The effect of stacked defibrillation on return of spontaneous circulation and neurologic outcome; swine cardiac arrest model

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The effect of stacked defibrillation on return of spontaneous circulation and neurologic outcome; swine cardiac arrest model

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A Masters Thesis

Submitted to the Department of Medicine

And the Graduate School of Yonsei University

in partial fulfillment of the

requirements for the degree of

Master of Medical Science

Soyeong Kim

January 2021

This certifies that the master′s thesis of

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January 2021

ACKNOWLEDGEMENTS

연세대학교 원주의과대학에서 사회인으로써 첫걸음을 내딛었을 때 모든 것이 낯설었고 때로는 어려운 일도 많았으나, 돌이켜보면 그 시작이 저의 20 대의 터닝포인트가 아니었을까 생각합니다. 이러한 생각을 가질 수 있게끔 늘 곁에서 아낌없는 지도와 힘을 주신 차경철 교수님께 가장 큰 감사를 드립니다. 교수님이 늘 자랑하고 싶은 멋진 제자가 될 수 있도록 열심히 노력하겠습니다. 항상 좋은 연구자가 될 수 있도록 많은 가르침을 주시는 존경하는 황성오 교수님, 바쁘신 와중에도 학위를 위해 자문을 주신 김현 교수님께도 감사드리며, 그간 힘들고 어려운 일에도 늘 웃으며 격려해주시고 도움을 주셨던 정우진 교수님, 노영일 교수님, 김태윤 선생님께도 감사의 인사를 드립니다.

연구원을 시작할 때부터 가장 큰 버팀목이 되어 준 성실 선생님, 그리고 연구원 생활에 힘이 되어준 강찬영 선생님을 비롯한 연구원들, 김형태, 김은아, 홍주희, 이지원, 박은지 선생님과 모든 응급구조사들에게도 깊은 감사를 드립니다.

항상 곁에서 응원해주시는 부모님과 언니, 동생에게도 모두 감사드리며 그간 주신 아낌없는 사랑을 보답할 수 있도록 늘 정진하며 살겠습니다.

2021 년 1 월

김소영 올림

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Abstract

The effect of stacked defibrillation on return of spontaneous circulation and neurologic outcome; swine cardiac arrest model

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Purpose: Defibrillation is the most important treatment for resuscitation of cardiac arrest patient due to ventricular fibrillation or pulseless ventricular tachycardia. Current cardiopulmonary resuscitation (CPR) guidelines recommend performing single shock after 2 minutes of chest compressions. However, there is a controversy over whether number and mode of electrical shock is optimal to successful

defibrillation. This study aimed to verify the effective defibrillation strategy by comparing the resuscitation outcomes between single shock and stacked shock for ventricular fibrillation in swine model of cardiac arrest.

Materials and Methods: Fifty-four pigs were randomly assigned to 1-shock, 2 and 3-shock groups. After inducing ventricular fibrillation (VF) and a downtime of 2 min, basic life support was begun with a 30:2 compression-to-ventilation ratio for 8 min. Subsequently, 20 min of advanced life support including asynchronous ventilation every 10 chest compressions with 15 L/min oxygen was delivered. According to the study protocol, animals of 1-shock group received a single shock, animals of 2-shock group received two consecutive shocks, and animals of 3 shock group received three consecutive shocks. Animal with restoration of spontaneous circulation (ROSC) underwent post-cardiac arrest care including mechanical ventilation, hemodynamic stabilization with fluids or vasopressor, and targeted temperature management (36.0°C) for 12 h. The neurologic deficit score (NDS) was evaluated at 48 h after ROSC. Hemodynamic measurements and resuscitation outcomes including rate of successful defibrillation, ROSC, 24 h survival and 48 h survival, and neurological deficit score were compared between the groups.

Results: Hemodynamic parameters, arterial blood gas profiles, troponin I and cardiac output were not different between the groups during CPR. Chest compression fraction was the highest in the 1-shock group and followed by the 2-shock and 3-shock groups. There was significant difference in CCF between the 1-shock group and the 3-shock group, although there was no difference between the 1-shock group and the 2-shock group or the 2-shock group and 3-shock group. Rate of successful defibrillation, ROSC, 24 h survival and 48 h survival was higher in the 2-shock group and 3-shock group than 1-shock group ($p = 0.005$, 0.021, 0.015 and 0.021 respectively). NDS at 48-hours was not different between the groups ($p = 832$).

Conclusions: A stacked defibrillation strategy was superior to single shock strategy for successful defibrillation and better resuscitation outcomes in treating ventricular fibrillation in a swine model of cardiac arrest. A two-stacked defibrillation strategy could be a better alternative to the single defibrillation strategy recommended in the current CPR guidelines.

Key words: Cardiopulmonary resuscitation, Heart arrest, Electric defibrillation

I. Introduction

Electrical shock is a treatment that uses high-voltage direct current to remove abnormal electrical excitation of the heart and restore it to sinus rhythm. It is divided into defibrillation and cardioversion, depending on the type of arrhythmia. In particular, electrical defibrillation is the removal of fibrillation by delivering strong electricity directly to the heart of a patient with ventricular fibrillation (VF). It is the most widely used treatment of VF ever since it was first reported by Prevost and Batelli in 1899.[1] The study on electrical defibrillation was developed later by Hooker, kowenhoven, and Langwort. In a study conducted by Beek et al. in 1947, internal defibrillation was first performed on humans, and in a study conducted by Zoll et al. in 1956, external defibrillation was first performed on humans.[2-4] Currently, Defibrillation is used not only in VF, but also in patients with pluseless ventricular tachycardia (pVT).

Defibrillation is the most effective treatment for these patients.[5, 6] Patient with an initial shockable rhythm, such as VF or pVT is likely to good resuscitation outcome.[7] Because shockable rhythms occurs in short cardiac arrest times and are more likely to be converted by defibrillation.[8, 9] Therefore, it is most important

for patients with refractory ventricular fibrillation (RVF) to succeed in defibrillation as soon as possible.

In the cardiopulmonary resuscitation (CPR) guidelines announced before 2005, ‘three-stacked shock’ was recommended. Three-stacked shock is a method of performing three consecutive defibrillation in a patient with initial rhythm is VF or pVT. However, current CPR guidelines recommend the single defibrillation every 2 min because successful defibrillation is most frequently observed in the first shock during three-stacked shocks and minimizing interruption of chest compression is one of the important factors to promote good resuscitation outcomes.[10-15] However, unsuccessful single defibrillation can deteriorate resuscitation because successful defibrillation rate could be decreased by about 10% every minute.[16] In addition, the results of the study mainly targeted patients with VF and pVT that occurred outside of the hospital, and it is unclear whether this strategy will benefit patients with VF and pVT that occurred in-hospital cardiac arrest (IHCA). Accordingly, the current European Resuscitation Council (ERC) CPR guidelines recommend three-stacked defibrillation in case of monitoring patients with an initial rhythm of VF or pVT.[17, 18] In addition, most experiments with poor prognosis for three-stacked shock may not have provided sufficient compression for brief pause between each single defibrillation for rhythm

confirmation and charging, and these factors may have influenced the study results. Therefore, there is no distinct evidence that single defibrillation is more effective in resuscitation than three-stacked defibrillation. Recent studies have recommended double sequential defibrillation (DSD) to treat shockable rhythms that do not recovery after repetitive defibrillation. It is performed two-stacked defibrillation with two defibrillators, and some effects have been reported in recent studies. However, currently there is insufficient randomized controlled trials of DSD. [19-21] For this reason, there is no previous study that directly compared the effect of the number of sequential defibrillations on resuscitation. In addition, the method of 'performing single defibrillation every 2 minutes' recommended in the current guidelines was determined only with the common opinion of experts without a scientific basis.

This study aimed to verify the effective defibrillation strategy by comparing the resuscitation outcomes between performed single shock and stacked shock in swine model of cardiac arrest.

II. Materials and Methods

1. Study design

This laboratory study was designed to compare the probability of successful defibrillation and resuscitation outcomes using single, 2- or 3-stacked defibrillation in swine models of cardiac arrest. This study was approved by the Institutional Animal Care and Use Committee of Yonsei University Wonju College of Medicine, Wonju, Republic of Korea (YWC-200228-1).

2. Animal preparation

Fifty-four male Yorkshire pigs (weight 35-49 kg) were used in this study. The pigs were allowed full access to water and food until the day before the experiment and were then fasted from midnight. The pigs were initially sedated with intramuscular ketamine (15 mg/kg) and xylazine (2 mg/kg), followed by inhaled 3% isoflurane. After sedation, the pigs were placed in the prone position, and endotracheal intubation was performed with a cuffed endotracheal tube. Next, Animals were placed in the supine position and ventilated with oxygen and nitrous oxide via a volume-controlled ventilator (Drager Fabius GS, Drager Medical Inc.,

Telford, PA). The tidal volume of 10 mL/kg and ventilation rate of 18 breaths/min were set initially and then modified to maintain arterial oxygen saturation from 94 to 98% and end-tidal carbon dioxide ($ETCO_2$) from 35 to 45 mmHg. Electrocardiography (ECG) with lead II and $ETCO_2$ were continuously monitored. Under aseptic conditions, the right femoral artery was cannulated using a 5.5-French (Fr) introducer sheath via the Seldinger technique, and aortic blood pressure was continuously recorded using a 5-Fr micromanometer-tipped catheter that was introduced into the femoral artery. An introducer sheath was placed in the right external jugular vein, and right atrial pressure was recorded via a 5-Fr micromanometer-tipped catheter. The right internal carotid artery was exposed, and a vascular flowmeter (Transonic system, Inc., Ithaca, NY) was used to monitor the carotid blood flow. An introducer sheath placed via the right internal jugular vein was used as an insertion route for a 5-Fr pacing catheter to induce VF and infuse saline and epinephrine. An introducer sheath placed via the left external jugular vein was used as an insertion route for a Swan-Ganz pulmonary artery catheter (Edwards Lifesciences, Irvine, CA) to measure cardiac output. Left femoral artery cannulation was also performed for arterial blood sampling. Once the catheters were in place, a 100-unit/kg intravenous (IV) heparin bolus was administered to prevent thrombosis.

3. Study protocol

The pigs were randomized to three groups according to the result indicated in a sealed, opaque envelope opened by an investigator before the induction of cardiac arrest. The randomization envelopes, which contained different defibrillation methods (1-shock, 2-shock, or 3-shock group), were randomized by shaking the box and drawing an envelope from the top of the resulting pile. Pre-defined energy was calculated based on 2 J/kg for the first shock and 4 J/kg for the consecutive shocks. Because the minimum unit of energy selection with the defibrillator was 25 J, the pre-defined defibrillation energy for the first shock was 75 J for pigs weighing 34-37 kg, or 100 J for pigs weighing 38-49 kg, and the consecutive shock was 150 J for pigs weighing 34-37 kg, 175 J for pigs weighing 38-43 kg and 200 J for pigs weighing 44-49 kg.

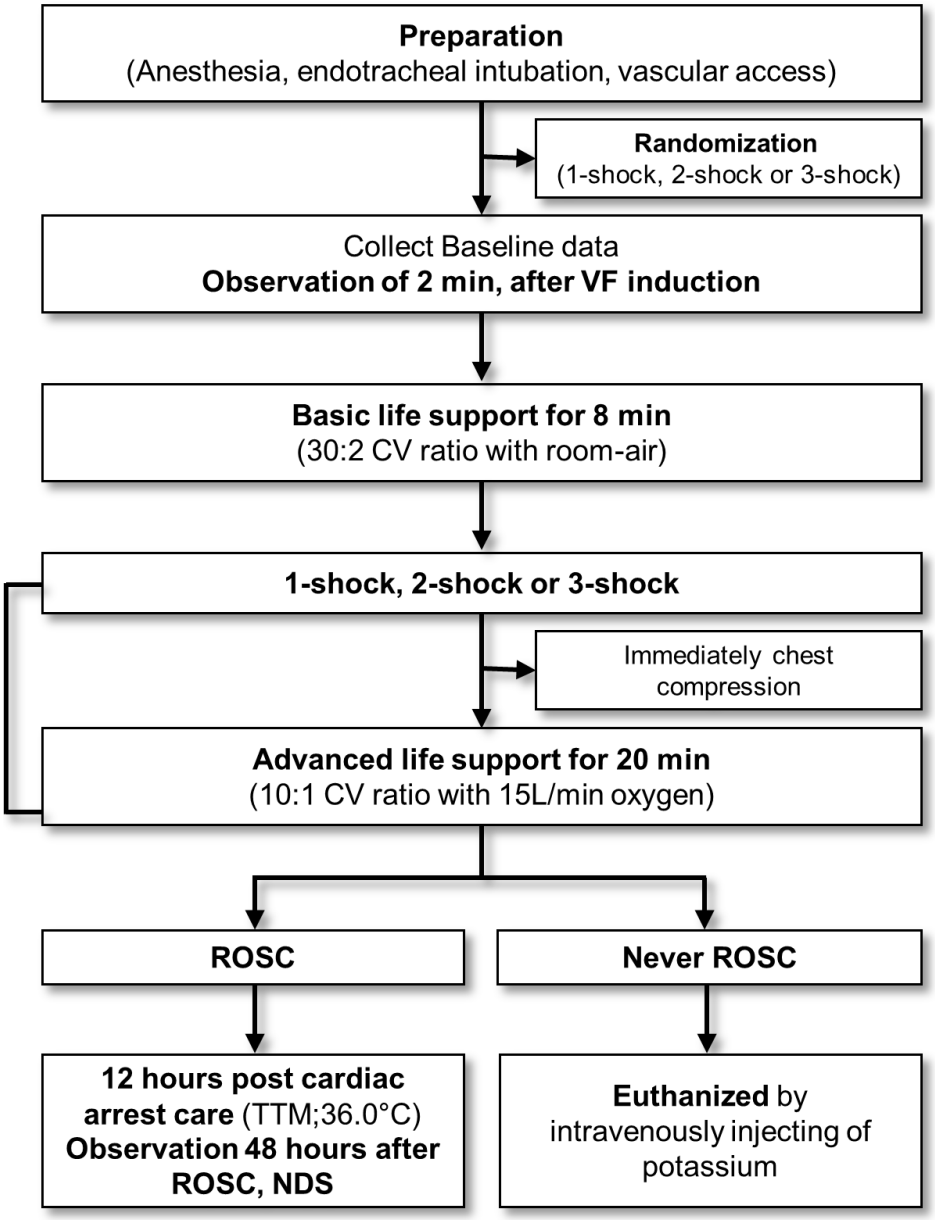
After baseline data were collected, a pacing catheter was positioned in the right ventricle. VF was induced by delivering an alternating electrical current at 60 Hz to the endocardium, which was confirmed by the ECG waveform and a decrease in aortic pressure. Once VF was induced, the endotracheal tube was disconnected from the ventilator, and the pigs were observed for 2 min without any procedure or treatment. After 2 min of untreated VF, basic life support (BLS) was performed for

8 min to mimic a BLS situation in which a bystander recognizes cardiac arrest and calls for help. Mechanical chest compression (LUCAS2, Stryker Medical, Kalamazoo, MI) with a depth of 5 cm was used during the entire experimental period. Following 30 chest compressions given at a rate of 100 chest compressions/min, 2 consecutive ventilations were performed. Positive pressure ventilation at approximately 300 mL of tidal volume was delivered using a resuscitator bag (Silicone resuscitator 87005133, Laerdal Medical, Stavanger, Norway).

Defibrillation was performed after 8 min of BLS if the ECG rhythm was shockable, and consecutive defibrillation was performed as indicated. Chest compression was performed immediately after defibrillation and continued until consecutive defibrillation or rhythm check. During the next 10 min after BLS, chest compression was changed to a continuous mode, and ventilation with 15 L/min of oxygen was delivered every 10 chest compressions, mimicking advanced cardiac life support (ACLS). One milligram of epinephrine with 20 mL of saline was delivered every 4 min until the return of spontaneous circulation (ROSC) or the end of the experiment.

If a pig did not achieve ROSC at 30 min after VF induction, the experiment was terminated, and the animal was considered dead. When a pig achieved ROSC,

mechanical ventilation with inhalation anesthesia was re-initiated. Postcardiac arrest care, which included an injection of intramuscular ketoprofen (1 mg/kg) for pain control, IV infusion of normal saline (80 mL/h) to prevent dehydration, maintenance of arterial oxygen saturation between 94% and 98%, maintenance of $ETCO_2$ between 35 and 45 mmHg and controlling body temperature at 36.0℃ with a temperature management system (Artic Sun, BD, NJ) was performed for 12 h. After post-cardiac arrest care, the pig was moved to breeding room and observed for 48 h after ROSC. The neurologic deficit score (NDS) was determined by another researcher who was blinded to our study 48 h after ROSC. The NDS includes the type of behavior and level of consciousness, breathing pattern, cranial nerve function and motor and sensory function. An NDS of 0-40 is considered as the absence of neurologic deficit and an NDS of 400 as brain death.[22] After the neurologic examination, the animals were euthanized by IV injection of potassium.



VF, ventricular fibrillation; CV, compression-ventilation; ROSC, return of spontaneous circulation; TTM, targeted temperature management; NDS, neurologic deficit score

Fig 1. Study protocol

4. Measurements

Data were digitized using a digital recording system (PowerLab, ADInstruments, Colorado Springs, CO). Aortic and right atrial pressures and carotid blood flow (CBF) were continuously recorded and analyzed at baseline, at 2 min, and then every 4 min until 30 min elapsed. Coronary perfusion pressure (CPP) during CPR was calculated as the difference between the aortic and right atrial pressures in the mid-diastolic phase using an electrical subtraction unit. Arterial blood gas analyses, including pH, $PaCO_2$, PaO_2, HCO_3^-, oxygen saturation, and lactate, were performed using a blood gas analyzer (i-STAT1, Abbott Laboratories, Abbott Park, IL) at baseline, at ROSC, at 1 h after ROSC, at 2 h after ROSC, at 6h after ROSC and at 12 h after ROSC. Cardiac output via the thermo dilution technique (VGS Vigilance Monitor, Edwards Lifesciences) was measured at the same time aforementioned. Troponin I was analyzed using a troponin I analyzer (Triage Meter Cardio3, Abbott Laboratories, Chicago, IL) to compare myocardial injury followed by defibrillation energy or frequency, and it was measured at baseline, at ROSC, and at 12 h after ROSC. Once a pig achieved ROSC, the measurement of hemodynamic parameters was discontinued owing to the possibility of bias from spontaneous circulation.

Chest compression fraction (CCF) was defined as the proportion of time spent performing chest compressions during ACLS. Successful defibrillation was defined as termination of VF irrespective of restoration of circulation or recurrence of VF. Time to successful defibrillation was defined as the time (min) of termination of VF at the first time. ROSC was defined as the maintenance of aortic perfusion pressure over 20 min. The 48 h survival rate and NDS at 48 h were evaluated as outcome variables.

5. Sample size

The sample size was selected with reference to the preliminary study based on the results from 9 pigs per group because ROSC followed by two-stacked defibrillation under recent CPR guidelines had never previously been evaluated. In the preliminary study, ROSC was observed in 2 out of 9 pigs (22%) in the single-shock group and in 6 out of 9 pigs (67%) in the 2-shock and 3-shock groups. The sample size was calculated as 18 pigs per group using tests for two proportions with a two-sided alpha value of 0.05 and a statistical power of 90%.

6. Data analysis

Continuous variables are presented as means ± standard deviations. Analysis of variance or the Kruskal-Wallis test and post-hoc analysis was used to compare the continuous variables between the 1-shock, 2-shock and 3-shock groups, as appropriate. The nominal variables are reported as counts and percentages and were compared using the chi-square or Fisher' exact test, as appropriate. A linear mixed-model analysis was used to compare hemodynamic parameters, including aortic systolic pressure, aortic diastolic pressure, right atrial systolic pressure, right atrial diastolic pressure, CBF, CPP, and $ETCO_2$, between the three groups. The statistical results are presented as group-time interaction. A repeated measure analysis of variance was used to compare cardiac output and troponin I during post-cardiac arrest care between the three groups. A value of $p < 0.05$ was considered significant. In the post-hoc analysis of the Kruskal-Wallis test, we performed Bonferroni correction because the family-wise type I error would be increased at a 5% significance level in multiple comparison. The formula for compensating is shown below and p-values < 0.142 were regarded as significant in this analysis.

Formula for compensating for the family-wise type I error = $1- (1 - 0.05)^k$

(k: the number of multiple comparison)

Analyses were performed using SPSS Statistics 23.0 for Windows (IBM Corp., Chicago, IL).

III. Results

1. Baseline characteristics

Eighteen male pigs from each group were enrolled in the study. There were no significant differences in baseline characteristics such as body weight, aortic and right atrial pressures, CPP, CBF, ETCO2, arterial blood gas profiles, troponin I and cardiac output (Table 1).

Table 1. Baseline characteristics

Parameters	Defibrillation group			p-value
	1-shock (n = 18)	2-shock (n = 18)	3-shock (n = 18)	
Body weight (kg)	41.4 ± 5.0	42.3 ± 3.7	42.2 ± 3.8	0.907
$ETCO_2$ (mmHg)	42.3 ± 7.2	45.2 ± 10.3	39.5 ± 6.9	0.095
ABGA				
pH	7.479 ± 0.061	7.459 ± 0.063	7.493 ± 0.053	0.228
$PaCO_2$	39.8 ± 6.6	41.5 ± 7.2	38.1 ± 6.7	0.144
PaO_2	127 ± 34	114 ± 24	124 ± 26	0.551
HCO_3^-	29.3 ± 2.4	28.7 ± 1.8	30.0 ± 2.6	0.750
SaO_2	98 ± 1	98 ± 1	99 ± 1	0.126
Lactate	2.1 ± 0.6	2.2 ± 0.7	2.0 ± 0.6	0.626
Troponin I (ng/mL)	0.06 ± 0.05	0.06 ± 0.08	0.07 ± 0.08	0.937
Cardiac output (L/min)	3.5 ± 1.1	4.0 ± 1.0	3.9 ± 0.9	0.421

* Variables are presented as mean ± standard deviation

§ $ETCO_2$, end tidal carbon dioxide; ABGA, arterial blood gas analysis

2. Hemodynamic parameters during CPR

There were no significant differences between the groups in the group-time interaction analyses of hemodynamic parameters such as aortic systolic and diastolic pressures, right atrial systolic and diastolic pressures, CPP, CBF, and $ETCO_2$ during CPR (Fig 2-9).

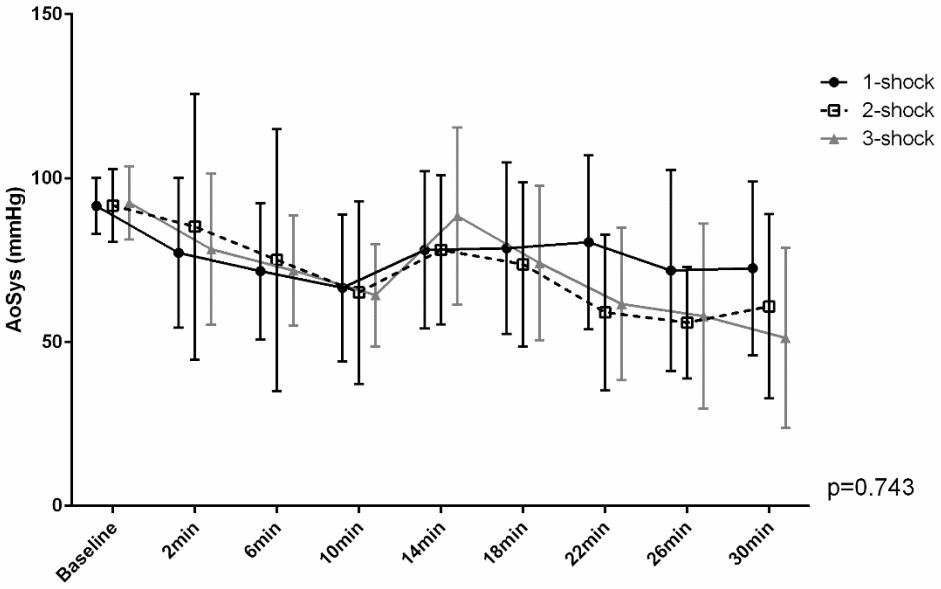


Fig 2. Aortic systolic pressure (AoSys) during CPR

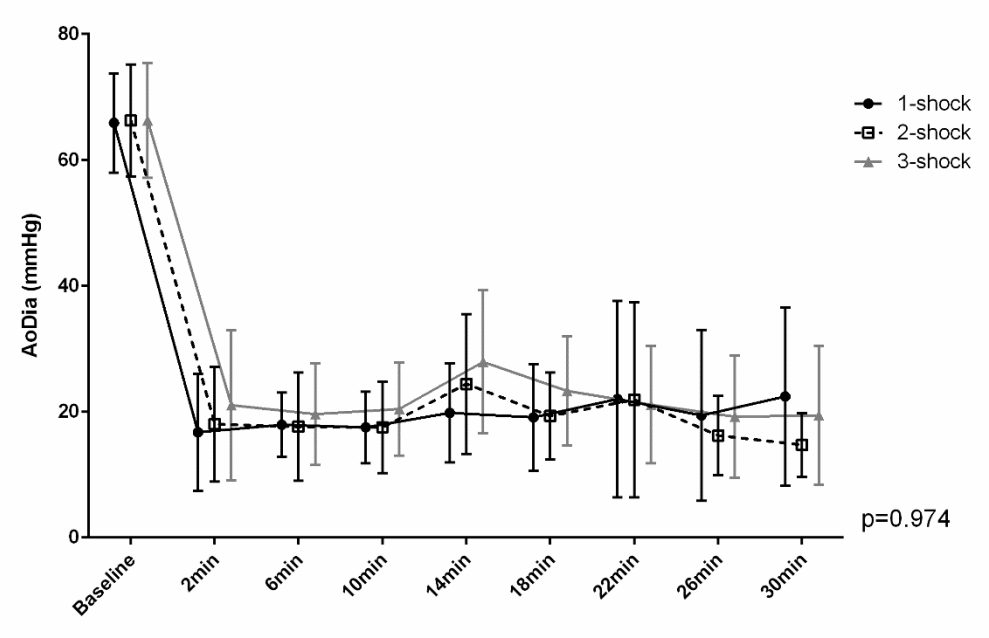


Fig 3. Aortic diastolic pressure (AoDia) during CPR

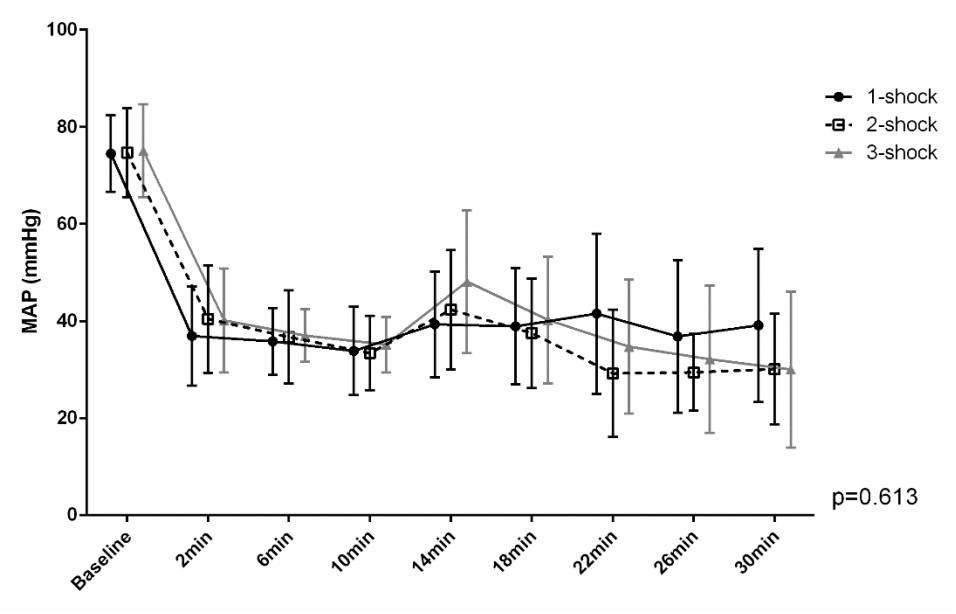


Fig 4. Mean aortic pressure (MAP) during CPR

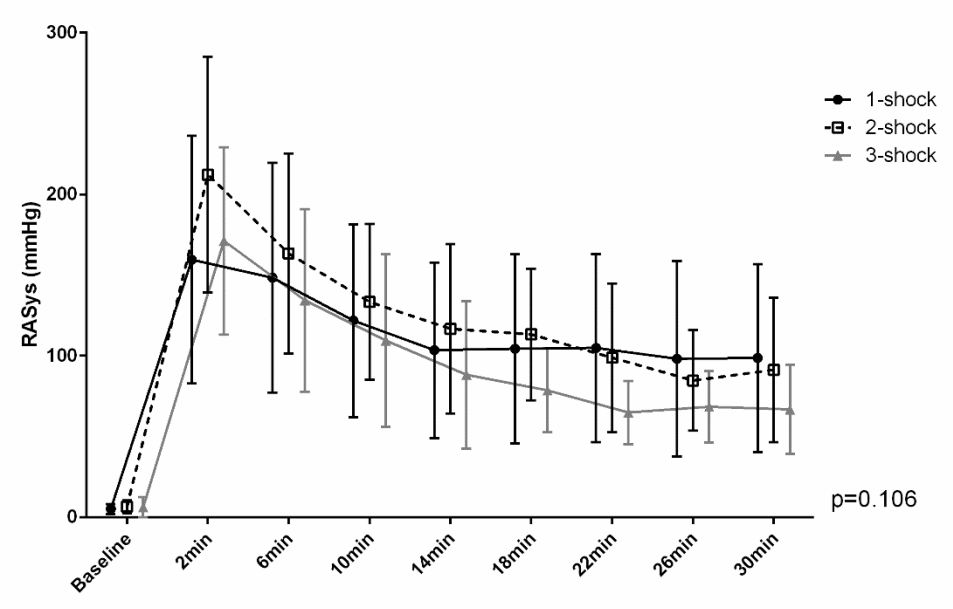


Fig 5. Right atrial systolic pressure (RASys) during CPR

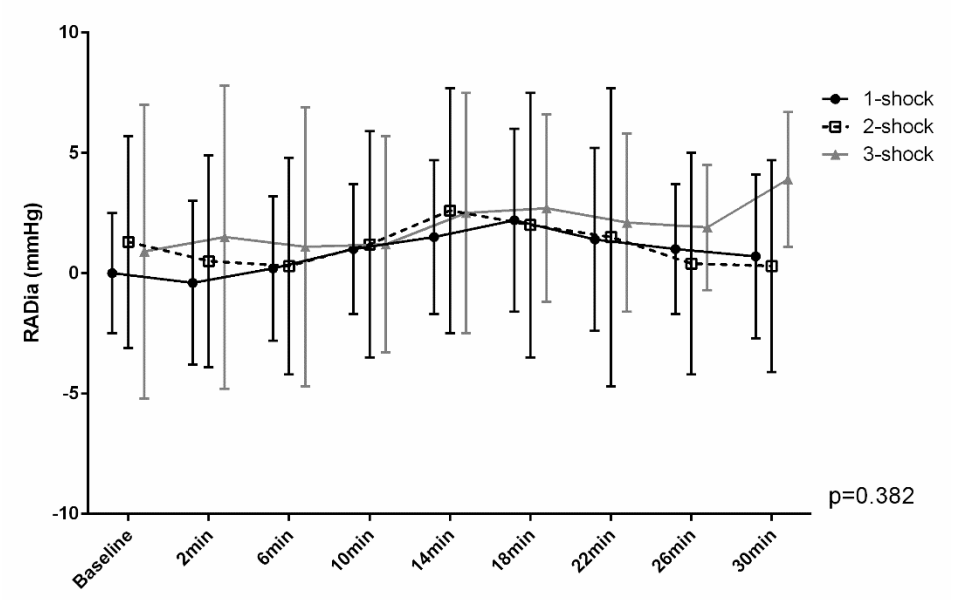


Fig 6. Right atrial diastolic pressure (RADia) during CPR

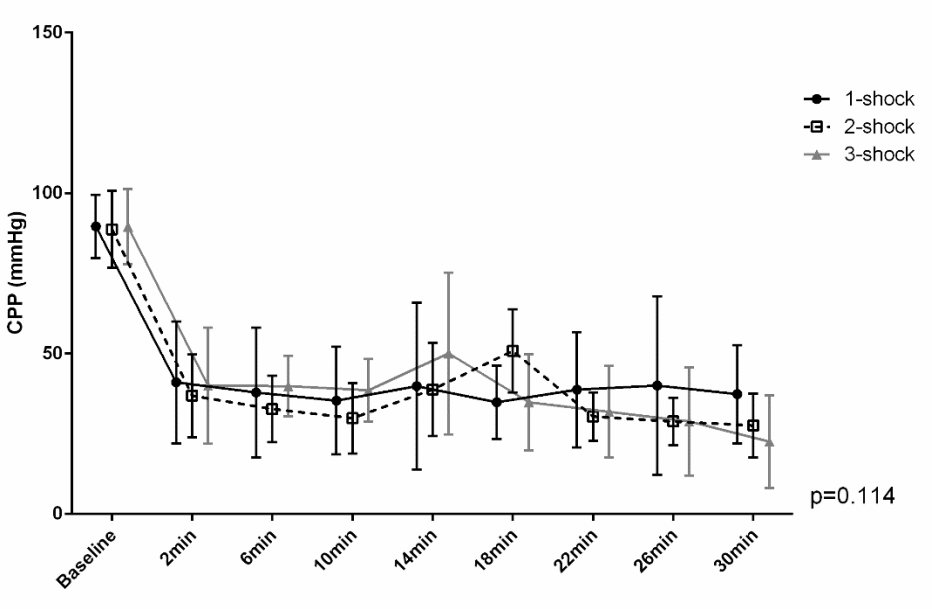


Fig 7. Coronary perfusion pressure (CPP) during CPR

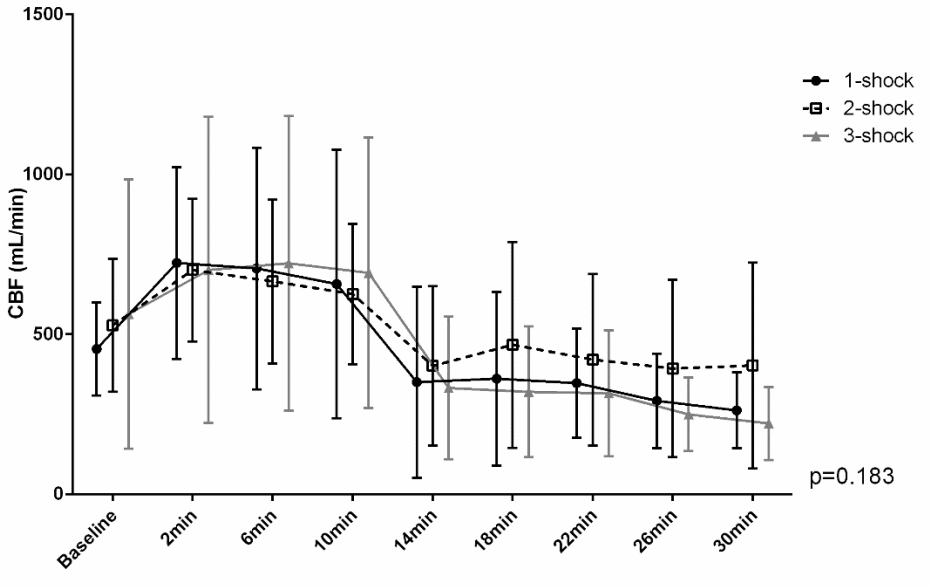


Fig 8. Carotid blood flow (CBF) during CPR

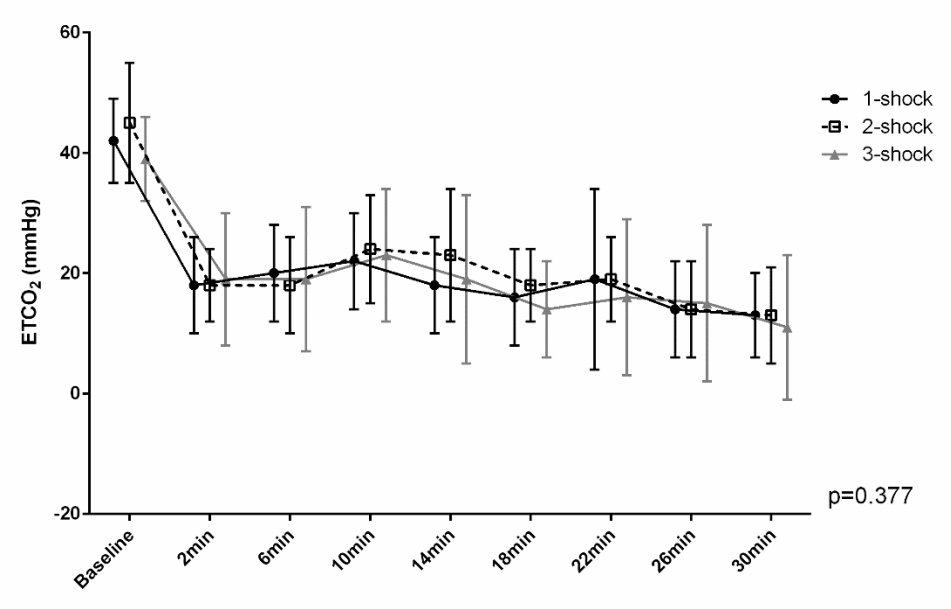


Fig 9. End tidal carbon dioxide ($ETCO_2$) during CPR

3. Comparison of defibrillation profiles between the groups

Successful defibrillation was more frequently observed in 2- or 3-shock groups than in the 1-shock group ($p = 0.005$). Total defibrillation frequency and cumulative energy of defibrillation were not different between the groups (Table 2).

Table 2. Comparison of defibrillation profiles

Parameters	Defibrillation group			p-value
	1-shock (n = 18)	2-shock (n = 18)	3-shock (n = 18)	
Successful defibrillation, n (%)	8 (44)	15 (83)	16 (89)	0.005
Total defibrillation frequency	9 ± 3	13 ± 7	17 ± 10	0.142
Cumulative energy of defibrillation (J)	1594 ± 518	2240 ± 1392	2969 ± 1806	0.117

4. Comparison of chest compression fraction during ACLS between the groups

CCF was the highest in the 1-shock group and followed by the 2-shock and 3-shock groups (96.2 ± 3.3, 94.7 ± 2.4 and 92.1 ± 4.1, respectively, $p<0.001$). In the post-hoc analysis, there was a significant difference in CCF between the 1-shock and the 3-shock groups ($p < 0.001$), although there was no difference between the 1-shock and the 2-shock groups ($p = 0.022$) or the 2-shock and 3-shock groups ($p = 0.040$).

5. Hemodynamic parameters during post-cardiac arrest care

There were no significant differences between the groups in the group-time interaction analyses of hemodynamic parameters such as aortic systolic and diastolic pressures, right atrial systolic and diastolic pressures, CPP, CBF, and $ETCO_2$ during post-cardiac arrest care (Fig 10-17).

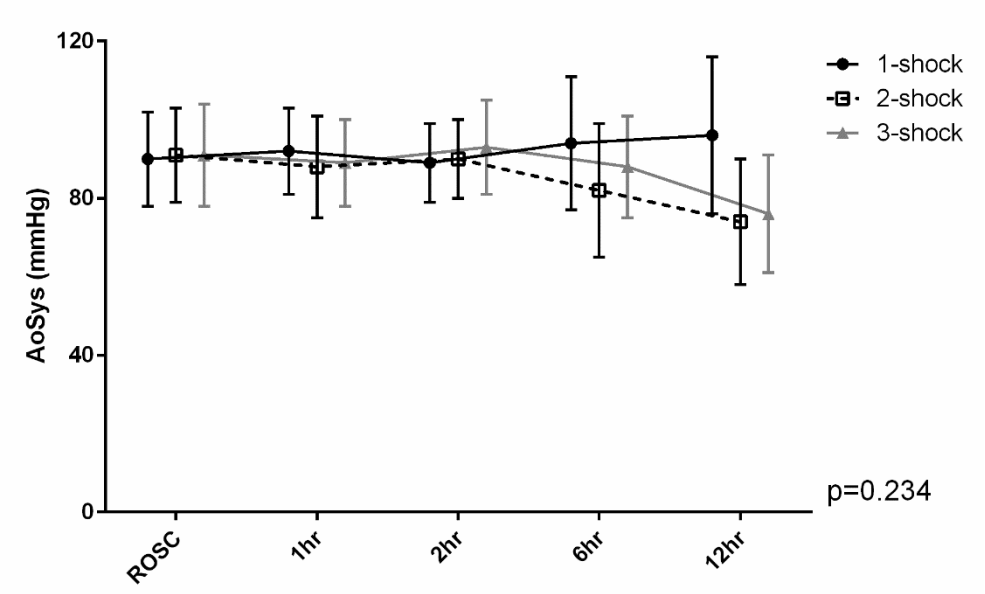


Fig 10. Aortic systolic pressure (AoSys) during post-cardiac arrest care

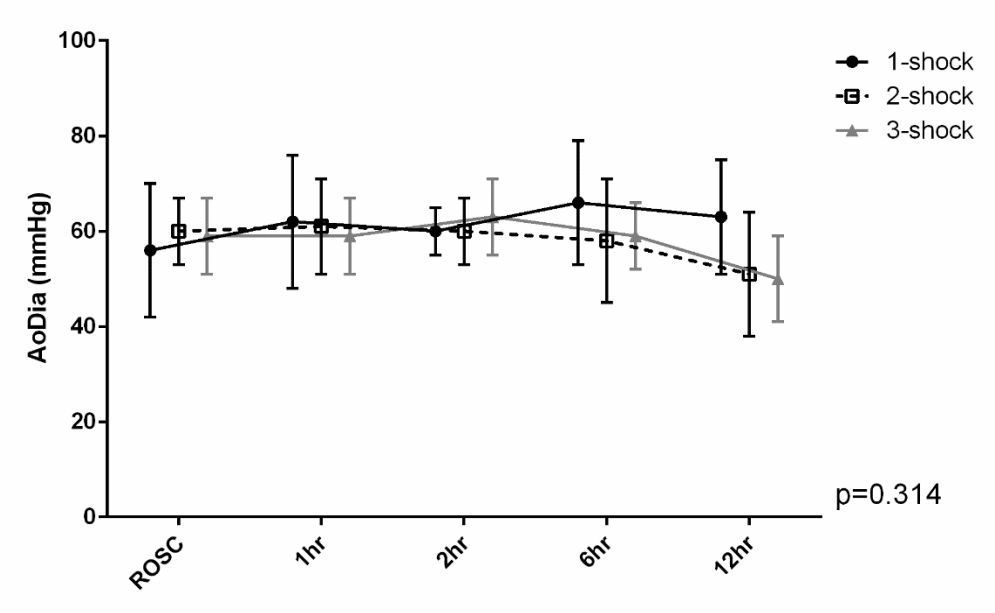


Fig 11. Aortic diastolic pressure (AoDia) during post-cardiac arrest care

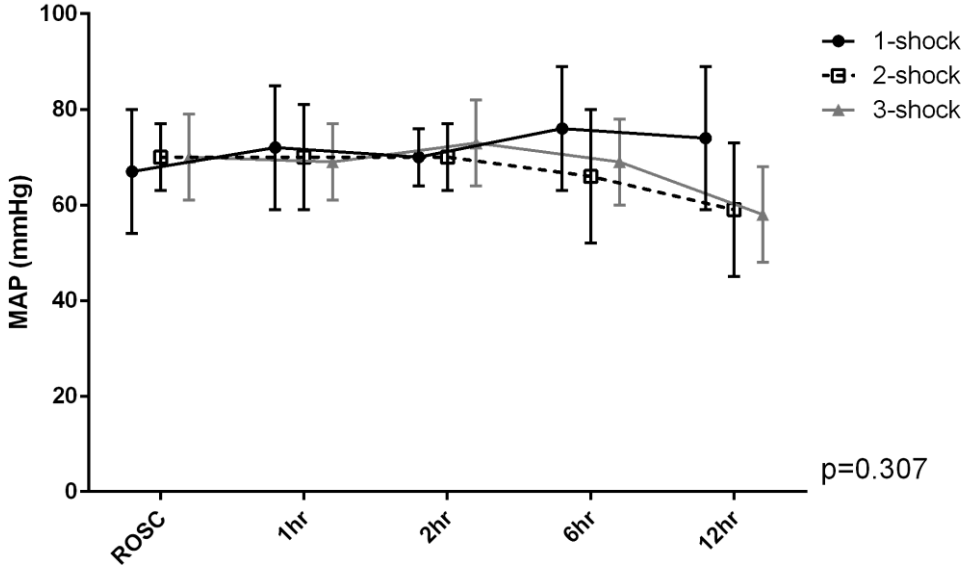


Fig 12. Mean aortic pressure (MAP) during post-cardiac arrest care

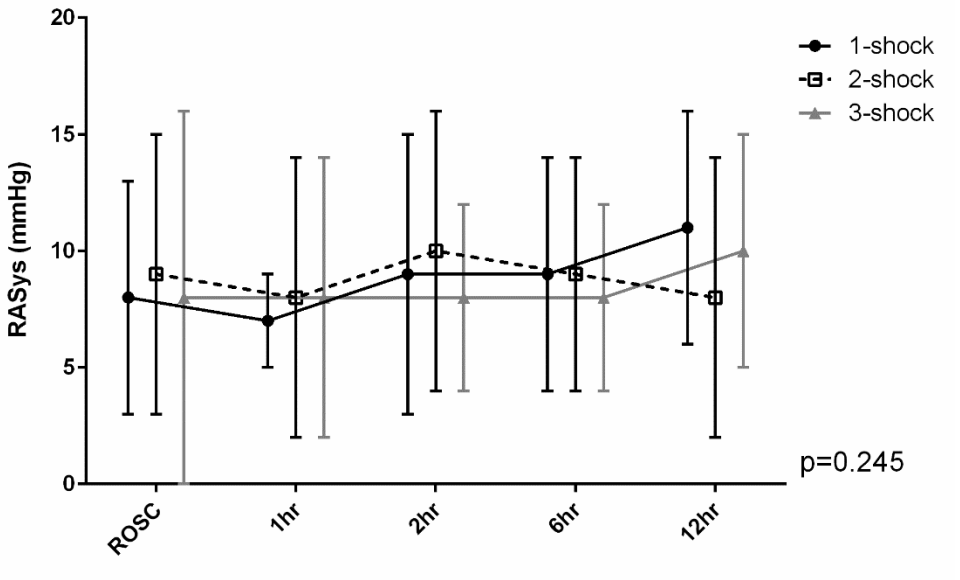


Fig 13. Right atrial systolic pressure (RASys) during post-cardiac arrest care

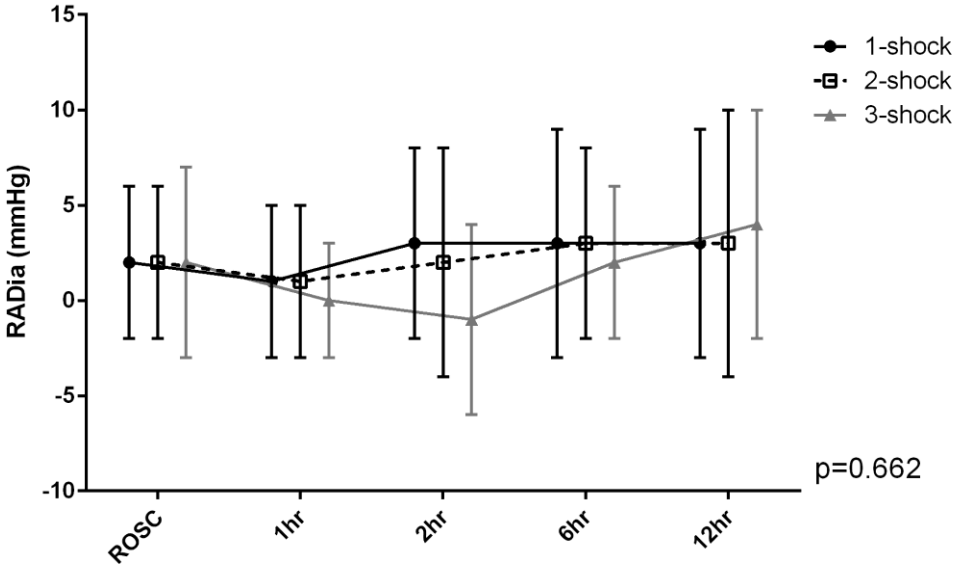


Fig 14. Right atrial diastolic pressure (RADia) during CPR

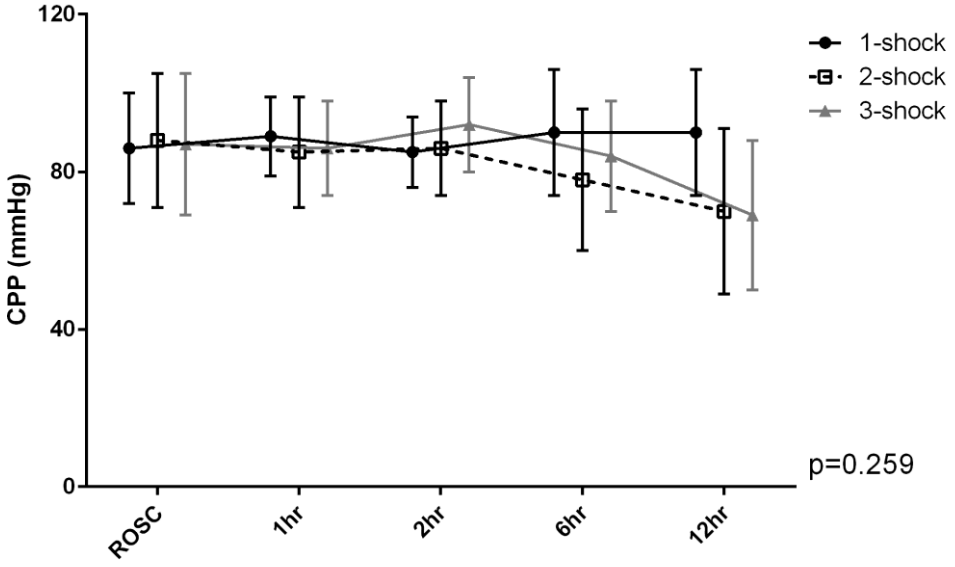


Fig 15. Coronary perfusion pressure (CPP) during post-cardiac arrest care

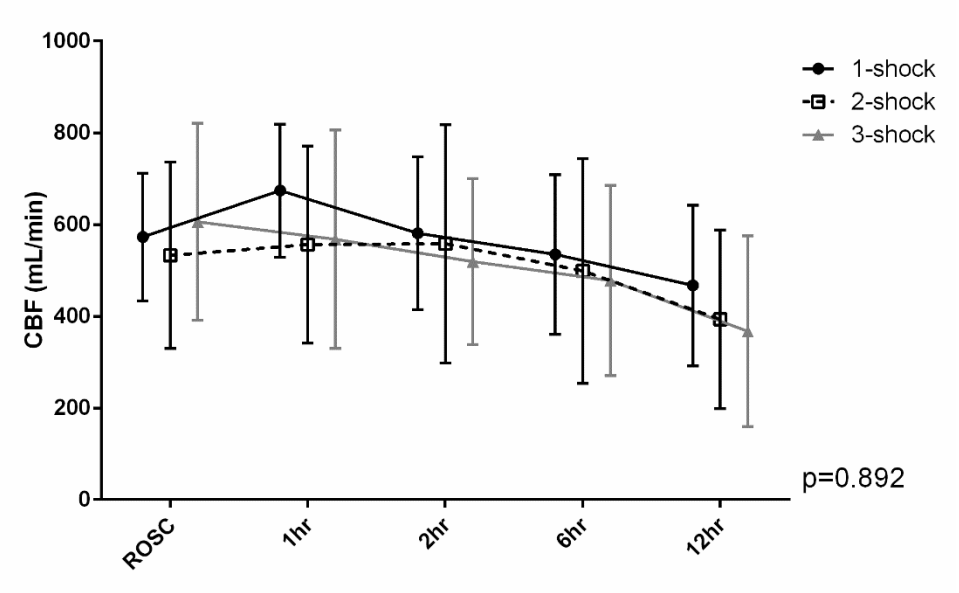


Fig 16. Carotid blood flow (CBF) during post-cardiac arrest care

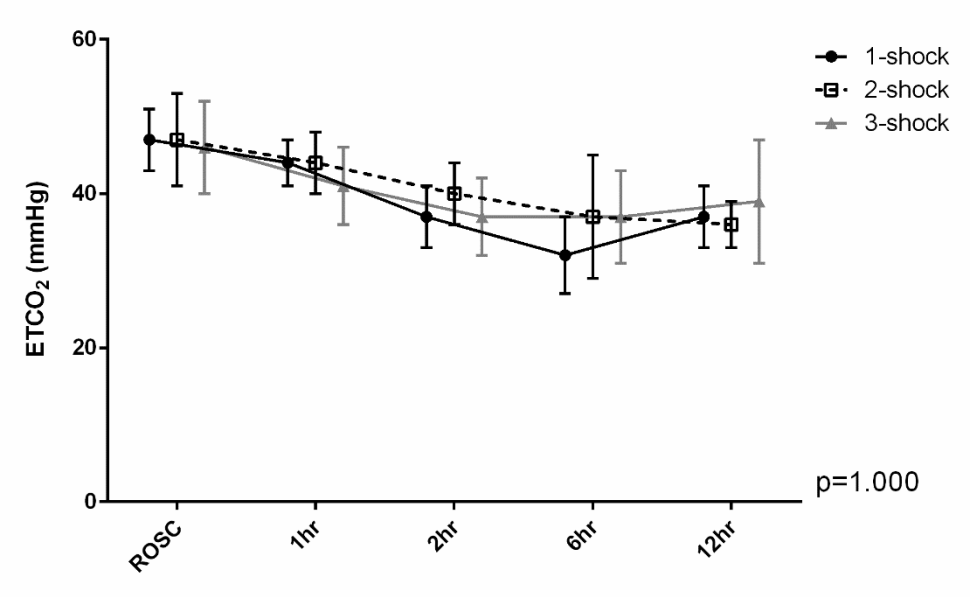


Fig 17. End tidal carbon dioxide ($ETCO_2$) during post-cardiac arrest care

6. Comparison of cardiac output, lactate, and troponin I during post-cardiac arrest care between the groups

Cardiac output, lactate and troponin I measured during post-cardiac arrest care were not different between the groups (p = 0.258, 0.941 and 0.525, respectively) (Table 3) (Fig 18 and 20).

Table 3. Comparison of cardiac output, lactate and troponin I during post-cardiac arrest care

Parameter / Defibrillation group	Baseline	ROSC	1hr	2hr	6hr	12hr	p-value
Cardiac output (L/min)							0.258
1 shock (n = 5)	4.1 ± 1.4	5.4 ± 2.4	7.4 ± 2.7	6.7 ± 1.5	8.6 ± 2.6	5.4 ± 1.8	
2 shock (n = 11)	4.1 ± 1.0	3.8 ± 1.9	5.7 ± 2.3	6.0 ± 2.0	6.6 ± 2.0	5.5 ± 2.5	
3 shock (n = 13)	4.0 ± 1.0	5.9 ± 2.5	6.7 ± 1.5	7.2 ± 1.7	6.5 ± 1.9	4.3 ± 1.9	
Lactate (mmol/L)							0.941
1 shock (n = 5)	2.1 ± 0.6	8.3 ± 2.8	6.9 ± 1.4	4.9 ± 0.9	1.6 ± 0.6	1.2 ± 0.4	
2 shock (n = 11)	2.4 ± 0.6	9.0 ± 2.7	6.9 ± 2.0	4.8 ± 1.5	1.6 ± 0.4	1.1 ± 0.3	
3 shock (n = 13)	2.1 ± 0.6	9.0 ± 2.5	7.1 ± 1.5	4.4 ± 1.0	1.9 ± 0.5	1.4 ± 0.5	
Troponin I (ng/mL)							0.525
1 shock (n = 5)	0.04 ± 0.02	0.21 ± 0.15				3.31 ± 4.46	
2 shock (n = 11)	0.07 ± 0.1	0.36 ± 0.36				5.56 ± 3.40	
3 shock (n = 13)	0.08 ± 0.09	0.23 ± 0.15				5.12 ± 3.05	

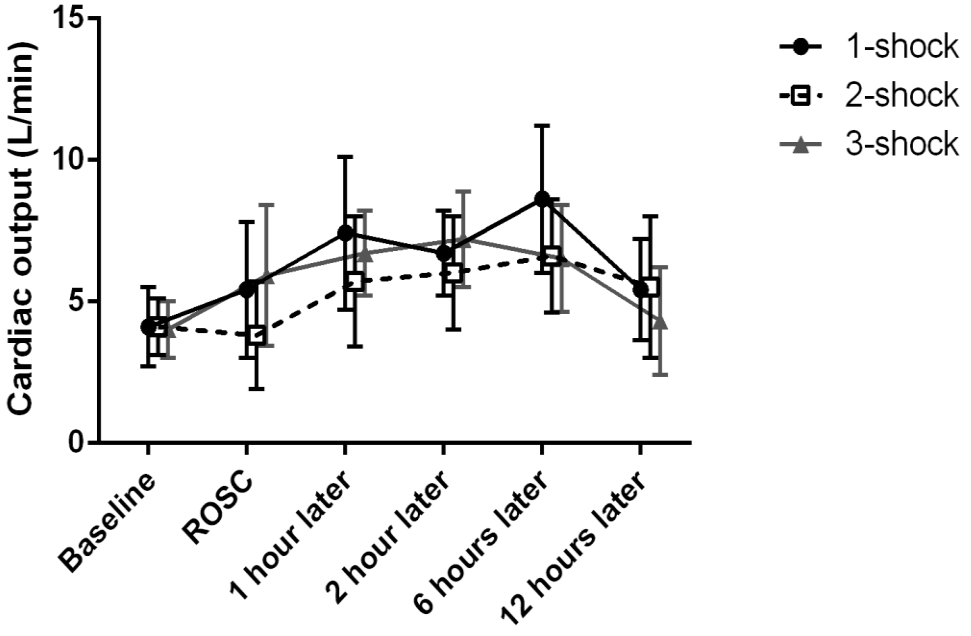


Fig 18. The comparison of cardiac output during post-cardiac arrest care between the groups

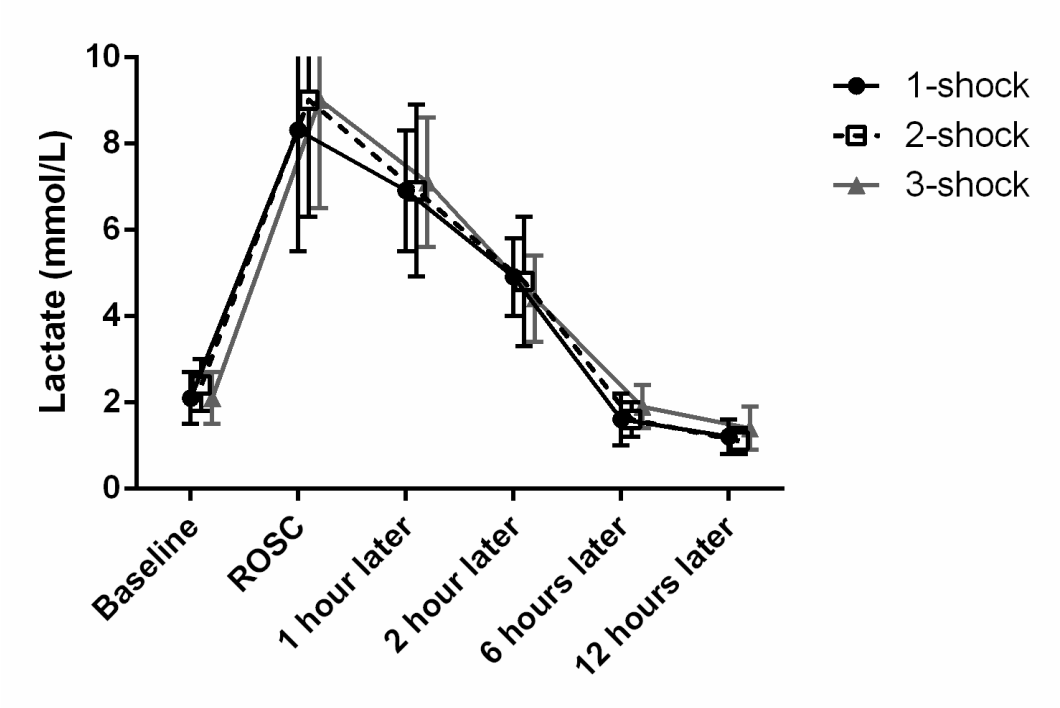


Fig 19. The comparison of lactate during post-cardiac arrest care between the groups

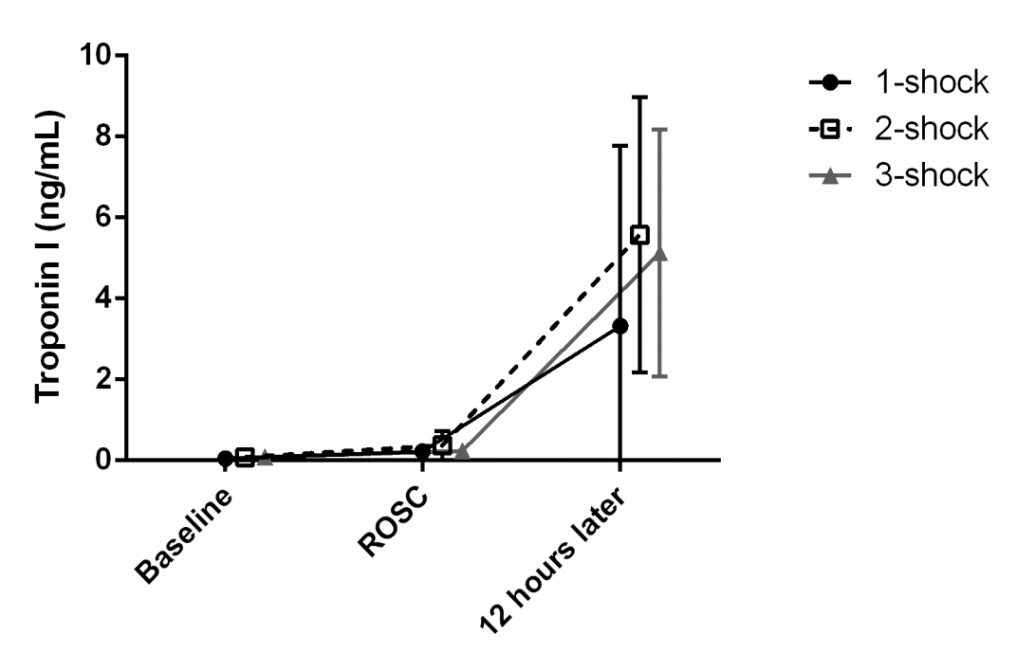


Fig 20. The comparison of troponin I during post-cardiac arrest care between the groups

7. Outcomes

ROSC was more frequently observed in the 2-shock(61.1%) and 3-shock(72.2%) groups than in the 1-shock group (27.8%, p = 0.021) (Fig. 21). 24 hour survival was more frequently observed in the 2-shock (61.1%) and 3-shock (66.7%) groups than in the 1-shock group (22.2%, p = 0.015) (Fig. 22). 48 hour survival was also more frequently observed in the 2-shock (55.6%) and 3-shock (66.7%) groups than in the 1-shock group (22.2%, p = 0.021) (Fig. 23). The NDS of pigs that survived for 48 hour were 80 ± 179 in the 1-shock group, 56 ± 118 in the 2-shock group, and 54 ± 110 in the 3-shock group, and there was no statistically significant difference (p = 0.832) (Fig. 24).

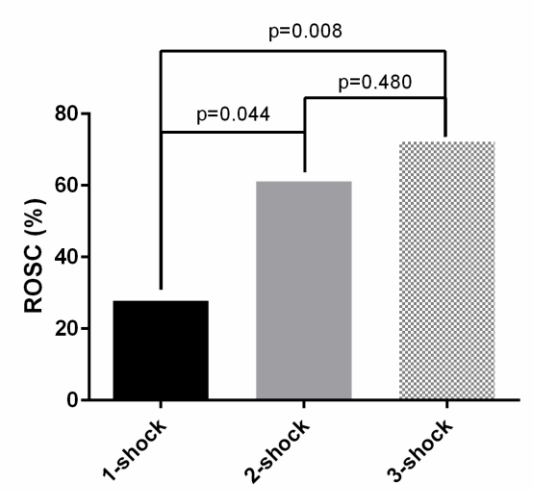


Fig 21. The comparison of ROSC rate between the groups

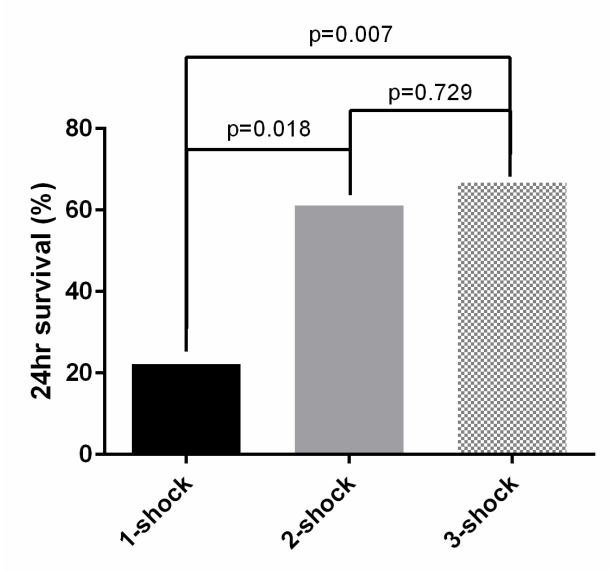


Fig 22. The comparison of 24-hour survival rate between the groups

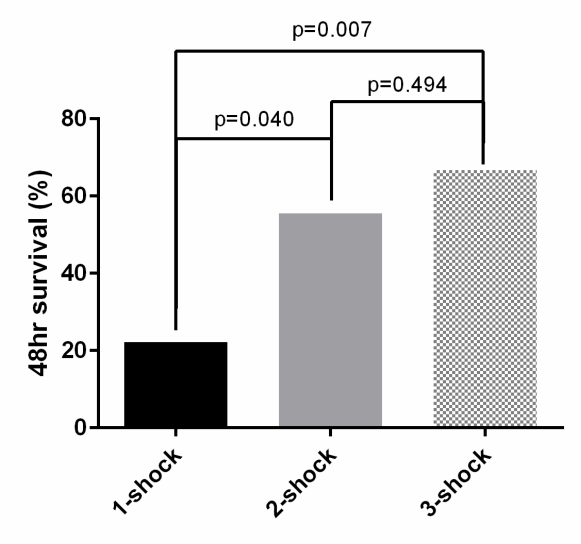


Fig 23. The comparison of 48-hour survival rate between the group

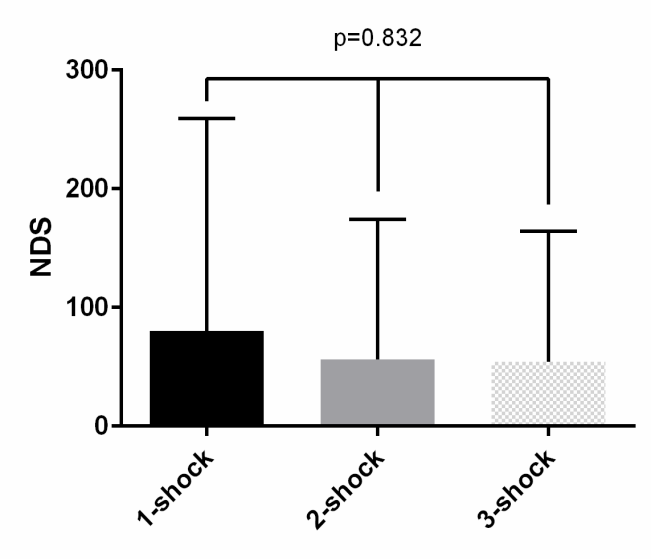


Fig 24. The comparison of neurologic deficit score (NDS) between the groups

IV. Discussion

In our study, a higher rate of ROSC and better 24h and 48h survivals were observed for the 2- or 3-shock groups than for the 1-shock group. However, the neurologic outcome was not different between the groups. The three-stacked defibrillation strategy was changed to single shock defibrillation and immediate CPR since the 2005 CPR guidelines were announced.[23, 24] It was based on a high probability of successful defibrillation of the first shock using biphasic defibrillators and reduction of the survival rate resulted from prolonged interruption of chest compression for rhythm analysis.[25-27] However, we should consider consecutive shock in patients with VF/pVT because about 50% of them are refractory to the first shock.[28, 29] For a consecutive shock according to recent CPR guidelines, we should wait for 2 min while performing CPR but it can reduce the chance to resuscitate a cardiac arrest patient because the rate of successful defibrillation is reduced by 7% - 10% per minute.[16, 30] Furthermore, we should consider that the resuscitation outcomes in the three-stacked defibrillation group in the studies favoring the single defibrillation strategy might have been affected by frequent interruption of chest compression for rhythm analysis and no chest compression during capacitor charging, which is strongly discouraged in recent guidelines.[31, 32] A “modified stacked shock strategy” in in-hospital cardiac arrest

in an observational study implied that early and stacked defibrillation with minimally interrupted CPR can promote better resuscitation outcomes.[33] The recent European Resuscitation Council CPR guideline also advised performing three-stacked defibrillation and immediate CPR without rhythm analysis in witnessed and monitored VF/pVT.[34] Therefore we should keep in mind that stacked defibrillation could be an option to resuscitate a patient with refractory VF/pVT. However, this strategy had been investigated only a monitored in-hospital cardiac arrest situation; thus, there is a knowledge gap of the effectiveness of the stacked defibrillation in an out-of-hospital cardiac arrest situation. Our study showed that the 2- or 3-stacked defibrillation with minimally interrupted CPR resulted in more favorable outcomes including successful defibrillation, ROSC, 24 h survival and 48 h survival than single defibrillation. Furthermore it showed that all stacked defibrillation strategies can keep CCF > 90%, which was much higher than the recommended CCF in recent CPR guidelines.[30, 34] Especially, the 2-shcok strategy, firstly evaluated in this study, showed a similar CCF and better resuscitation outcomes than the single defibrillation strategy; thus, the two-stacked defibrillation would be a better alternative to single defibrillation to promote better resuscitation outcomes.

Post-cardiac arrest myocardial dysfunction followed by single or stacked defibrillations was evaluated through serial cardiac output and troponin I

examinations and there was no difference between the groups in our study. There were heterogeneous reports associated with the relationship between a cumulative dose of defibrillation and myocardial injury or dysfunction, although there is a concern about the risk of myocardial injury secondary to defibrillation.[35, 36] However, in previous clinical studies, it was verified that frequency or cumulative energy of defibrillation have been not association with resuscitation outcomes.[37, 38] Therefore, we can focus on early successful defibrillation for promoting ROSC or survival in out-of-hospital cardiac arrest rather than risk of post-cardiac arrest myocardial dysfunction.

The neurologic outcome was not different between the groups in the present study. This discrepancy between ROSC and favourable neurologic outcome was also noticed in previous investigations humans.[39, 40] The various factors contributing to survival and favourable neurologic outcomes in out-of-hospital cardiac arrest have been noticed, and the patient factors are one of most important ones.[41] Even though the pigs enrolled in this study were bred in a similar environment and the same experimental protocol was used during the intervention and post-cardiac arrest care, undetected individual factors such as underlying disease or development or aggravation of systemic illness during experiment and pre- and post-cardiac arrest care might have affected the neurologic outcome.

Further study is needed to verify the effect of stacked defibrillation on neurologic outcome.

Our study has some limitations. First, this study was designed using a swine cardiac arrest model. Therefore, it would be difficult to apply the results to humans, although the swine model was chosen because a two-stacked defibrillation strategy is not recommended in the current guidelines. Second, we did not use any antiarrhythmics drugs, including amiodarone or lidocaine, to terminate refractory VF or pulseless VT. Our study was designed to verify the effect of various defibrillation strategies on resuscitation outcomes, and these outcomes would have been different if we had used antiarrhythmics drugs. Third, although we performed modified targeted temperature management for 12 h, neurologic outcomes may have improved if we had performed a full period of targeted temperature management as conducted with humans. Lastly, this study did not include histopathologic injury determination, which would show different cerebral injury patterns.

V. Conclusion

A stacked defibrillation strategy was superior to single shock strategy for successful defibrillation and better resuscitation outcomes in treating ventricular fibrillation in a swine model of cardiac arrest. A two-stacked defibrillation strategy could be a better alternative to the single defibrillation strategy recommended in the current CPR guidelines.

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Abstract in Korean

심장정지 동물 모델에서 연속 제세동 횟수가 자발순환회복률 및 신경학적 예후에 미치는 영향

<지도교수: 차경철>

연세대학교 대학원 의학과
김소영

배경과 목적

제세동은 심실세동이나 무맥성 심실빈맥으로 인한 심정지 환자의 소생에 가장 중요한 치료이다. 현재의 심폐소생술 지침은 2 분간의 가슴압박 이후 리듬을 확인하여 1 회만 제세동을 시행할 것을 권유하고 있다. 그러나 이러한 심폐소생술 지침은 과학적인 근거 없이 전문가들의 공통 의견으로만 결정되었으며, 가장 효율적인 제세동 횟수에 대해서는 연구가 부족하다. 본 연구의 목적은 심정지 동물 모델에서 연속 제세동 횟수에 따른 자발순환회복률과 신경학적 예후를 비교하는 것이다.

대상 및 방법

체중 35-49 kg 의 돼지 53 마리를 각각 1 회, 2 회, 3 회 연속 제세동을 시행하는 그룹으로 나누었다. 돼지의 심장에 전기를 가하여 심실세동을 유발하고 2 분간 관찰한 후 초기 8 분동안 30:2 의 가슴압박-인공호흡 비율로 기본소생술을 시행하였다. 이 후 10 분 부터는 가슴압박의 중단 없이 10 번의 가슴압박 당 한 번의 인공호흡을 시행하는 전문소생술을 실시하였다. 실험 도중 자발순환이 회복된 경우는 12 시간 동안 36 도로 체온 조절을 실시하며, 48 시간 동안 경과관찰 후 신경학적 예후를 평가하였다.

결과

심실세동을 유발하기 전의 대동맥 수축기 및 이완기압, 평균동맥압, 우심방 수축기 및 이완기압, 관상동맥 관류압, 호기말이산화탄소분압과 동맥혈 산소분압, 심근효소 수치 및 심박출량은 세 군에서 유의한 차이가 없었다. 심폐소생술과 심정지 후 치료 중 측정한 대동맥 수축기 및 이완기압, 평균동맥압, 우심방 수축기 및 이완기압, 관상동맥 관류압, 호기말이산화탄소분압의 결과는 세 군에서 유의한 차이가 없었다.

가슴압박실시율은 1 회 제세동을 시행한 그룹이 가장 높았고 ($p < 0.001$), 1 회 제세동을 시행한 그룹과 3 회 연속 제세동을 시행한 그룹에서 유의한 차이가 있었으나 ($p < 0.001$), 1 회 또는 2 회 연속 제세동을 시행한 그룹과, 2 회 또는 3 회 연속 제세동을 시행한 그룹에서는 차이가 없었다 ($p = 0.022$, 0.040).

2 회 또는 3 회 연속 제세동을 시행하는 그룹에서 제세동 성공률, 자발순환회복률과 24 시간, 48 시간 이후 생존율이 높았으며 ($p = 0.005$, 0.021, 0.015, 0.021), 신경학적인 예후는 세 군에서 차이가 없었다. ($p = 0.832$)

결론

돼지 심정지 모델에서 연속된 제세동 시행 방법은 1 회의 제세동 시행 방법보다 심실세동을 치료할 때 더 좋은 예후를 보인다. 이에 따라 2 회 제세동을 시행하는 방법은 현재 심폐소생술 지침에서 권고하는 1 회 제세동 시행 방법에 대한 더 좋은 대안이 될 수 있다.

핵심 되는 말: 심폐소생술, 심정지, 제세동