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ORIGINAL RESEARCH

Comparison of Resuscitation Outcomes Between 2- or 3-Stacked Defibrillation Strategies With Minimally Interrupted Chest Compression and the Single Defibrillation Strategy: A Swine Cardiac Arrest Model

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BACKGROUND: There is controversy over whether the number and mode of electrical shock are optimal for successful defibrillation.

METHODS AND RESULTS: Fifty-four pigs were randomly assigned to 3 groups. After inducing ventricular fibrillation and a 2-minute downtime, basic life support was initiated with a 30:2 compression/ventilation ratio for 8 minutes. Subsequently, 20 minutes of advanced life support, including asynchronous ventilation, every 10 chest compressions with 15 L/min of oxygen, was delivered. Animals of the single shock group received a single shock, animals of the 2-stacked shock group received 2 consecutive shocks, and animals of the 3-stacked shock group received 3 consecutive shocks. Animals with the return of spontaneous circulation underwent post–cardiac arrest care for 12 hours. The rates of successful defibrillation, return of spontaneous circulation, 24-hour survival, and 48-hour survival and neurological deficit score were compared between the groups. Hemodynamic parameters, arterial blood gas profiles, troponin I, and cardiac output were not different between the groups. There was a significant difference in chest compression fraction between the single and 3-stacked shock groups ($P<0.001$), although there was no difference between the single and 2-stacked shock groups ($P=0.022$) or the 2-stacked and 3-stacked shock groups ($P=0.040$). The rates of successful defibrillation, return of spontaneous circulation, 24-hour survival, and 48-hour survival were higher in the 2- and 3-stacked shock groups than in the single shock group ($P=0.021$, $P=0.015$, and $P=0.021$, respectively). Neurological deficit score at 48 hours was not different between the groups.

CONCLUSIONS: A stacked shock strategy was superior to a single shock strategy for successful defibrillation and better resuscitation outcomes in treating ventricular fibrillation.

Key Words: cardiac arrest ■ cardiopulmonary resuscitation ■ chest compression ■ defibrillation ■ outcomes

Defibrillation is the most effective treatment for patients experiencing cardiac arrest with ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT). It should be performed as soon as possible to convert these shockable rhythms into perfusing rhythms.[1–4] Current cardiopulmonary resuscitation (CPR) guidelines recommend the single defibrillation strategy every 2 minutes because successful defibrillation is most frequently observed in the first shock during 3-stacked shock. Minimizing chest compression

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CLINICAL PERSPECTIVE

What Is New?

- The 2- or 3-stacked shock strategy with minimally interrupted chest compression was superior to a single shock strategy for successful defibrillation and better resuscitation outcomes in a swine cardiac arrest model.

What Are the Clinical Implications?

- Because the effect of stacked shock strategy on resuscitation outcomes in out-of-hospital cardiac arrest has not been proved in the era of emphasis of minimally interrupted chest compression, the study protocol is ready to be translated clinically.
- The study suggests 2-stacked defibrillation with minimally interrupted chest compression might be a good alternative to single shock strategy.

Nonstandard Abbreviations and Acronyms

CCF	chest compression fraction
$ETCO_2$	end-tidal carbon dioxide
NDS	neurological deficit score
pVT	pulseless ventricular tachycardia
ROSC	return of spontaneous circulation

interruption is one of the important factors to promote good resuscitation outcomes.[5,6] However, we may lose the chance to revive a patient with unsuccessful defibrillation with a single shock because the probability of survival could be decreased by ≈10% every minute.[7] Furthermore, the recommendations were based on indirect evidence comparing resuscitation outcomes between patients with or without minimally interrupted chest compression during CPR.[8,9] Double sequential defibrillation was introduced for the alternative 2-stacked defibrillation method to terminate refractory VF/pVT; however, the effect has been controversial, and it is inconvenient to prepare another defibrillator during CPR.[10–12] Therefore, a new defibrillation strategy for promoting early successful defibrillation under high-quality CPR needs to be investigated.

This study aimed to verify the effective defibrillation strategy by comparing the resuscitation outcomes between single shock and stacked shocks with minimally interrupted chest compression during CPR. The authors hypothesized that the stacked defibrillations could improve the resuscitation outcomes compared with the single defibrillation.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Design

This laboratory study was designed to compare the probability of successful defibrillation and resuscitation outcomes using single, 2-stacked, or 3-stacked defibrillation in a swine model 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).

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, endotracheal intubation was performed with a cuffed endotracheal tube, and the pigs were 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 mm Hg. Electrocardiography with lead II and $ETCO_2$ were continuously monitored. Under aseptic conditions, the right femoral artery was cannulated using a 5.5F introducer sheath via the Seldinger technique, and aortic blood pressure was continuously recorded using a 5F 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 5F micromanometer-tipped catheter. The right internal carotid artery was exposed, and a vascular flowmeter (Transonic Systems, 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 5F pacing catheter to induce VF and to 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 heparin bolus was administered to prevent thrombosis.

Study Protocol

According to the result indicated in a sealed opaque envelope opened by an investigator before the induction of cardiac arrest, the pigs were randomized to 3 groups. The randomization envelopes, which contained different defibrillation methods (single shock, 2-stacked shock, or 3-stacked shock group), were randomized by shaking the box and drawing an envelope from the top of the resulting pile. Predefined energy was calculated on the basis of 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 predefined defibrillation energy for the first shock was 75 J for pigs weighing 34 to 37 kg or 100 J for pigs weighing 38 to 49 kg. The consecutive shock was 150 J for pigs weighing 34 to 37 kg, 175 J for pigs weighing 38 to 43 kg, and 200 J for pigs weighing 44 to 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, confirmed by the electrocardiographic waveform and a decrease in aortic pressure. Once VF was induced, the endotracheal tube was disconnected from the ventilator; pigs were observed for 2 minutes without any procedure or treatment. After 2 minutes of untreated VF, basic life support was performed for 8 minutes to mimic a basic life support 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).

The manual biphasic defibrillator (D500, Mediana, Republic of Korea) was used for defibrillation, and the first defibrillation was performed after 8 minutes of basic life support. In the single shock group, chest compression was performed immediately after defibrillation and continued for 2 minutes until the next rhythm check; a consecutive shock was delivered as indicated. This “shock–chest compression” strategy continued until the return of spontaneous circulation (ROSC) or 30 minutes after VF induction. In the 2- or 3-stacked shock group, electrocardiographic rhythm was checked immediately after defibrillation, and if it was a shockable rhythm, chest compression was performed while recharging the defibrillator; then, the consecutive shock was delivered. If the electrocardiographic rhythm was nonshockable, chest compression continued for 2 minutes until the next rhythm check. This shock–rhythm check, chest compression during recharging, and consecutive shock strategy continued until ROSC or 30 minutes after VF induction. During the next 20 minutes after basic life support, 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. One milligram of epinephrine with 20 mL of saline was delivered every 4 minutes until ROSC or the end of the experiment (Figure 1).

If a pig did not achieve ROSC at 30 minutes after VF induction, the experiment was terminated, and the animal was considered dead. When a pig achieved ROSC, mechanical ventilation with inhalation anesthesia was reinitiated. Post–cardiac arrest care, which included an injection of intramuscular ketoprofen (1 mg/kg) for pain control, intravenous 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 mm Hg, and controlling body temperature at 36.0 °C with a temperature management system (Artic Sun, BD, NJ), was performed for 12 hours. After post–cardiac arrest care, the pig was moved to a breeding room and observed for 48 hours after ROSC. The neurological deficit score (NDS) was determined by another researcher blinded to our study 48 hours after ROSC. The NDS includes behavior type and consciousness level, breathing pattern, cranial nerve function, and motor and sensory function. An NDS of 0 to 40 is considered the absence of neurological deficit, and an NDS of 400 is considered as brain death.[13] After the neurological examination, the animals were euthanized by intravenous injection of potassium.

Measurements

Data were digitized using a digital recording system (PowerLab, AD Instruments, Colorado Springs, CO). Aortic and right atrial pressures, $ETCO_2$, and carotid blood flow were continuously recorded and analyzed at baseline, at 2 minutes, and then every 4 minutes until 30 minutes elapsed. Coronary perfusion pressure during CPR was calculated as the difference between the aortic and right atrial pressures in the middiastolic phase using an electrical subtraction unit. Arterial blood gas analyses, including pH, partial pressure of carbon dioxide, partial pressure of oxygen, bicarbonate, oxygen saturation, and lactate, were performed using a blood gas analyzer (i-STAT1, Abbott Laboratories, Abbott Park, IL) at baseline, at ROSC, and at 1, 2, 6, and 12 hours after ROSC. Cardiac output via the thermodilution technique (VGS Vigilance Monitor, Edwards Lifesciences) was measured simultaneously. Troponin I was analyzed using a troponin

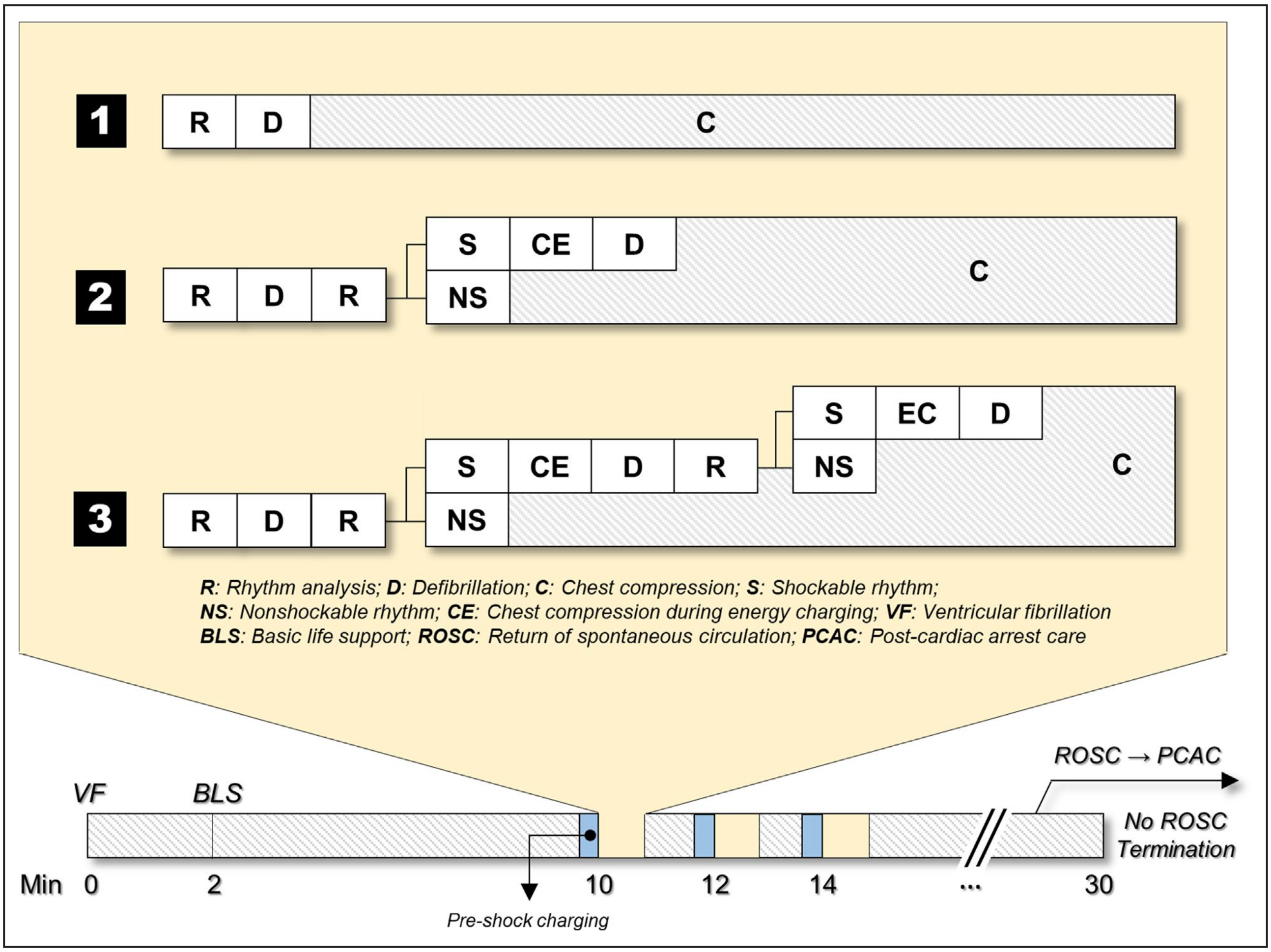

Figure 1. Study protocol.
BLS indicates basic life support; C, chest compression; CE, chest compression during charging; D, defibrillation; NS, nonshockable rhythm; PCAC, post–cardiac arrest care; R, rhythm analysis; ROSC, return of spontaneous circulation; S, shockable rhythm; and VF, ventricular fibrillation.

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 hours after ROSC. Once a pig achieved ROSC, the measurement of hemodynamic parameters was discontinued because of the possibility of bias from spontaneous circulation. Chest compression fraction (CCF) was defined as the proportion of time spent performing chest compressions during advanced cardiac life support. Successful defibrillation was defined as the frequency of pig experienced termination of VF irrespective of the restoration of circulation or recurrence of VF. The successful defibrillation per episode was calculated as the frequency of successful defibrillation per shocks attempted. To evaluate the usefulness of stacked defibrillation, the rate of successful defibrillation was compared between the first shock and the second or third shock in 2- and 3-stacked shock groups, respectively. ROSC was defined as maintaining aortic perfusion pressure over 20 minutes after the restoration of perfusing rhythm. The 24-hour survival rate, 48-hour survival rate, and NDS at 48 hours after ROSC were evaluated as outcome variables.

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 2-stacked defibrillation under recent CPR guidelines had never previously been evaluated. In the preliminary study, ROSC was observed in 2 of 9 pigs (22%) in the single shock group and in 6 of 9 pigs (67%) in the 2- and 3-stacked shock groups. The sample size was calculated as 18 pigs per group using tests for 2 proportions with a 2-sided α value of 0.05 and a statistical power of 80%.

Statistical Analysis

Continuous variables are presented as medians and interquartile ranges (IQRs). ANOVA or the Kruskal-Wallis test and post hoc analysis were used to compare the continuous variables between the single shock, 2-stacked shock, and 3-stacked shock groups, as appropriate. The nominal variables are reported as counts and percentages and were compared using the χ^2 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, carotid blood flow, coronary perfusion pressure, and $ETCO_2$, between the 3 groups. The statistical results are presented as group-time interaction. A repeated measure ANOVA was used to compare cardiac output and troponin I during post–cardiac arrest care between the 3 groups. $P<0.05$ 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 comparisons. The formula for compensating this is as follows:

$$\text{Formula for compensating family} \\ -\text{wise type I error} = 1-(1-0.05)^k$$

$$(k:\ \text{the number of multiple comparison}),$$

and a $P<0.0142$ was regarded as significant in this analysis. Analyses were performed using SPSS Statistics 23.0 for Windows (IBM Corp, Chicago, IL).

RESULTS

Baseline Characteristics

Eighteen male pigs from each group were enrolled in the study. There were no significant differences in baseline characteristics between the groups (Table 1).

Hemodynamic Parameters During CPR and Post–Cardiac Arrest Care

There were no significant differences between the groups in the group-time interaction analyses of hemodynamic parameters (Figure S1). There was also no significant difference between the groups in the group-time interaction analyses of hemodynamic parameters during post–cardiac arrest care (Figure S2).

Comparison of Vasopressor Infusion Profiles Between the Groups

There was no difference in the total dose of epinephrine administered between the groups (median, 5 [IQR, 3–5] mg in the single shock group, 5 [IQR, 4–5] mg in the 2-stacked shock group, and 2 [IQR, 1–5] mg in the 3-stacked shock group; $P=0.55$). There was no difference in norepinephrine infusion frequency during post–cardiac arrest care between groups (80% in the single shock group, 36% in the 2-stacked shock group, and 62% in the 3-stacked shock group; $P=0.268$).

Comparison of Defibrillation Profiles Between the Groups

Successful defibrillation was more frequently observed in the 2- or 3-stacked group than in the single shock group ($P=0.005$). Successful defibrillation was more frequently observed in the second or third shocks than in the first shock in the 2- or 3-stacked group. The successful defibrillation per episode and cumulative energy of defibrillation were not different between the groups (Table 2, Figure 2 and Figure S3).

Table 1. Baseline Characteristics

Parameter	Defibrillation group			*P* value
	Single shock (n=18)	2-Stacked shock (n=18)	3-Stacked shock (n=18)	
Body weight, kg	42 (38–46)	44 (38–45)	43 (39–45)	0.907
$ETCO_2$, mm Hg	41 (37–46)	42 (39–50)	38 (34–44)	0.095
ABGA values				
pH	7.488 (7.433–7.532)	7.460 (7.404–7.502)	7.502 (7.455–7.538)	0.228
$Paco_2$	39 (35–42)	42 (36–47)	36 (34–39)	0.144
Pao_2	123 (104–142)	115 (98–134)	122 (104–147)	0.551
Bicarbonate	29.7 (27.2–31.3)	28.5 (27.6–30.0)	28.5 (27.6–30.3)	0.750
Sao_2	99 (99–99)	99 (98–99)	99 (98–99)	0.126
Lactate	2.1 (1.8–2.4)	2.4 (1.8–2.7)	1.9 (1.6–2.6)	0.626
Troponin I level, ng/mL	0.05 (0.02–0.07)	0.05 (0.02–0.07)	0.04 (0.02–0.08)	0.937
Cardiac output, L/min	3.2 (2.6–5.5)	3.9 (3.2–4.7)	3.9 (3.2–5.5)	0.421

Variables are presented as median (interquartile range). ABGA indicates arterial blood gas analysis; $ETCO_2$, end-tidal carbon dioxide; and Sao_2, oxygen saturation.

Table 2. Comparison of Defibrillation Profiles

Parameter	Defibrillation group			P value
	Single shock (n=18)	2-Stacked shock (n=18)	3-Stacked shock (n=18)	
Successful defibrillation, n (%)	8 (44)	15 (83)	16 (89)	0.005
Successful defibrillation per episode, %	12.2	21.5	18.4	0.176
Cumulative energy of defibrillation, J	1850 (1294–1913)	1963 (875–3400)	2000 (1675–4819)	0.117

Variables are presented as frequency (percentage), percentage, or median (interquartile range).

Comparison of CCF During Advanced Cardiac Life Support Between the Groups

CCF was the highest in the single shock group, followed by the 2- and 3-stacked shock groups (median, 98 [IQR, 96–98], 95 [IQR, 93–96], and 93 [IQR, 92–95], respectively; *P*<0.001). In the post hoc analysis, there was a significant difference in CCF between the single shock and 3-stacked shock groups (*P*<0.001), although there was no difference between the single shock and 2-stacked shock groups (*P*=0.022) or the 2- and 3-stacked shock groups (*P*=0.040).

Comparison of Cardiac Output, Lactate, and Troponin I During Post–Cardiac Arrest Care Between the Groups

Cardiac output, lactate, and troponin I measured in pigs with sustained ROSC during post–cardiac arrest care were not different between the groups (*P*=0.258, *P*=0.941, and *P*=0.525, respectively) (Table 3).

Outcomes

ROSC was more frequently observed in the 2-stacked (61.1%) and 3-stacked (72.2%) shock groups than in the single shock group (27.8%; *P*=0.021), although time to ROSC was not different between groups (median, 20 [IQR, 15–24] minutes in the single shock group, 18 [IQR, 14–24] minutes in the 2-stacked shock group, and 16 [IQR, 14–23] minutes in the 3-stacked group; *P*=0.830). The 24-hour survival was more frequently observed in the 2-stacked (61.1%) and 3-stacked (66.7%) shock groups than in the single shock group (22.2%; *P*=0.015). The 48-hour survival was also more frequently observed in the 2-stacked (55.6%) and 3-stacked (66.7%) shock groups than in the single shock group (22.2%; *P*=0.021) (Figure 3). The median NDSs of pigs that survived for 48 hours were 0 (IQR, 0–200) in the single shock group, 0 (IQR, 0–75) in the 2-stacked shock group, and 0 (IQR, 0–75) in the 3-stacked shock group; there was no significant difference (*P*=0.832).

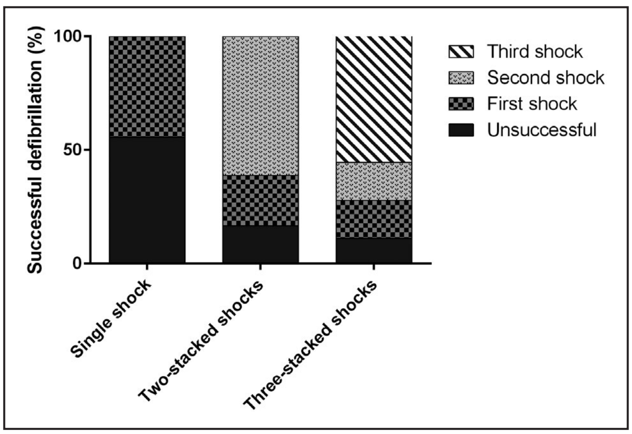

Figure 2. The rate of successful defibrillation per order of attempted shocks.

DISCUSSION

In our study, a higher rate of ROSC and better 24- and 48-hour survival were observed for the 2- and 3-stacked shock groups than for the single shock group. However, the neurological outcome was not different between the groups. The 3-stacked defibrillation strategy was changed to a single shock defibrillation and immediate CPR since the 2005 CPR guidelines were announced.[14,15] 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.[16–18] However, we should consider additional shock in patients with VF/pVT because a significant proportion of them recurred and about half of them occurred within 2 minutes.[19,20] According to recent CPR guidelines, we should wait for 2 minutes while performing CPR for a consecutive shock. However, it can reduce the chance to resuscitate a patient experiencing cardiac arrest because the probability of survival is reduced by 7% to 10% per minute.[5,7] Furthermore, we should consider that the resuscitation outcomes in the 3-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.[8,21] A "modified stacked shock strategy" in in-hospital cardiac arrest in

Table 3. Comparison of Cardiac Output, Lactate, and Troponin I Levels During Post–Cardiac Arrest Care

Parameter/defibrillation group	Baseline	ROSC	1 hour	2 hours	6 hours	12 hours	*P* value
Cardiac output level, L/min							0.258
Single shock (n=5)	3.2 (2.6–5.5)	5.9 (3.0–7.6)	7.3 (4.9–9.9)	7.2 (5.5–7.8)	8.8 (6.2–11.0)	5.3 (3.7–7.2)	
2-Stacked shock (n=11)	3.9 (3.2–4.7)	5.3 (4.3–6.8)	5.3 (4.3–6.8)	6.2 (4.4–7.4)	6.7 (5.0–7.8)	4.5 (3.5–7.6)	
3-Stacked shock (n=13)	3.9 (3.2–5.5)	6.5 (5.7–7.8)	6.5 (5.7–7.8)	7.3 (5.5–8.5)	6.8 (4.8–8.1)	3.7 (3.1–5.3)	
Lactate level, mmol/L							0.941
Single shock (n=5)	2.1 (1.8–2.4)	8.4 (5.6–11.0)	6.4 (5.7–8.5)	5.2 (4.0–5.7)	1. 7 (1.0–2.1)	1.3 (0.9–1.5)	
2-Stacked shock (n=11)	2.4 (1.8–2.7)	9.2 (6.7–10.5)	7.2 (4.8–8.4)	5.1 (3.8–5.7)	1.6 (1.3–1.8)	1.2 (0.8–1.3)	
3-Stacked shock (n=13)	1.9 (1.6–2.6)	8.4 (7.1–10.8)	6.8 (5.9–7.8)	4.4 (3.8–5.0)	1.7 (1.5–2.4)	1.5 (1.3–1.6)	
Troponin I level, ng/mL							0.525
Single shock (n=5)	0.05 (0.02–0.07)	0.19 (0.07–0.37)				1.15 (0.95–7.83)	
2-Stacked shock (n=11)	0.05 (0.02–0.07)	0.21 (0.16–0.57)				5.2 (2.96–10.00)	
3-Stacked shock (n=13)	0.04 (0.02–0.08)	0.14 (0.11–0.40)				4.17 (2.74–8.24)	

Variables are presented as median (interquartile range). ROSC indicates return of spontaneous circulation.

an observational study implied that early and stacked defibrillation with minimally interrupted CPR can promote better resuscitation outcomes.[22] The recent European Resuscitation Council CPR guideline also advised considering the use of up to 3-stacked shocks in witnessed and monitored VF/pVT.[6] 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 in 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-hour survival, and 48-hour survival, than a single defibrillation. In the 2- or 3-stacked shock groups, the higher rate of successful defibrillation of the second or third shock than that of the first shock indicates that the stacked defibrillation strategy can promote successful defibrillation. Furthermore, it showed that all stacked defibrillation strategies can keep CCF >90%, which was much higher than the recommended CCF in recent CPR

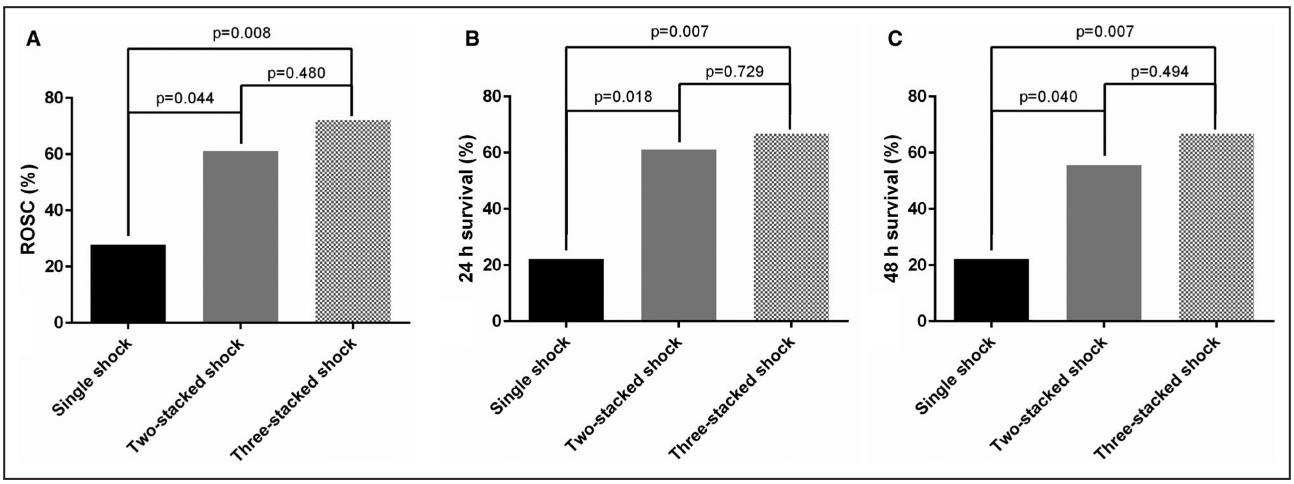

Figure 3. Comparison of the return of spontaneous circulation (ROSC) rate, 24-hour survival and 48-hour survival between the groups.

guidelines.[5,6] Especially, the 2-stacked defibrillation strategy, first evaluated in this study, showed a similar CCF and better resuscitation outcomes than the single defibrillation strategy; thus, 2-stacked defibrillation would be a better alternative to single defibrillation to promote improved resuscitation outcomes.

Although it is difficult to clearly explain why the stacked defibrillation showed superiority in ROSC and survival, the depletion of myocardial ATP might be one of the reasons. Because CPR has little effect in restoring myocardial ATP in prolonged VF, delayed defibrillation might reduce the chance of ROSC.[23] Further studies to investigate the mechanism whereby stacked defibrillation with minimally interrupted chest compression can promote successful defibrillation will be needed.

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.[24,25] However, in previous clinical studies, it was verified that the frequency or cumulative energy of defibrillation is not associated with resuscitation outcomes.[26,27] Therefore, we can focus on early successful defibrillation for promoting ROSC or survival in out-of-hospital cardiac arrest rather than the risk of post–cardiac arrest myocardial dysfunction.

The neurological outcome was not different between the groups in the present study. This discrepancy between ROSC and favorable neurological outcome was also noticed in previous human investigations.[28,29] The various factors contributing to survival and favorable neurological outcomes in out-of-hospital cardiac arrest have been noticed, and the patient factors are one of the most important.[30] Although 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 and before and after cardiac arrest care might have affected the neurological outcome. Further study is needed to verify the effect of stacked defibrillation on neurological 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 2-stacked defibrillation strategy is not recommended in the current guidelines. Second, we did not use any antiarrhythmic drugs, including amiodarone or lidocaine, to terminate refractory VF or pVT. 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 antiarrhythmic drugs. Third, escalation of defibrillation energy from second shock would be a confounder as higher energy rather than stacked defibrillation, although only one animal in the 2-stacked shock group was restored spontaneous circulation with the second shock. Fourth, although we performed modified targeted temperature management for 12 hours, neurological outcomes may have improved if we had performed a full period of targeted temperature management as conducted with humans. Fifth, the staked defibrillation strategy in this study could be applied only for experienced healthcare providers familiar with rhythm analysis. The proposed reintroduction of stacked shocks with rhythm analysis would only apply to the emergency medical services system-attended arrests with manual defibrillators and not automated external defibrillators. Mechanical chest compression would also not be applicable in some emergency medical services systems, although it was performed to control the quality of CPR in this experiment. Last, this study did not include histopathologic injury determination, which would show different cerebral injury patterns.

CONCLUSIONS

A stacked defibrillation strategy was superior to a single shock strategy for successful defibrillation and better resuscitation outcomes in treating VF in a swine model of cardiac arrest. A 2-stacked defibrillation strategy could be a better alternative to the single defibrillation strategy currently recommended in the CPR guidelines.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Figures S1–S3

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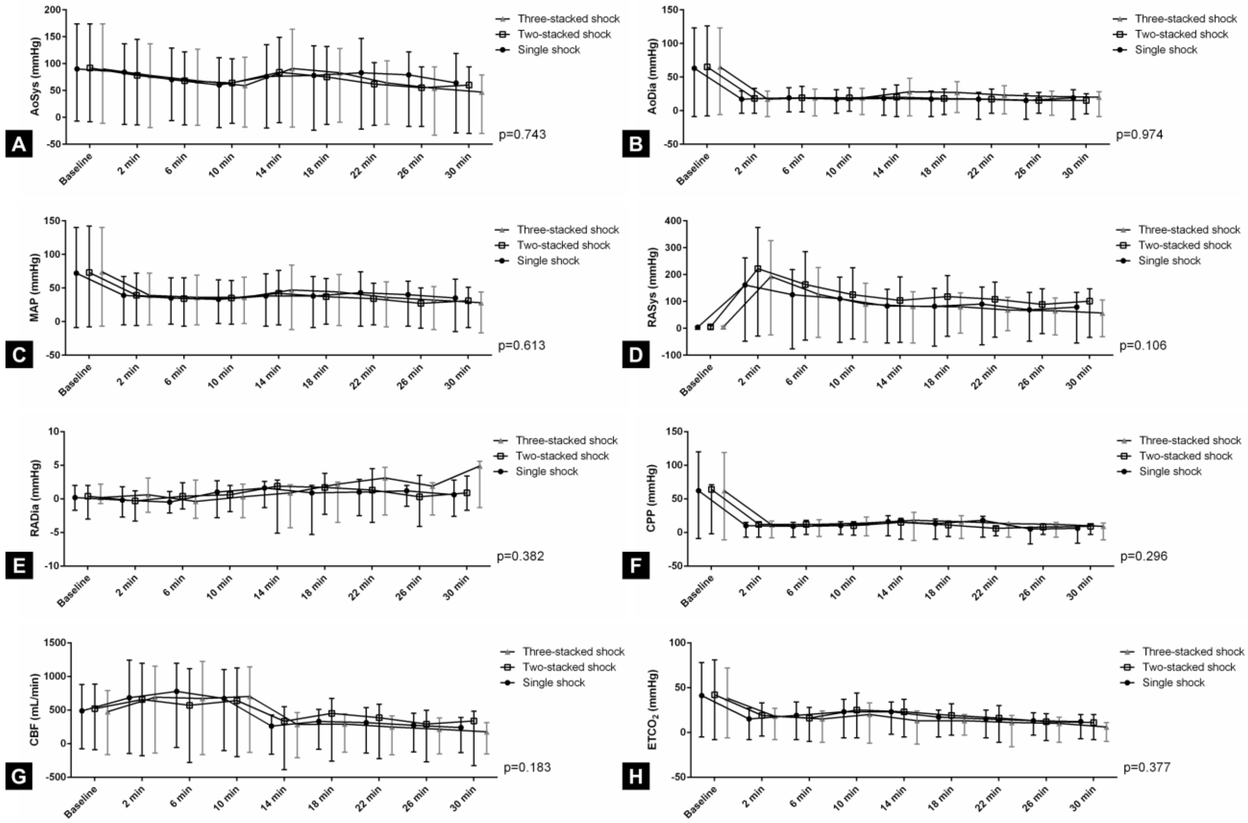
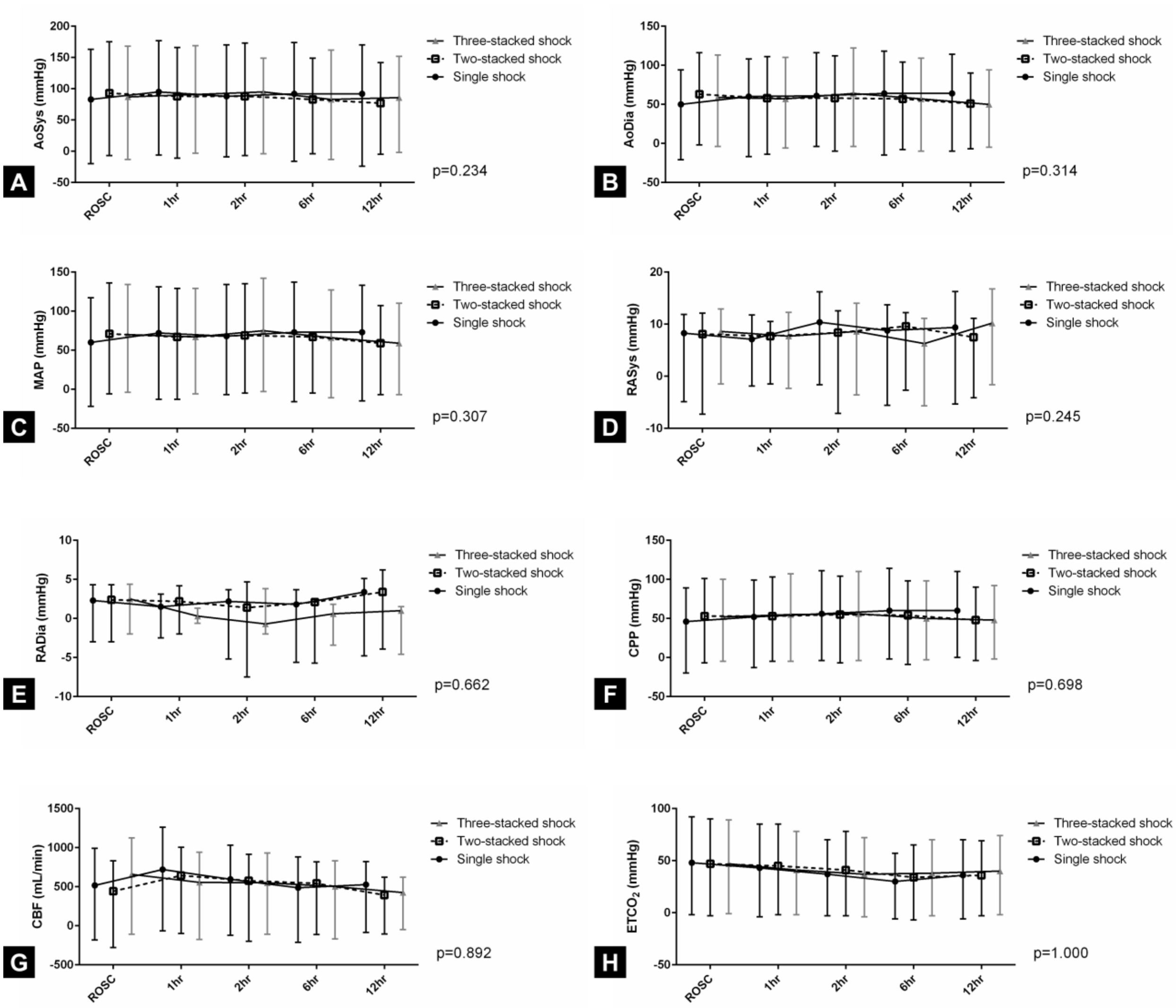
SUPPLEMENTAL MATERIAL

Figure S1. Comparison of hemodynamic parameters during CPR.



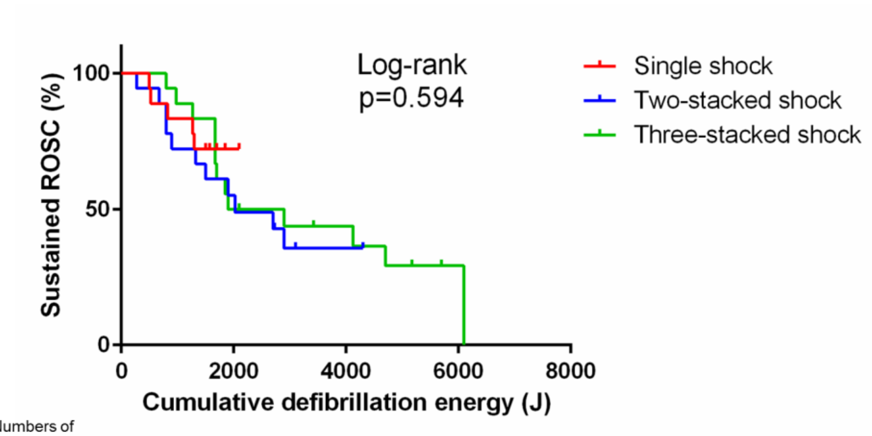
AoSys = aortic systolic pressure, AoDia = aortic diastolic pressure, MAP = mean aortic pressure, RASys = right atrial systolic pressure, RADia = right atrial diastolic pressure, CPP = coronary perfusion pressure, CBF = carotid blood flow, $ETCO_2$ = end-tidal carbon dioxide.

Figure S2. Comparison of hemodynamic parameters during post-cardiac arrest care.



AoSys = aortic systolic pressure, AoDia = aortic diastolic pressure, MAP = mean aortic pressure, RASys = right atrial systolic pressure, RADia = right atrial diastolic pressure, CPP = coronary perfusion pressure, CBF = carotid blood flow, $ETCO_2$ = end-tidal carbon dioxide.

Figure S3. Kaplan-Meier curve for probability of sustained return of spontaneous circulation (ROSC) by cumulative defibrillation energy.



Numbers of survived pigs

Single	18	13	4				
Two-stacked	18	12	9	5	4		
Three-stacked	18	16	9	8	6	3	1