Defibrillation delivered during the upstroke phase of manual chest compression improves shock success*

Yongqin Li, PhD; Hao Wang, MD; Jun Hwi Cho, MD; Weilun Quan, PhD; Gary Freeman, MSEE; Joe Bisera, MSEE; Max Harry Weil, MD, PhD; Wanchun Tang, MD

Objective: **The current standard of manual chest compression during cardiopulmonary resuscitation requires pauses for rhythm analysis and shock delivery. However, interruptions of chest compression greatly decrease the likelihood of successful defibrillations, and significantly better outcomes are reported if this interruption is avoided. We therefore undertook a prospective randomized controlled animal study in an electrically induced ventricular fibrillation pig model to assess the effects of timing of defibrillation on the manual chest compression cycle on the defibrillation threshold.**

Design: **Prospective, randomized, controlled animal study.**

Setting: **University-affiliated research laboratory.**

Subjects: **Yorkshire-X domestic pigs (*Sus scrofa*).**

Interventions: **In eight domestic male pigs weighing between 24 and 31 kg, ventricular fibrillation was electrically induced and untreated for 10 secs. Manual chest compression was then performed and continued for 25 secs with the protection of an isolation blanket. The depth and frequency of chest compressions were guided by a cardiopulmonary resuscitation prompter. Animals were randomized to receive a biphasic electrical shock in five different compression phases with a predetermined energy setting. A control phase was chosen at a constant 2 secs after discontinued chest compression. A grouped up–down defibrillation threshold testing protocol was used to compare the success rate at different coupling phases. After a recovery interval of 4 mins, the sequence was repeated for a total of 60 test shocks for each animal.**

Measurements and Main Results: **No difference in coronary perfusion pressure before delivering of the shock was observed among the six study phases. The defibrillation success rate, however, was significantly higher when shocks were delivered in the upstroke phase of manual chest compression.**

Conclusion: **Defibrillation efficacy is maximal when electrical shock is delivered during the upstroke phase of manual chest compression. (Crit Care Med 2010; 38:910–915)**

Key Words: cardiac arrest; ventricular fibrillation; defibrillation threshold; upstroke phase; manual chest compression

For more than 40 yrs, since the landmark report by Kouwenhoven et al (1), manual closed chest compression (CC) has been the standard for providing cardiac and cerebral perfusion to victims during episodes of sudden cardiac arrest (2). However, despite technique refinement, development of support devices such as automatic external defibrillators, and intensive training/retraining programs, the survival rates remain abysmal (3–5).

The current standard of manual cardiopulmonary resuscitation (CPR) requires pauses for rhythm analysis and shock delivery (6, 7). However, interruptions of CC for these requirements greatly degrade the CC quality. Performances of good-quality CC together with minimal or no interruption during CPR are essential for improving survival rates (8–12). One of the most significant changes in the 2005 American Heart Association/International Liaison Committee on Resuscitation guidelines was the re-evaluation and renewed emphasis on the importance of CC for the treatment of cardiac arrest and, in particular, on the importance of reducing interruptions in CC during CPR (13).

With the protection of a pair of medical gloves (14) or an isolation blanket (15), pausing of manual CC can be eliminated and electrical shock can be safely delivered during uninterrupted manual CC. Recent advances in rhythm detection algorithms also make it feasible to deliver an electrical shock during the ongoing manual CC (16–21). However, the optimal phasic relationship between defibrillation shock and CC is still unknown. The objective of this study was to compare the transthoracic defibrillation threshold (DFT) at different compression–decompression phases during uninterrupted manual CC in a porcine model of cardiac arrest. The primary objective of the study was to characterize the phase dependency of DFT during manual CC and to identify potentially optimal phases in CC cycles during which defibrillation efficacy reaches the highest level.

MATERIALS AND METHODS

Institutional Review. This study was approved by the Institutional Animal Care and Use Committee of the Weil Institute of Critical Care Medicine. All animals received humane care in compliance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research and the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory

***See also p. 1005.**

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For information regarding this article, E-mail: drsheart@aol.com

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Study Design. This prospective, randomized, single-center controlled trial was designed to compare the DFT at different coupling phases between manual CC and electrical shocks in a porcine model of cardiac arrest, in which each pig served as its own control.

The baseline 50% defibrillation threshold (DFT50) was estimated using a standard protocol of up and down with three reversals in the control phase (22–24). Ventricular fibrillation was electrically induced and allowed to continue for 10 secs. The testing shock started with initial defibrillation energy of 2 J/kg. The succeeding shock energy was increased or decreased by 20%, depending on failure or success of the previous test, until a reversal from failure to success or from success to failure had occurred. After the first reversal, testing energy was changed by 10% until the third reversal. The baseline DFT was calculated as the average of all the energy delivered, including the next step after the third reversal and excluding the first test energy. However, the data from baseline DFT testing were not included in the final data analyses.

A novel grouped up-and-down DFT testing protocol was then used in the study. In this protocol, the subjects to be compared in DFT were organized in a DFT testing group. In this study, five different coupling phases plus a control phase were our testing subjects, which are shown in Figure 1: 1) downstroke; 2) early upstroke; 3) middle of upstroke; 4) late upstroke; and 5) precompression (immediately before downstroke). The control group was chosen at 2 secs after discontinued CC. The testing defibrillation energy remained unchanged until all the subjects in the group had one DFT test. We termed this energy the group testing energy. The succeeding group testing energy could be increased or decreased by 10% depending on the aggregated group defibrillation success probability to maintain it at approximately 50%. The baseline DFT energy calculated from the standard up-and-down method was used as the initial group testing energy. The same grouped up–down DFT testing procedure was repeated ten times, resulting in a total of 60 testing shocks for each animal, ten from each of the testing coupling phases, respectively. A dose–response curve was then constructed based on the measured energy and the observed outcome in each of the coupling phase. The energy that corresponded to the 50% probability of the defibrillation success was calculated with a logistic function.

Animal Preparation. The animals were fasted overnight except for free access to water in this prospective study. Anesthesia was initiated by intramuscular injection of ketamine (20 mg/kg) and completed by ear vein injection of sodium pentobarbital (30 mg/kg). Additional doses of sodium pentobarbital (8 mg/kg) were injected at intervals of approximately 1 hr to maintain anesthesia. A cuffed endotracheal tube was advanced into the trachea. Animals were mechanically ventilated with a volume controlled ventilator (Model MA-1; Puritan-Bennett, Carlsbad, CA) with a tidal volume of 15 mL/kg, peak flow of 40 L/min, and F_{IO_2} of 0.21. $PetCO_2$ was monitored with an infrared capnometer (Model 01R-7101A; Nihon Kohden Corp, Tokyo, Japan). Respiratory frequency was adjusted to maintain $PetCO_2$ between 35 and 40 mm Hg. Aortic pressure was measured using a fluid-filled catheter advanced from the right femoral artery into the thoracic aorta. The right atrial, pulmonary arterial pressure, and blood temperature were measured using a 7-Fr thermodilution-tipped catheter positioned in the pulmonary artery. Electrocardiogram signal was obtained using three adhesive electrodes applied to the shaved skin of the right upper, left upper, and lower limbs. The position of catheters was confirmed by characteristic pressure morphology and/or fluoroscopy. A pair of adult defibrillation pads was placed in a lateral-to-lateral configuration, with the positive electrode placed at the right anterolateral thorax and the negative electrode placed at the left anterolateral thorax so that the heart was directly interposed between two electrodes. The animal was then put on a pig tray, which was located on the top of a base platform with four load cells embedded for the measurement of compression forces and for synchronizing the timing of defibrillation.

Experimental Protocol. Baseline measurements were obtained, including the aortic pressure, right atrial pressure, pulmonary arterial pressure, $PetCO_2$, electrocardiogram, and DFT50, together with arterial blood gases and arterial blood lactate. The intravascular pressures, $PetCO_2$, and electrocardiogram were continuously measured and recorded on a PC-based data acquisition system supported by WinDaq hardware/software (DATAQ Instruments, Inc, Akron, OH) as previously described (25–27).

Ventricular fibrillation was electrically induced by applying a 5 mA AC current through a 5-Fr pacing catheter (EP Technologies, Mountain View, CA) in the right ventricle. After 10 sec of untreated ventricular fibrillation, manual CC was performed for 25 secs. A test shock was then delivered in one of the five different testing phases during compressions or in the control phase with a predetermined randomized order. Immediately after the delivery of the attempted electrical shock, compression was stopped, and rhythm was checked by the electrocardiogram waveform together with aortic pressure measurement. If the shock failed to defibrillate, a 200-J rescue shock was delivered to the animal with the same defibrillator. The rescue shock could be repeated if needed until the animal was brought back to sinus rhythm. However, the

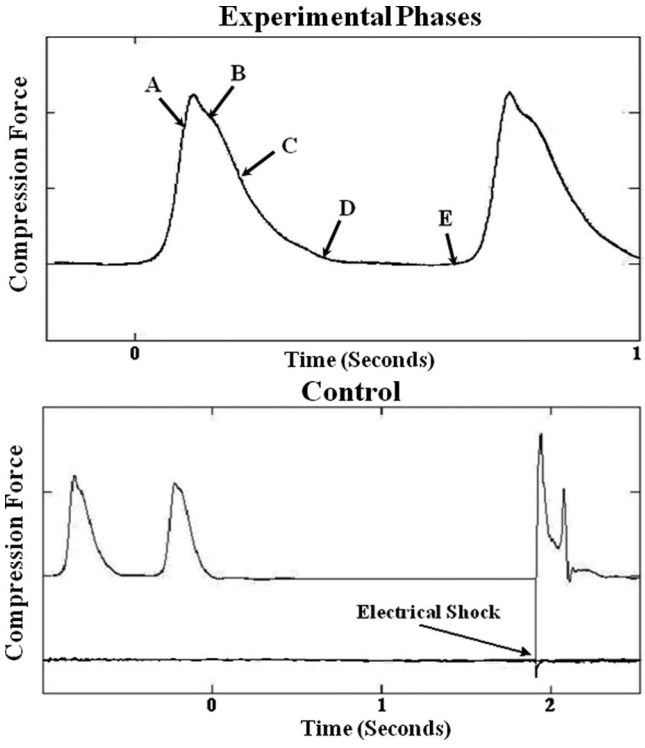

Figure 1. Waveform of different coupling phases between manual chest compression and timing of delivering an electrical shock based on the load cell voltage measurement. *Upper panel*, experimental phases; (*lower panel*) control.

rescue shocks were not included in the data analyses. The body temperature was monitored and maintained within 37.5 ± 0.5°C. A minimum 4-min waiting period was required between each of the test shocks to ensure hemodynamic stability.

The outcome of each of the shocks was recorded. The defibrillation voltage and current waveforms delivered to the animal were continuously recorded with a custom-designed LabView system (LabView 8.2; National Instruments, Austin, TX). The transthoracic impedance of the animals and the energy delivered to the animals were calculated and reported by the software in real time.

Defibrillation and Recording Systems. Manual CC was performed by the same physician from our group with the protection of an isolation blanket. The depth and the frequency of compression were guided by a CPR prompter (Real CPR Help; ZOLL Medical Corporation, Chelmsford, MA) and also adjusted by monitoring the coronary perfusion pressure (CPP) during compression to maintain a CPP level of >20 mm Hg. The CPR prompter is a CPR feedback device with a built-in metronome set to 100 beat/min and a visual prompt to feed back the measured compression depth. The CPP was calculated by the difference of diastolic aortic pressure and diastolic right atrium pressure, which was synchronized/recorded during chest compression by the WinDaq software. To record compression cycle, a flat plate with four load cell force transducers (MLP-200; Transducer Techniques Inc, Temecula, CA), mounted underneath was used. The animal was fixed on a V-shaped tray placed on top of the plate. When the chest was compressed, the compression force was sensed by the load cells and transformed into a calibrated voltage signal (10 mV/lbs; range, 0–5 V), which was simultaneously recorded (Fig. 1) and sent to the defibrillator to trigger the electrical shock at predetermined phases of CC (phases A to E in Fig. 1). The onset of each compression was detected by the defibrillator. The compression phases were determined by the elapsing time related to the onset of each compression.

A modified external biphasic defibrillator (E-Series; ZOLL Medical Corporation, Chelmsford, MA) was used, which allowed defibrillation shocks to be delivered at predetermined phases in CC cycles with an increased energy resolution of 5 J. The accuracy of synchronization was in 4 msec. The defibrillation voltage, current, and the compression force signal that the animals received were recorded with a high-speed USB data acquisition system (USB-6211; National Instruments, Austin, TX) and LabView software at a sample rate of 4000 Hz.

Data Inclusion and Statistical Analysis. The grouped up-and-down DFT testing method used in this study required that the testing energy should be chosen and delivered so that the resulting aggregated group success rate was close to 50%. If the resulting aggregated group success rate was at some distance from 50%, the testing energy was either too high or too low and, therefore, the data in that group were excluded for the data analyses. In this study, only those group data that had aggregated group success rate in the range of 33% to 67% were included for analysis. The data inclusion criteria required that group data be excluded if there were only one (or less) out of six or five (or more) out of six successful defibrillations in a round of tests in a DFT testing group. To simplify the qualification, the phases that had the same compression characters and demonstrated the same trend of increasing or decreasing defibrillation efficacy would be combined into one phase.

Data were presented in mean ± SD; the 95% confidence intervals were also presented. A standard chi-square test was used for defibrillation success rate comparison. A standard two-sided, paired Student's t test was performed for those paired continuous data, and a standard two-sample Student's t test was used for the combined continuous data. A p value $<.05$ was considered significant.

RESULTS

Eight male domestic pigs weighing between 24 and 31 kg (27.4 ± 2.6 kg) were used for this study. There were no significant differences in baseline measurement between the animals. The heart rate, mean arterial pressure, cardiac output, and ejection fraction did not show significant differences at the beginning and the end of the experiments (Table 1).

A total of 480 test defibrillations were delivered, and 279 resulted in defibrillation success (58.1%); all of the failed attempts were successfully defibrillated with a single rescue shock. However, only 39 testing groups, which had 127 successful shocks and 107 failed shocks (54.3%), were included for the final analysis based on our inclusion criteria of aggregated group success rate between 33% and 67%. The experimental results are listed in Table 2. The CPP in Table 2 was measured immediately before each of the shock deliveries. No differences among CPP, delivered shock voltage, energy, and current were observed among the six testing phases. However, the defibrillation success rates were significantly higher in the upstroke phases B, C, and D and significantly lower in the precompression phase E compared with control phase as shown in Figure 2. Because groups B, C, and D all fell in upstroke

Table 1. Hemodynamic characteristics between the initial and end of experiments (n = 8)

	Heart Rate, beats/min	Mean Arterial Pressure, mm Hg	Cardiac Output, liters/min	Eject Fraction, %
Initial	136 ± 22	111 ± 18	5.5 ± 1.4	66.4 ± 3.1
End	153 ± 26	116 ± 24	4.3 ± 0.4	61.2 ± 6.0
p value	NS	NS	NS	NS

NS, nonsignificant.

Table 2 Primary experiment results

		Experimental Phases				
Parameters	Control	Phase A	Phase B	Phase C	Phase D	Phase E
CPP, mm Hg	31.8 ± 13.7 (27.4–36.2)	29.8 ± 11.7 (26.0–33.6)	31.7 ± 13.5 (27.3–36.1)	31.6 ± 15.1 (26.7–36.5)	30.8 ± 14.2 (26.2–35.4)	31.4 ± 13.5 (27.0–35.8)
Voltage, V	566 ± 78 (541–591)	592 ± 84 (565–619)	604 ± 87 (576–632)	598 ± 79 (572–623)	584 ± 78 (559–609)	575 ± 83 (548–602)
Energy, J	63.4 ± 15.6 (58.3–68.5)	65.4 ± 16.2 (60.1–70.7)	66.2 ± 15.9 (61.0–71.4)	66.7 ± 16.1 (61.5–71.9)	64.7 ± 16.4 (59.4–70.1)	64.0 ± 16.1 (58.8–69.2)
Current, A	13.9 ± 1.9 (13.3–14.5)	13.5 ± 1.9 (12.9–14.1)	13.4 ± 1.8 (12.8–14.0)	13.5 ± 1.8 (12.9–14.1)	13.6 ± 1.9 (13.0–14.2)	13.8 ± 1.9 (13.2–14.4)
Impedance, Ohm	40.7 ± 2.9 (39.8–41.6)	44.1 ± 3.3[b] (43.0–45.2)	45.3 ± 3.8[b] (44.1–46.5)	44.3 ± 3.4[b] (43.2–45.4)	43.2 ± 4.3[a] (41.8–44.6)	42.0 ± 3.9 (40.7–43.3)
Success rate, %	44	51	69[a]	82[b]	64[a]	15[b]
50% DFT, J	79.1 ± 6.7 (73.5–84.7)	80.3 ± 6.2 (75.1–85.5)	71.6 ± 6.4[a] (66.2–76.9)	65.5 ± 13.3[a] (54.4–76.6)	67.1 ± 10.7[a] (58.2–76.0)	88.0 ± 7.3[a] (81.9–94.1)

CPP, coronary perfusion pressure; DFT, defibrillation threshold.
[a]Compared with control, $p < .05$; [b]compared with control, $p < .01$. Thirty-nine shocks were applied in each of the experimental phases.

phases of CC and they all demonstrated significant differences in increased defibrillation efficacy, data from these three phases were pooled in a single phase denoted as the upstroke phase (Table 3). Comparison of defibrillation parameters and defibrillation success rate were then performed between the upstroke phase to control phase, to downstroke phase (A), and to precompression phase (E), respectively, with a two-sample Student's *t* test and chi-square test. The defibrillation success rate was significantly higher in the upstroke phase compared with the control phase (65% vs. 44%, $p = .001$), downstroke phase (65% vs. 51%, $p = .011$), and precompression phase (65% vs. 15%, $p = .000$) (Fig. 3).

The load cell voltage that was proportional to the applied force on the animal was also recorded. As shown in Figure 4, when the shock was delivered in the downstroke of the CC (*bottom panel*), the combined force from the downward compression from the CPR performer plus the upward heave of the animal resulting from the shock-induced tetanic contraction was almost doubled as compared with that of the shock delivered in either the control phase (*top panel*) or in upstroke of CC (*middle panel*).

DISCUSSION

It is a common practice in clinical setting to use a pair of defibrillation paddles and to compress the defibrillation pads while delivering shocks for those patients who failed multiple shocks (28, 29). This maneuver is actually similar to the shocking in downstroke of manual CC (phase A) in this study. In our study, we noticed a trend of defibrillation efficacy, which was a slight improvement in phase A compared with the control phase. However, it did not reach the statistical significance (51% vs. 44%, $p = .14$). This finding was consistent with the results reported previously by Cohen at al (30). In their study, the transthoracic impedance was significantly reduced by compressing two defibrillation pads. They related this improved cardioversion success to the increased cardioversion current as a result of reduced impedance. In contrast to their findings, our data showed a 10% increase in the transthoracic impedance measured between the two shock pads in the downstroke phase (Table 2). We suspected that the active compression with movement during the downstroke phase was not *a priori* identical to the effects of continuous constant applied pressure on the chest. In our study, there was no direct compression pressure applied on the defibrillation pads because the pads were placed in the lateral-to-lateral position. However, compression pressure resulted in a distortion of normal heart geometry so that in the pad-to-pad direction, the projected area of the heart was reduced while the heart length was increased. Both changes in the heart geometry resulted in an increase in transthoracic impedance measured by the defibrillation pads. Despite the differences in the transthoracic impedance, both studies have shown a moderate improvement in defibrillation efficacy if the shock was delivered in the downstroke of manual CC compared with the conventional hands-off defibrillation.

The most profound finding in this study was that the defibrillation efficacy was maximal when a shock was delivered during the upstroke phase in the CC cycles compared with the downstroke phase as well as hands-off defibrillation. The defibrillation success rate was increased by 21% when shock was delivered in the upstroke compared with the control phase and increased by 14% compared with the downstroke phase. This may help with the future design of defibrillators, which will be capable of delivering synchronized shocks during the upstroke of CC. Although the combined upstroke phase has a different sample size compared with control and other phases, the statistical method of the two-sample Student's *t* test and chi-square test in this

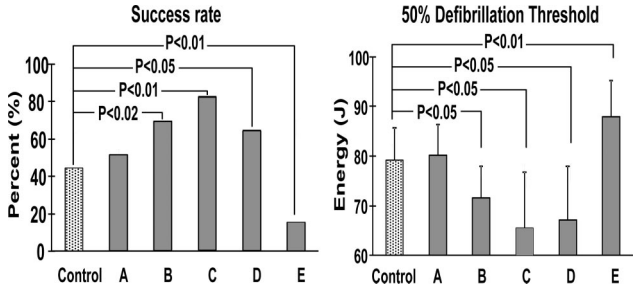

Figure 2. The primary experimental results based on various intervals of defibrillation during uninterrupted compression. (*A*) downstroke; (*B*) early upstroke; (*C*) middle of upstroke; (*D*) late upstroke; and (*E*) precompression (immediately before downstroke). The 50% defibrillation thresholds were represented with mean ± SD.

Table 3. Experiment results based on pooled data in upstroke phases

Parameters	Control	Experimental Phases		
		Downstroke (Phase A)	Upstroke (Phases B + C + D)	Precompression (Phase E)
Number of shocks	39	39	108	39
CPP, mm Hg	31.8 ± 13.7 (27.4–36.2)	29.8 ± 11.7 (26.0–33.6)	31.7 ± 14.0 (29.0–34.4)	31.4 ± 13.5 (27.0–35.8)
Voltage, V	566 ± 78 (541–591)	592 ± 84 (565–619)	595 ± 81 (580–610)	575 ± 83 (548–602)
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Success rate, %	44	51	65[a]	15[a]
50% DFT, J	79.1 ± 6.7 (73.5–84.7)	80.3 ± 6.2 (75.1–85.5)	68.1 ± 10.2[a](59.6–76.6)	88.0 ± 7.3[b] (81.9–94.1)

CPP, coronary perfusion pressure; DFT, defibrillation threshold.
[a]Compared with control, $p < .01$; [b]compared with control, $p < .05$.

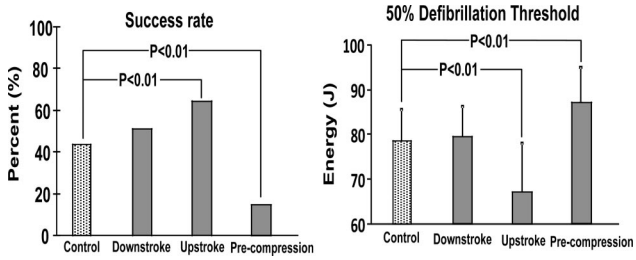

Figure 3. The combined experimental results based on three different phases: the downstroke phase, the upstroke phase, and the precompression phase that is immediately before the downstroke. The 50% defibrillation thresholds were represented with mean ± SD.

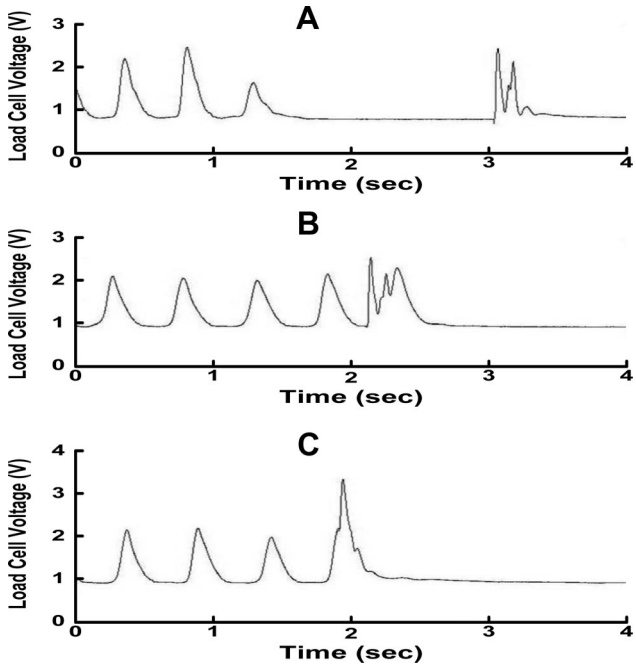

Figure 4. The recordings of the load cell voltage. (*A*) Recordings in the control. (*B*) Recordings in the upstroke phase. (*C*) Recordings in the downstroke phase.

study did not necessarily request an equal sample size for each group.

The study also identified a worst phase for defibrillation during the uninterrupted manual CC compared with the control phase (15% vs. 44%, $p = .005$). The worst phase was denoted as phase E in Figure 1, located immediately before the onset of compression. We suspect that the immediate compression force (in the range of 20–40 msec) following the shocks delivered interfered with the normal defibrillation process and resulted in low defibrillation success.

The mechanisms by which probability of shock success was improved by timing the shock in the upstroke of CC are still unclear. Based on an earlier study by Noc et al (31), that CPP was a highly predictive indicator of the likelihood of successful defibrillation, the outcome of defibrillation in each phase should be equivalent because the same energy level of electrical shocks was applied. We suspect that the difference in defibrillation success in different coupling phases may have resulted from geometric and physical changes of the heart during CC. It is perceptible that during early upstroke, heart chambers remain in reduced volumes, which are approximately equal to the volumes at the end of downstroke. Small heart volume reduces the shunting effect and energy requirement for defibrillation. A previous study has demonstrated that the compression pressure produced by CC empties blood from the heart chambers or air from the lungs, which might change the defibrillation energy and current requirement (28). The decrease in blood volume during compression, thus reducing the cardiac preload and cardiac size, may result in a significantly lowered defibrillation energy requirement (32). Furthermore, without external force in early upstroke, cardiac muscle strain decreases. This also favors reduced energy requirements for defibrillation (33–38).

There are several limitations in our study. First, we have identified a significant reduction in the defibrillation energy requirement in the upstroke of manual CC. However, the mechanisms underlying this finding are still not clear. Further studies such as computer simulations based on a chest–torso volume conductor model and three-dimensional optical mapping experiments may reveal more mechanistically detailed information. Second, we did not study the effect of different defibrillator pad placements on the defibrillation efficacy. We used only lateral-to-lateral pad placement. The findings in this study may not be extrapolated into other pad placements. Third, this study used a 10-sec ventricular fibrillation animal model followed by 25 secs of CPR before defibrillation. Both the ventricular fibrillation and CPR duration were substantially shorter than the time to first shock for most patients with cardiac arrest. Fourth, the grouped up–down defibrillation threshold protocol used in this study, more or less, did not adhere to the classic work that was developed by McDaniel and Schuder (24). Also, the aggregated defibrillation threshold differed from the individual threshold in terms of probability of defibrillation success. In addition, the anesthetized animals were young, healthy, free from underlying disease, and without any pharmacologic interventions. Therefore, the results of the present study may not be easily translated into clinical sudden cardiac arrest in an in- or out-of-hospital setting.

CONCLUSIONS

Defibrillation efficacy is maximal when electrical shock is delivered during the upstroke phase of manual chest compression. However, shocks should be avoided during the precompression phase, which is immediately before the start of the next compression cycle.

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