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Original Article

Effect of high-energy defibrillation on success rate of defibrillation and cardiac trauma in ventricular fibrillation pig model

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Abstract: This study aimed to explore effect of increased two-phase wave energy defibrillation on success rate of defibrillation and cardiac trauma based on current recommend energy using ventricular fibrillation pig model built by electrical stimulation in right ventricle. Twenty-four pigs were randomly divided recommend energy group (200 J), high-energy group (300 J) and ultra-high energy group (360 J). Total and the first defibrillation success rate, rate of return of spontaneous circulation (ROSC) and the time of spontaneous circulation restoration were recorded. Left ventricular ejection fractions (LVEF) were examined before induced fibrillation, at 0 h and 24 h after ROSC, and change of serum BNP and serum markers were detected at 0 h, 2 h and 6 h after ROSC, respectively. Change of brain and neurological function, and pathomorphological changes of myocardial cells were observed under light microscope and electron microscope at 24 h after ROSC. Total defibrillation success rate in the ultra-high energy group was higher than the recommend energy group ($P<0.05$), but no significant difference was detected when other pairwise comparisons ($P>0.05$). LVEF was similar in each group at different time points ($P>0.05$), and no significant difference of serum BNP was detected between different groups at different time points ($P>0.05$). Myohemoglobin, troponin I and CK-MB had not significant difference between the three groups ($P>0.05$), while heart-type fatty acid binding protein was higher in the ultra-high energy group at 2 h and 6 h ($P<0.05$). Myocardial cells in each group were detected pathological changes under light microscope and electron microscope, but no significant difference was detected between groups. Mild damage in cerebral function was detected in the three groups, and no significant difference was detected pairwise comparison. The total success rate was higher using 360 J, and heart-type fatty acid binding protein was higher than the other groups. These findings implicate that ultra-high energy may have certain advantages, which may provide valuable reference for determining the optimal defibrillation energy.

Keywords: High-energy defibrillation, ventricular fibrillation pig model, cardiac trauma, success rate of defibrillation

Introduction

Sudden Cardiac Arrest (SCA) is a condition in which the function of effective ejection in heart suddenly stops, which further leads to serious ischemia and oxygen deficiency in some important tissues and organs (such as heart and brain). Patient may lose a life if the patient is not timely treated. In China, about 500,000 patients die of cardiac arrest every year [1] and 80% of them have ventricular tachycardia and ventricular fibrillation (VF) in electrocardiogram, which is the main cause of death of 63% cardiac patients. A series of literatures indicate that thoracic electric defibrillation is the most effective method to terminate VF when patient appears VF [2-8]. Timely and effective electric defibrillation can obtain better effect, and further protect cardiac contractive function, reduce recurrence of VF and generation of cardiac failure and myocardial ischemia, which contributes to improve prognosis and survival rate of patient.

However, it is still controversial what is the optimal electrical defibrillation energy. Although the 2010 edition of cardiopulmonary resuscitation (CPR) guidelines by American Heart Association

(AHA) recommends that the electrical defibrillation energy is 120-200 J, and the energy can be gradually improved if first defibrillation is not success [9]. The recommend energy is mainly derived from specialist, and no high quality evidence-based supports. In clinic, the most recommended energy (200 J) can not one time terminate defibrillation, but no relevant report indicate whether improved energy can improve success rate of defibrillation. Simultaneously, it is also controversial whether high energy can cause cardiac trauma. Some reports indicated that improved energy may increase damage of heart because of more current conveyance, so patient is difficult to recovery [10-17]. However, another literature showed that current used range of high energy is secure, and no significant difference of damage in heart is found between high energy and recommend energy [3].

This study aimed to explore effects of enhanced energy on success rate of defibrillation and cardiac trauma according to current recommended energy by establishing pig model of VF, which would provide reference for selecting the clinical optimal energy.

Methods

Animals

Twenty-four healthy adult male pigs (16-18 weeks, weight: 30±5 kg) were obtained from farms of experimental animals in Sichuan province. These animals were used to perform experiment after 3 days in our laboratory, and they were fasted 12 h pre-operation with freedom drinking water. They were randomly divided into three groups: the recommend energy group (200 J, 9), the high-energy group (300 J, 8) and the ultra-high energy group (360 J, 7).

Pig model of VF and sampling

Pigs were intravenously injected 5% ketamine (2 mg/kg), and disposable 7.5 trachea cannula with guide wire was fed into. Anesthesia respirator was connected, electrode slice was placed, and these could ensure effective conduction of defibrillating current. Heart rates of pigs were monitored by adjusting monitor, and the artery puncture was performed on the left side of femoral. Blood pressure transducer and heart were adjusted to the same level and zero calibration, which was used to continuously monitor arterial blood pressure. Bipolar pacemaker electrode wires were implanted to induce VF. After VF was maintained 5 min, closed cardiac massage was performed, and breathing machine was simultaneously connected. After 2 min of closed cardiac massage, electric defibrillation was performed, and recovery of return of spontaneous circulation (ROSC) was estimated by 2 min of closed cardiac massage. Cardiac compression was stopped if recovery.

Once ROSC was found, apex tudor cavity section was obtained using Sonoma-100 portable pa/device to detect ejection fraction value in left ventricular at different time points: basic status, 0 h, 24 h after ROSC. Blood samples were collected and stored at different time points, and cerebral performance category (CPC) was scored after 24 h. Ventricular myocardial tissues in the left ventricular apex and close to valvula bicuspidalis of left atrium were collected, and these tissues were rapidly put into 10% formaldehyde fixed fluid to fix 2 d that were used to perform examination of light microscope. Cardiac muscle tissues in the left ventricular apex were put into 4% lutaraldehyde to fix 4 h, and then they were stored at 4°C to perform examination of electron microscope.

Evaluation criteria of evaluation indexes

The criterion of success of defibrillation: VF was stopped at least 5 s after electric shock [8]. ROSC criterion: carotid pulsation or the average arterial pressure was larger than 50 mmHg and maintain at least 5 min [18]. The recovery time of ROSC was from chest compression to recovery time, and evaluation criterion of CPC was 5 grades in the published literature [19].

Examination of pathological and serum indexes

Histopathological examinations of collected atrial myocardial tissues were detected using light microscope and electric microscope. Serum indexes, including Cardiac troponin I (cTnI), Myoglobin (Mb), Creatine kinase-MB (CK-MB), Brain natriuretic peptide (BNP), Heart fatty acid-binding protein (hFABP), were detected at different time points using detection kits.

Statistical analysis

Measurement data with normal distribution were described using mean ± standard devia-

Table 1. Comparison of basic complications in different groups (M ± SD)

Basic complications	Recommend energy group	High-energy group	Ultra-high energy group	*F* value	*P* value
Weight (kg)	31.2±2.6	39.0±13.7	29.2±4.9	1.83	0.20
Basic heart rate (times/min)	92.8±28.2	96.2±21.8	87.6±16.7	0.18	0.84
Mean arterial pressure (mmHg)	91.6±24.0	86.6±21.3	76.0±15.4	0.73	0.50
$ETCO_2$ (mmHg)	36.0±6.6	34.8±9.2	38.0±2.2	0.29	0.75
LVEF (%)	50.8±8.8	58.6±18.3	49.2±7.2	0.82	0.47

Note: *P*<0.05 indicates statistical difference.

Table 2. Comparison of the first success rate of defibrillation between groups (times)

Groups	Number of success times (%)	Number of failure times (%)	Total times	*P* value
Recommend energy group	5 (55.6%)	4 (44.4%)	9	
High-energy group	5 (62.5%)	3 (37.5%)	8	0.651
Ultra-high energy group	3 (42.9%)	4 (57.1%)	7	

Note: *P*<0.05 indicates statistical difference.

Table 3. The recovery rate of ROSC (counts of pigs)

Groups	Number of recovery of ROSC (%)	Number of unrecovered of ROSC (%)	Total	*P* value
Recommend energy group	5 (55.6%)	4 (44.4%)	9	
High-energy group	5 (62.5%)	3 (37.5%)	8	0.807
Ultra-high energy group	5 (71.4%)	2 (38.6%)	7	

Note: *P*<0.05 indicates statistical difference.

tion ($\bar{x}$±s), measurement data with abnormal distribution were described using median ± range interquartile, and enumeration data were described using counts and percentage. One-way analysis of variance (ANOVA) analysis or repeated measures analysis of variance was analyzed if measurement data were normal distributed and homogeneity of variance, or else rank sum test was used to estimate the difference among groups. Enumeration data were analyzed using χ^2 test or Fisher's exact test. Differences were considered significant when $P<0.05$, and all statistical analyses were performed using SPSS 21.0 software.

Results

Effect of different energies on success of defibrillation

Pigs in each group were homogeneous, and no significant differences of indexes, including weights, heart rates, average aterial blood pressures, $ETCO_2$ and LVEF were detected ($P>0.05$, **Table 1**).

No significant difference of $ETCO_2$ values was detected among groups at different time points ($F=0.83$, $P=0.52>0.05$), and pairwise comparison did not show significant different ($P>0.05$). Although the ultra-high energy group used less epinephrine, no significant difference was detected among groups ($F=0.295$, $P=0.747>0.05$), and pairwise comparison showed similar results ($P>0.05$).

For comparison of total success rate of defibrillation, the three groups had no statistical difference ($\chi^2=4.261$, $P=0.119>0.05$), but the ultra-high energy group was obviously improved than the recommend energy group ($P=0.040<0.05$), although no significant difference was detected between the other pairwise comparisons ($P>0.05$). The first success rate did not show significant different among the three groups ($P=0.651>0.05$) and between pairwise groups ($P>0.05$, **Table 2**).

The time of ROSC was similar among the three groups ($F=0.867$, $P=0.445>0.05$), and further pairwise comparison did not show statistical difference ($P>0.05$). No significant difference of recovery rate of ROSC was detected among the three groups ($P=0.087>0.05$) and between pairwise groups ($P>0.05$, **Table 3**).

Effect of different energies on CPC at 24 h after ROSC

Comparison of CPC at 24 h after ROSC did not show statistical difference among groups ($\chi^2=0.120$, $P=0.942>0.05$). Similarly, no significant difference was detected between pairwise

Table 4. Comparison of CPC at 24 h after ROSC among groups

Groups	24 h CPC after ROSC					χ^2 value	*P* value
	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5		
Recommend energy group	2	1	2	0	0	0.120	0.942
High-energy group	2	1	1	1	0		
Ultra-high energy group	3	0	1	1	0		

Note: *P*<0.05 indicates statistical difference.

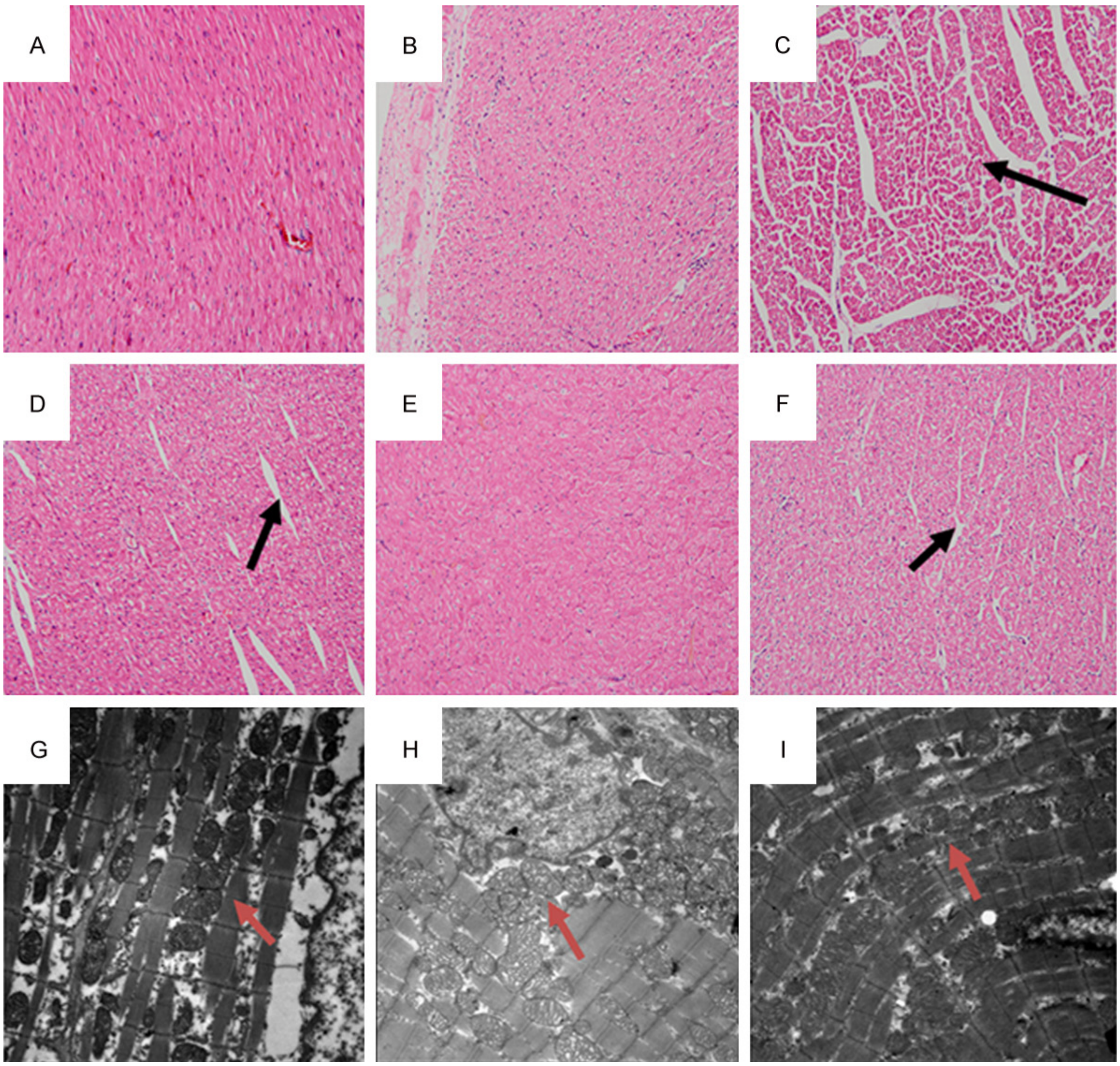

Figure 1. Pathological changes of sliced atrial tissues under light microscope (A-C, HE staining, 200×), ventricular tissues under light microscope (E, F, HE staining, 200×), and electro microscopic (G-I, 1500×). (A, D, G) The recommend energy group; (B, E, H) the high-energy group; (C, F, I) the ultra-high energy group.

groups: the recommend and high-energy groups (Z=-1.225, *P*=0.221>0.05), the recommend and ultra-high energy groups (Z=-0.775, *P*=0.439>0.05), and the high and ultra-high energy groups (Z=-1.247, *P*=0.212>0.05) (**Table 4**).

Effect of different energies on cardiac trauma

No significant difference was detected in heart gross anatomy between different groups at 24 h after ROSC. The recommend energy group showed that myocardial cells were neat

Table 5. Comparisons of serum Mb value (μg/L) and hFABP value (pg/mL) at different time points

Indicators	Monitor time	Recommend energy group	High-energy group	Ultra-high energy group	*P* value
Serum Mb	Basic status before induced quiver	295.9±65.2	369.5±93.4	427.0±181.94	0.283
	1 h after ROSC	448.7±156.2	809.6±435.0	1076.3±678.0	0.343
	2 h after ROSC	608.8±502.5	669.1±320.5	1041.0±714.2	0.765
	6 h after ROSC	322.2±133.3	606.2±251.0	1059.0±689.7	0.343
Serum hFABP	Basic status before induced quiver	5.7±0.8	7.3±2.7	8.3±5.2	0.491
	1 h after ROSC	22.6±15.0	35.9±30.0	87.9±60.5	0.074
	2 h after ROSC	8.6±3.3*	13.0±9.8*	61.0±53.8	0.041
	6 h after ROSC	12.7±12.1*	11.3±5.5*	72.7±61.7	0.032

Note: *P*<0.05 indicates statistical difference. *: compared with high energy group, change of serum fatty acid binding protein has statistical difference.

Table 6. Comparisons of serum cTnI value (μg/L) and creatine kinase-MB value (IU/L) at different time points

Indicators	Monitor time	Recommend energy group	High-energy group	Ultra-high energy group	*P* value
Serum cTnI	Basic status before induced quiver	0.045±0.041	0.038±0.032	0.018±0.004	0.680
	4 h after ROS	1.560±0.000	5.245±4.779	13.857±12.924	0.108
	6 h after ROS	3.883±3.061	3.710±3.257	14.484±12.390	0.772
	24 h after ROS	1.560±0.000	2.536±2.429	4.662±3.721	0.590
Serum creatine kinase-MB	Basic status before induced quiver	380.4±57.3	397.6±60.1	348.8±42.7	0.379
	4 h after ROS	558.6±145.0	349.6±102.5	500.8±108.0	0.055
	6 h after ROS	527.8±130.2	496.8±177.3	577.4±269.6	0.818
	24 h after ROS	388.2±24.6	375.6±100.9	506.2±127.1	0.156

Note: *P*<0.05 indicates statistical difference.

arrangement, nucleus were normal, and no inflammatory cell infiltration was detected. The high-energy group showed that myocardial cells were neat arrangement, nucleus were normal, but a few inflammatory cells were effused. Compared with the two groups, we found that myocardial cells in the ultra-high energy group were slight swollen, some myocardial fibers were dissolved fracture, interval broadened, small part of blood capillary expanded with inflammatory cell infiltration (**Figure 1C**). Results of left ventricular myocardium under light microscope in each group indicated that no significant damage was found in inner and outer membrane of left ventricle. The recommend energy group showed that part of myocardial fibers interval broadened (**Figure 1D**), the high-energy group detected a few inflammatory cells were effused without angiotelectasis (**Figure 1E**), and the ultra-high energy group showed slight swollen in myocardial cells, part of broadened myocardial fibers interval, a few angiotelectasis, and around with inflammatory cell infiltration (**Figure 1F**).

In the recommend energy group, Z line of myocardial cells was neat, some myofibril fractured and shortened, mitochondria cristae was complete (**Figure 1G**). The high-energy group indicated clear Z line, but muscle between tow mitochondria increased, arrangement was disorder, cristae was slightly damaged with some cavity formation (**Figure 1H**). In the ultra-energy group, light and shades of Z line were clear, muscle wire arrangement was neat, but mitochondria was obviously increased with malalignment and increased volume, some cristae fractured and dissolved (**Figure 1I**).

For comparison of LVEF at different times, different groups did not show statistical difference (F=0.673, P=0.556>0.05), and pairwise comparison also did not show significant difference (P>0.05). Serum BNP values and Mb values had not statistical difference among the three groups (F=1.516, P=0.259>0.05) and pairwise groups (P>0.05) (**Table 5**).

Serum hFABP rose to the highest after ROSC, but the hFABP values were different among the three groups (F=4.475, P=0.035<0.05). Specifically, statistical difference was detected between the recommend and ultra-high energy groups (F=5.391, P=0.019<0.05), the high and ultra-high energy groups (F=4.475, P=0.031<0.05), but no significant difference was detected between the recommend and high-energy groups (P>0.05) (**Table 5**).

Serum cTnI and CK-MB did not show significant difference among groups (F=1.691, P=0.225>0.05) and pairwise groups (P>0.05) (**Table 6**). Creatine kinase-MB in the three groups rose to the highest value at 4 h and 6 h after ROSC, and gradually reduced at 24 h (**Table 6**).

Discussion

Although the first success rate of defibrillation has not significant different among groups, the high-energy has higher total success rate than low energy. Similar to Stiell et al. [4], compared with gradually improved energy, no significant difference is detected in the first success rate of defibrillation in the stable low energy. However, in the total success rate of defibrillation, gradually improved energy has obvious advantage. In clinic, we found that increased energy can contribute to improve success rate, and the main reason may be stronger electric current generated by high energy [20]. The current may preferably terminate cardiac entricular fibrillation, then cardiac generates effective shrink and recover effective function of cardiac pumping, so can achieve the aim of defibrillation.

ROSC is correlated with the quality of chest compressions, the duration of cardiac arrest and time and energy of defibrillation [21]. Herein, except for energy of defibrillation, other factors are consistent, and the energy is the main factor that influences ROSC. Time and recovery rate of ROSC have not significant difference between groups, which indicates that increased energy (360 J) can not increase recovery rate of ROSC based on the recommend energy. Therefore, the optimal energy should be further determined through more clinical studies. Different energies have not different effects on cerebral function of recovery of pigs through evaluation of functional classification at 24 h after ROSC. Animals indicate damaged functional classification than before experiment, which is consistent with irreversible damage caused by the brain ischemia hypoxia more than 3 min [22]. Therefore, it is important that quality of cardiopulmonary resuscitation should be improved, time of ROSC should be shortened, and irreversible damage should be reduced. Moreover, although LVEF is reduced in each group at 0 h after ROSC, no significant difference is detected between groups. LVEF cannot recover the basic complications at 24 h, but it is improved than the value at 0 h. The phenomenon shows myocardial stunning. The study implicates that the selected energy has not significant effect on LVEF in successful resuscitation animals with VF.

Similar to recent studies [23-25], the recommend energy group is detected broadened interval of myocardial fibers, breakage and shortened fibers, chaos arrangement of mitochondria. The ultra-high energy group shows that swollen myocardial cell, increased mitochondria, chaos arrangement, increased volume, and some cristae fractured and dissolved (**Figure 1**). These results show that electric defibrillation may lead to damage in myocardial, but different energies have not significant difference. Caterine et al. [26] and Trouton et al. [27] believed that the damage in myocardial is caused by malfunction of mitochondria and free radical, and Maixent et al. [28] found that Na^+-K^+-ATP enzymatic activity reduces to 50% caused by electric defibrillation. At present, the mechanism of damage may be associated with mitochondria damage, oxygen radical and cell membrane potential. After damage in myocardial, application of multiple indicators can improve sensitivity and specificity of diagnose [29]. In the study, we found that serum cardiac markers are increased than the basic complications, which may be associated with myocardial injury caused by ischemia-reperfusion. Moreover, hFABP in the ultra-high group is higher than other groups at 1 h after ROSC, indicating the ultra-high energy can lead to more serious myocardial damage. In the study, healthy animals are used to perform the experiment, but patients always have basic heart disease and other complications in clinic. Whether patients with pathological changes of myocardial can suffer from basic disease and higher energy, which should be further studied and validated in future.

Individual difference in animals and collection of blood specimen may lead to biased result, cardiac output is not detected in heart function monitoring, and it is difficult to ensure consistent compressions. Despite of these limitations, the study proves that the total success rate of 360 J is higher than 200 J, and different energies can increase serum cardiac markers. These findings may provide reference for determining the optimal defibrillation energy.

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Disclosure of conflicts of interest

None.

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