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The effects of cardiopulmonary resuscitation under the diaphragmatic muscle on post-resuscitation hemodynamics after cardiac arrest in rabbit models.

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Abstract

The aim of this study was to compare standard cardiopulmonary resuscitation (S-CPR) and diaphragmatic muscle cardiopulmonary resuscitation (D-CPR) for cardiac arrest (CA) in rabbit models. Twenty rabbits were randomized into either the S-CPR group or the D-CPR group. CA lasting 8 min was induced in healthy New Zealand rabbits through abdominal operation and tracheal tube clamping. During end-expiration 5 min after vital signs stabilized, the aortic pressure and transcutaneous oxygen saturation levels were recorded, and restoration of spontaneous circulation (ROSC) and the 6-h survival rate were analyzed. Five rabbits in the S-CPR group and eight in the D-CPR group achieved ROSC; the survival rate in the S-CPR group and the D-CPR group was 40% and 50%, respectively. Blood pressure indices in each group were higher post-ROSC than at baseline. One minute after resuscitation, the blood pressure values in the D-CPR group were higher than those in the S-CPR group (aortic systolic pressure=54.9 ± 10.1 mmHg versus 42.1 ± 16.2 mmHg, respectively; aortic diastolic pressure=22.1 ± 7.4 mmHg versus 15.1 ± 7.3 mmHg, respectively; mean arterial pressure=33.0 ± 5.8 mmHg versus 21.4 ± 8.5 mmHg, respectively; and coronary perfusion pressure=17.5 ± 7.5 mmHg versus 9.2 ± 6.6 mmHg, respectively). Five minutes after resuscitation, blood pressure values in the D-CPR group remained statistically higher than those in the S-CPR group. However, no differences between the two groups existed after 5 min. When compared to S-CPR, D-CPR resulted in a higher ROSC rate and a higher survival rate in rabbit models; however, the results depend on higher atrial pressure and cardiac output.

Keywords: Cardio-pulmonary resuscitation, Diaphragm, Cardiac compression, Rabbit, Hemodynamics, Survival rate.

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Introduction

Cardiac arrest is a major cause of morbidity and mortality worldwide [1], and patients who survive cardiac arrest often develop severe neurological dysfunction due to hypoxic brain injury and reperfusion-induced cell death [2]. Cardiopulmonary resuscitation (CPR) remains the most commonly used resuscitation method for cardiac arrest (CA) [3], and it has been one of the most important determinants of patient survival. However, the quality of CPR, which is related to the depth and frequency of chest compressions [4], always determines the prognosis of CA [5]. On the other hand, standard CPR (S-CPR) can cause many complications including thoracic rib fractures and gastric rupture [6-12]. In addition, although open chest cardiac compression is thought to achieve better outcomes [13], it can also cause major damage and serious postoperative complications. Additionally, when CA happens during special situations such as open operation, S-CPR disable to act as a thorax pump and fails to ensure the blood supply to major organs because the abdominal cavity is open. Furthermore, the clinical success rate of resuscitation is low (about 10%) and the survival status of patients after resuscitation is not satisfying [14,15]. Therefore, although researchers worldwide have investigated several methods to improve clinical outcomes, they have seen little success [16,17]. Thus, our study aimed to provide theoretical evidence for the clinical applications of diaphragmatic muscle CPR (D-CPR) by comparing the effects of D-CPR and S-CPR on the circulatory function of rabbits before and after resuscitation.

Materials and Methods

Animal preparation

Twenty New Zealand rabbits weighing between 2.0 kg and 3.5 kg (irrespective of the sex) were provided by the animal experimental center of the General Hospital of the People's Liberation Army. The rabbits were randomly assigned into the D-CPR group (n=10) or the S-CPR group (n=10). Ketamine and sumianxin were used to induce anesthesia, the neck trachea was intubated, and the rabbits were connected to a ventilator. A multifunctional physiological monitor was connected to the left carotid artery and the right jugular vein to monitor ascending aortic pressure and right atrial pressure. The electrocardiogram (ECG) results and transcutaneous oxygen saturation (SpO_2) levels were monitored during the operation. The ear vein was intubated for transfusion and drug administration. The trachea was clipped at the end of an exhalation to initiate asphyxia. CA was considered successful if the ECG displayed obvious ventricular fibrillation waveforms or a flatline accompanied by a mean arterial pressure (MAP) less than 15 mmHg (1 mmHg=0.133 kPa) and the disappearance of arterial pressure differences or if the monitor displayed an arterial line waveform. We conducted D-CPR or S-CPR exactly 8 min after asphyxia with a massage frequency of 180-200 per min. We simultaneously used a ventilator to assist respiration (frequency: 40 per min, tidal volume: 20 ml/kg, concentration of inspired oxygen: 100%). After 2 min of massage, resuscitation drugs (adrenaline: 0.1 mg/kg, atropine: 0.05 mg/kg) were administered. After 5 min of massage, electric defibrillation was used if there was a ventricular fibrillation waveform on the monitor.

The ventilation mode, respiratory parameters, abdominal incision procedures, and salvage drugs were the same for both cardiac compression methods. For the S-CPR group, the compression depth is that resulting in the thoracic sagged to 1/3-1/2 of its thickness. For the D-CPR group, three or four fingers were inserted into the diaphragm below the heart (the finger pulp was used to place sterile gauze to prevent the fingertips from tearing the diaphragm because of uneven force), and the heart was crimped to the chest wall with a range of 2-3 cm. ROSC was successful when the ECG monitor indicated that the superventricular rhythm was recovered and the MAP was greater than 25 mmHg for more than 1 min.

Hemodynamic determination and treatment

After preparation of the animal models, the rabbits breathed ambient air for 5 min without any operation. After the hemodynamics stabilized, the aortic systolic pressure (AOS), aortic diastolic pressure (AOD), right atrial systolic pressure (RASP), right atrial diastolic pressure (RADP), respiratory rate (RR), heart rate (HR), and SpO_2 values were recorded. After asphyxia began, the ascending aortic pressure, right atrial pressure (RAP), ECG results, and SpO_2 levels were recorded until the animal achieved ROSC or the experiment was terminated (i.e., if the circulation did not recover after 30 min of massage). The MAP and central venous pressure (CVP, approximately equal to the mean RAP) were calculated. The formulas are as follows: coronary perfusion pressure (CPP)=AOD-RADP; RAP=1/3 × RASP+2/3 × RADP; and MAP=AOD+1/3 × AOS.

Statistical analysis

The statistical software used in this study was SPSS 15.0. The results are displayed using the mean ± standard deviation ($\bar{x} \pm s$). A t-test was adopted for comparisons among groups, a repeated-measures ANOVA was used for comparing data that changed over time, and a chi-square test (exact probability method) was adopted for categorical data. A $P<0.05$ was considered statistically significant.

Results

Comparison of the baselines values between the two groups

The baseline values (before CA) for weight, AOS, AOD, MAP, CVP, CPP, HR, RR, and SpO_2 were compared between the D-CPR group and S-CPR group. No significant differences between the two groups were found ($P>0.05$ for all values), indicating that the two groups were comparable (Table 1).

Table 1. *The basic value before CA ($\bar{x} \pm s$).*

Group	S-CPR	D-CPR	P-value
Number of animals	10	10	-
Weight (kg)	2.9 ± 0.3	2.6 ± 0.4	0.107
AOS (mmHg)	77.7 ± 10.9	75.0 ± 4.2	0.479
AOD (mmHg)	57.3 ± 11.4	54.0 ± 5.0	0.412
MAP (mmHg)	64.6 ± 10.3	60.0 ± 6.5	0.294
CVP (mmHg)	3.7 ± 3.1	2.6 ± 2.2	0.393
CPP (mmHg)	55.7 ± 10.8	52.4 ± 6.1	0.41
HR (times/min)	173 ± 21	171 ± 14	0.833
RR (times/min)	34 ± 7	35 ± 5	0.831
SpO_2 (%)	97 ± 1.3	96 ± 0.6	0.104

Comparison of ROSC between the two groups

Five rabbits in the S-CPR group and 8 rabbits in the D-CPR group achieved ROSC in 5-10 min, but this difference was not statistically significant ($P>0.05$). One rabbit in the D-CPR group received ventricular fibrillation and achieved ROSC after defibrillation twice; however, resuscitation lasted only 12 min while the survival time for the other rabbits who achieved ROSC was longer than 0.5 h (Table 2).

Table 2. *The distribution of survival time of animals from D-CPR group and S-CPR group.*

Group	Number of animals	Dead (number)	Survive(%(number))	ROSC rate (%)

			≤ 0.5h	≤ 2.0h	≤ 6.0h	
S-CPR	10	5	0 (0)	10 (1)	40 (4)	50
D-CPR	10	2	10 (1)	20 (2)	50 (5)	80

Change in hemodynamics 15 min after resuscitation

The differences in the frequency of massage and CVP between the two groups at 1 min and 5 min after resuscitation were not statistically significant (Table 3). However, the AOS, AOD, MAP, and CPP values for the D-CPR group were statistically significantly higher than those of the S-CPR group. The MAP and CPP values for the two groups after resuscitation increased significantly until the peak value was reached at 5 min, after which, they decreased gradually (Figure 1). At 1 min and 5 min after resuscitation, the MAP and CPP values for the D-CPR group were significantly higher than those of the S-CPR group ($P<0.05$). However, by 10 and 15 min after resuscitation, the differences between the two groups were no longer statistically significant. Within groups, the AOS, AOD, MAP, and CPP values after CA were significantly lower than the baseline values (Table 4).

Table 3. *Comparison of the change of hemodynamic in 15 min after resuscitation between two groups (xs).*

Time after frequency of resuscitation	Group	Animals	Massage (/min)	AOS (mmHg)	AOD (mmHg)	MAP (mmHg)	CVP (mmHg)	CPP (mmHg)
1 min	S-CPR	10	188 ± 8	42.1 ± 16.2	15.1 ± 7.3	21.4 ± 8.5	16.3 ± 8.5	9.2 ± 6.6
	D-CPR	10	188 ± 7	54.9 ± 10.1*	22.1 ± 7.4*	33.0 ± 5.8*	13.7 ± 3.1	17.5 ± 7.5*
5 min	S-CPR	10	195 ± 17	42.6 ± 10.7	16.1 ± 9.7	24.9 ± 8.4	17.9 ± 5.8	9.5 ± 8.2
	D-CPR	10	186 ± 7	57.0 ± 10.0*	25.5 ± 9.1*	36.0 ± 8.7*	13.6 ± 4.1	21.9 ± 9.7*

Note: Compare with the S-CPR group, *P<0.05

Table 4. *The ratio of measures and their basic values at different times.*

Time after resuscitation	Group	Animals	AOS	AOS	AOD	CPP
1 min	S-CPR	10	52.9%	26.4%	37.3%	16.5%
	D-CPR	10	73.2%	40.9%	54.1%	33.4%
5 min	S-CPR	10	55.3%	28.1%	38.5%	17.1%
	D-CPR	10	76.0%	47.2%	60.0%	41.8%

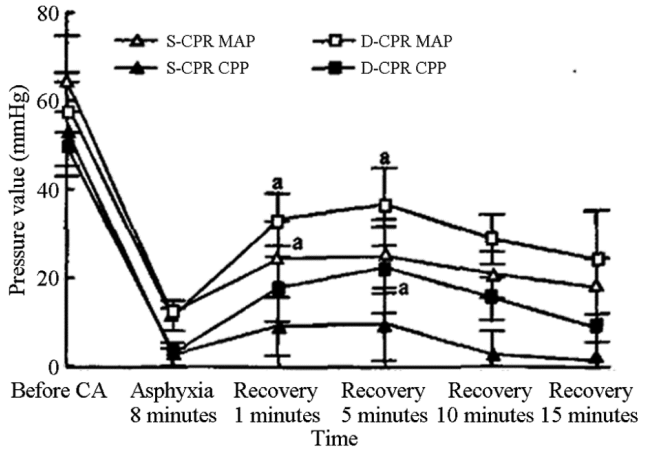

Figure 1. *Hemodynamic changes of animals resuscitated for 15 min in two groups.*

The MAP and CPP values for the S-CPR group were significantly higher than those of the D-CPR group immediately after ROSC; however, these values gradually decreased and became similar to those of the D-CPR group after ROSC (Figure 2). For the D-CPR group, the changes in the MAP and CPP values were steady beginning 5 min post-ROSC and the amount of dopamine used was very small during both the monitoring and maintenance phases.

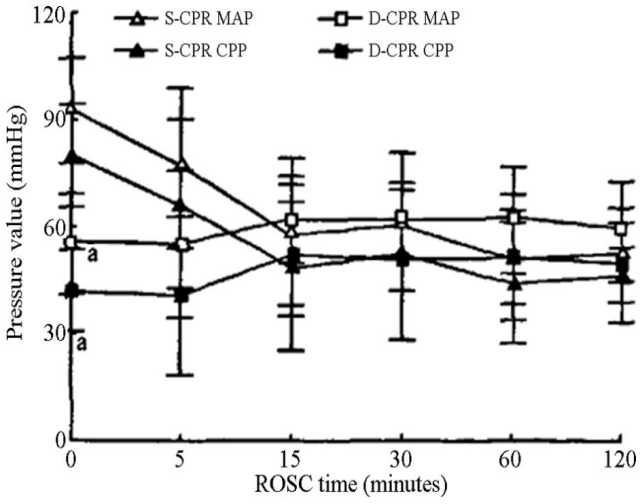

Figure 2. *Hemodynamic changes in two groups after ROSC.*

Complications

Autopsy reports showed that one rabbit in the S-CPR group had pulmonary edema and two had multiple fractured ribs, one of which also had hepatic rupture. One rabbit in the D-CPR group had a diaphragmatic tear at the point of diaphragmatic compression because of the pressure applied directly to the diaphragm by the fingers; however, this situation did not occur after applying gauze at the compression point on the diaphragm.

Discussion

Analysis of the change in hemodynamics

S-CPR is always used for CPR after clinical CA both domestically and abroad. However, experimental studies and clinical practice reveal that hemoperfusion for important organs is not very good for some patients and the success rate of resuscitation is below 30% [18], which might be related to the low perfusion pressure and low blood flow during the period of resuscitation [19-21].

This study revealed that the AOS, AOD, MAP, and CPP values of the D-CPR group were significantly higher than those of the S-CPR group 1 min and 5 min after resuscitation. However, the MAP and CPP values were not significantly different between the two groups 10 min and 15 min after resuscitation. This indicates that D-CPR may result in better hemodynamic effects during the early period of resuscitation (in 5-10 min) and benefit heart hemoperfusion. The decreasing effects of cardiac massage that occurred after more than 5-10 min post-resuscitation might be because of decreasing myocardial compliance caused by a long cardiac ischemia and hypoxia duration and a sample size reduction (since the animals continued to achieve ROSC more than 5-10 min post-resuscitation). The comparison within groups revealed that the MAP and CPP values 1 min after resuscitation were not significantly different from those 5 min after resuscitation; however, these values were still significantly lower than the baseline values for both groups. In addition, the MAP and CPP values reached 54.1% and 33.4% of the baseline values, respectively, 1 min after resuscitation, and 60.0% and 41.8% of the baseline values, respectively, 5 min after resuscitation. This reveals that D-CPR generates better hemodynamic effects when compared to S-CPR and is in favor of heart hemoperfusion during resuscitation, which might account for the high success rate of resuscitation in the D-CPR group. We also observed that performing CPR while crimping the heart to the chest wall under the diaphragm resulted in good outcomes and few complications for CA patients during liver transplantation and upper abdominal operations (for example, liver, gallbladder, pancreas, or spleen operations) [15-21].

Furthermore, in this study, the rates of ROSC were not significantly different between the D-CPR group and the S-CPR group; however, this might be related to the small sample size. Our study also revealed that both the MAP and CPP values decreased after more than 5 min of resuscitation, which might be related to decreasing myocardial compliance due to a long cardiac ischemia and hypoxia duration.

The D-CPR mechanism

Our study revealed that the AOS, AOD, MAP, and CPP values of the D-CPR group were significantly higher than those in the S-CPR group during resuscitation. This verifies that cardiac compression through the diaphragm could partially construct effective artificial circulatory support to maintain blood circulation and ensure hemoperfusion for important organs. The D-CPR can generate artificial circulation and ventilation *via* the thoracic, abdominal and heart pump mechanisms. D-CPR results in upward and downward motion of diaphragm and pressure changes in the abdominal cavity, which actives the “abdominal pump”. The piston effect of the diaphragm in the thoracic and abdominal cavities then transmits pressure changes in the abdominal cavity to the thoracic cavity, inducing thoracic pressure changes which indirectly activate the “thoracic pump”. The anatomical relationship of the heart and the diaphragm then activates the “heart pump, which results in blood flow. In addition, adequate coronary perfusion pressure (CPP) is important for successful CPR, and abdominal compression can significantly increase CPP. An advantage of abdominal pumping on the chest is that it would promote some ventilation. So rhythmic diaphragm compression CPR provides effective blood circulation and some oxygen supplement. It may be the reason why D-CPR has better hemodynamic effects when compared to S-CPR.

In conclusion, the evidence provided in this study indicates that D-CPR results in better outcomes when compared to S-CPR. These results provide additional experimental supporting the popularization of D-CPR in clinical practice. However, the situation in clinical practice is complicated and variable, and animal models cannot completely mimic a real clinical situation. Therefore, additional, large-scale experiments are needed to verify the results of our experiment.

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