥70% of drowning victims, and in ≥90% of open-heart patients, respectively [36]. This phenomenon was also observed in our study with shorter durations of CA (≤8 minutes), when immediate ROSC occurred with first pulsations of abdominal Corset. Similarly, we modeled the novel chest compressions technique in order to create intracardiac ESS with adequate BV. Unlike CPR, the technique adapts to and overcomes the pathophysiological conditions of CA (Figure 1). Thus, it can promote rapid ROSC in complete harmony with thoracic biomechanics, thereby less-traumatic, less-exhausting for rescuers. In addition, the rescuer can secure the victim's airway and easily check for heartbeats so as not to confuse CA with syncope or cardiogenic shock.

As stated by Feynman and demonstrated in our study, ESS-mediated endothelial function must be induced according to the Newton's principles by maintaining an almost physiological arterial pulse-pressure [37].

In both animal studies, near-physiological AP was successfully induced in beatless-heart, either invasively or noninvasively with pulsatile MCSs, in correspondence to cardiovascular biophysics and pathophysiological conditions.

For example, the right-heart circuit can adjust pressurized BV and ESS at five different anatomical zones to maintain low-level remodeling [38]. So, it is fundamental keep its low-level remodeling as delivery of ESS in high pulse-pressure can induce serious irreversible conditions such as Eisenmenger syndrome [39]. Therefore, in the 1st study, ESSs were delivered in alternating low-pressure pulsatile impacts on multiple C-zones at the right-heart-side, at a rate of 40 bpm according to the capillary pressure cycle [40].

At the left-heart circuit, ESS inside the Valsalva sinuses determines coronary ostia morphogenesis and may contribute to a severe hemodynamic deterioration [40]. Accordingly, in the 2nd study, pulsatile impacts of ESS were delivered from the aortic root to minimize the constitution of intravascular vortices [41]. However, this study showed significant hemolysis in the treated group (Gr-I) caused by the preliminary concept, which was subsequently resolved and tested effectively [33].

On the other hand, current CPR procedures contradict the most fundamental principles of hydrostatic circuits, leading to illusory and inconclusive benefits for CA victims. Oddly, most recent CPR publications ignore previously reported hemostatic data showing flattened zero AP and central venous pressure (CVP) exceeding ≥80 mmHg during chest compressions [42,43]. Such severe hemostatic disorders compromise invasive CPR procedures such as drug injections or ventilation due lack of interalveolar gas-exchanges [44].

Therefore, it is strongly recommended to use E-CPR promptly to salvage cellular metabolism instead of exhorting ROSC through a pointless Yoyo-perfusion mode of CPR [45]. However, E-CPR remains an invasive and time-consuming procedure requiring skilled squad and ultra-sound-guided installation through flattened arteries, which compromises its effectiveness in OHCA. In addition, suppression of ESS by the constant flow of E-CPR creates a vicious emerging cycle of energy losses and endothelial dysfunction. This phenomenon could be aggravated by ROSC, leading to countercurrent intravascular vortices (Reynolds stresses) [46].

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These issues were addressed in our study demonstrating significant restoration of endothelial function, confirmed by histopathological and biochemical results in piglets, animal models well-known for lack of coronary network [47]. Interestingly, as shown in (Figure 5), the supposedly stunned PA due to no-flow perfusion, in both groups, showed quasi complete recovery, like sham. These prove the crucial role of ESS in improving endothelial function via pulmonary collaterals and myocardial microcirculatory pathways. Evidence of restored endothelial function in vitro as demonstrated in (Table 1) and (Figures 6 and 7), can significantly improve postarrest multiorgan failure mortality caused by poor CPR perfusion.

Limitations: To avoid tedious repetitions of published materials and methods available in the literature for further details,, we limited our study to the means and potential for restoring ESS-mediated endothelial function under hemostatic condition of CA.

4. Conclusions

Optimal goal of CPR, namely rapid ROSC while ensuring adequate perfusion of vital organs, remains elusive, leading to high mortality and morbidity. Prioritizing rapid CFR-inducing ESS over exhorting heartbeat return may improve the dismal outcomes of CA.

5. Patents

S.N. author of several patents, available from the corresponding media.

Abbreviations

The following abbreviations are used in this manuscript:

CA	Cardiac arrest
CPR	Cardiopulmonary resuscitation
AED	Automated external defibrillators
ICD	Implantable cardioverter defibrillators
ECMO	Extracorporeal membrane oxygenation
CPB	Cardiopulmonary bypass
OHCA	Out-of-hospital cardiac arrest
ROSC	Return of spontaneous circulation
ESS	Endothelial shear stress
CFR	Circulatory flow restoration
MCS	Mechanical circulatory support
bpm	beats per minute
BV	Blood volume
AP	Arterial pressure
PA	Pulmonary artery
PAP	Pulmonary artery pressure
RV	Right ventricle
LV	Left ventricle
IV	Intravenous

CVD   Cardiovascular disease
CO   Cardiac output
CI   Cardiac index

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