Remote Ischemic Pre- and Postconditioning Improve Postresuscitation Myocardial and Cerebral Function in a Rat Model of Cardiac Arrest and Resuscitation*

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Objectives: Cardiac arrest and resuscitation are models of whole body ischemia reperfusion injury. Postresuscitation myocardial and cerebral dysfunction are major causes of high mortality and morbidity. Remote ischemic postconditioning has been proven to provide potent protection of the heart and brain against ischemia reperfusion injury. In this study, we investigated the effects of remote ischemic postconditioning on postresuscitation myocardial and cerebral function in a rat model of cardiac arrest and resuscitation.

Design: Prospective, randomized, controlled experimental study.

Setting: University-affiliated animal research institution.

Subjects: Twenty-eight healthy male Sprague-Dawley rats.

Interventions: The animals were randomized into four groups: 1) remote ischemic preconditioning initiated 40 minutes before induction of ventricular fibrillation, 2) remote ischemic postconditioning initiated coincident with the start of cardiopulmonary resuscitation, 3) remote ischemic postconditioning initiated 5 minutes after successful resuscitation, and 4) control. Remote ischemic pre- and postconditioning was induced by four cycles of 5 minutes of limb ischemia, followed by 5 minutes of reperfusion. Ventricular fibrillation was induced and untreated for 6 minutes while defibrillation was attempted after 8 minutes of cardiopulmonary resuscitation. The animals were then monitored for 4 hours and observed for an additional 68 hours after resuscitation.

Measurements and Main Results: Hemodynamic measurements and myocardial function, including cardiac output, left ventricular ejection fraction, and myocardial performance index, were measured at baseline and hourly for 4 hours after resuscitation. Postresuscitation cerebral function was evaluated by neurologic deficit score at 24-hour intervals for a total of 72 hours. Consequently, significantly better myocardial and cerebral function with a longer duration of survival were observed in the three groups treated with remote ischemic pre- and postconditioning.

Conclusions: In a rat model of cardiac arrest and resuscitation, remote ischemic pre- and postconditioning attenuated postresuscitation myocardial and cerebral dysfunction and improved the duration of survival. (Crit Care Med 2015; 43:e12–e18)

Key Words: cardiopulmonary resuscitation; cerebral function; myocardial function; postresuscitation; remote postconditioning; remote preconditioning

Sudden cardiac arrest (CA) remains a major public health issue. In the United States, it is estimated that CA occurs nearly half a million times annually, with approximately 290,000 out-of-hospital cases and 210,000 in-hospital cases (1, 2). Even if the initial success of cardiopulmonary resuscitation (CPR) is approximately 40%, hospital mortality is up to 71% (3). Recent changes in guidelines have improved the success of resuscitation and survival to hospital admission; however, survival after hospital discharge remains unchanged (4).

The pathophysiology of CA represents stages of cell injury that may be attributed initially to ischemia and then amplified following the return of spontaneous circulation (ROSC) (5). Prognosis after CA is primarily determined by the degree of ischemia reperfusion (IR) injury of the brain and heart. Most survivors from successful CPR suffer from significant neurological
disability and myocardial dysfunction (6, 7). This results in a significant postresuscitation in-hospital mortality (8).

Ischemic preconditioning (IPC), applied directly to the heart and brain, has been proven to provide powerful myocardial and cerebral protection against lethal ischemia and reperfusion injury in diverse animal studies (9, 10). An early study demonstrated that IPC induced by brief episodes of whole body ischemia significantly improved post-CPR myocardial function and survival (11). A recent study further demonstrated that IPC induced by episodes of brief ischemia of regional organ or remote limb significantly decreased the number of damaged neurons in CA1 hippocampus after asphyxia CA (12). However, in patients experiencing an unpredictable ischemic insult such as CA, the window of opportunity for IPC has passed.

Currently, ischemic postconditioning has also shown its potent protection of vital organs against IR injury caused by CA and resuscitation. In a pig model of CA, Segal et al (13) have demonstrated that ischemic postconditioning with four 20-second pauses during the first 3 minutes of CPR improved postresuscitation cardiac function and facilitated neurologic recovery. In addition, ischemic postconditioning via remote limb becomes an alternative ideal noninvasive and easily performed means of organ protection. A few studies have demonstrated that remote ischemic postconditioning (RpostC) is as effective as IPC in preventing IR injury to the heart and brain (14–17).

In the present study, we investigated the effects of RpostC on post-CPR myocardial and cerebral function. Since the time window of intervention may affect the effectiveness of postconditioning, we chose to implement RpostC either during CPR or after successful resuscitation. We hypothesized that RpostC initiated during CPR or after successful resuscitation are both as effective as remote ischemic preconditioning (RPC) in improving postresuscitation myocardial and cerebral dysfunction in a rat model of CPR.

MATERIALS AND METHODS
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 Animal Resources and published by the National Institutes of Health (8th edition, Washington, DC, National Academies Press, 2011). The protocol was approved by the Institutional Animal Care and Use Committee of the Weill Institute of Critical Care Medicine. Our established rodent model of CA and resuscitation was used (18). Healthy male Sprague-Dawley rats, aged 6–8 months, weighing between 450 and 550 g, were supplied by a single source breeder (Harlan Sprague-Dawley, Livermore, CA), which has consistently supplied healthy animals of relatively uniform age and weight.

Animal Preparation
Male Sprague-Dawley rats were fasted overnight except for free access to water. The animals were anesthetized by intraperitoneal injection of sodium pentobarbital (45 mg/kg). They were then placed on a surgical board in the supine position. Additional doses of sodium pentobarbital (10 mg/kg) were administered as required to maintain anesthesia. The trachea was orally intubated with a 14-G cannula (Abbocath-T; Abbott Hospital Products Division, North Chicago, IL) mounted on a blunt needle with a 145° angled tip. End-tidal CO$_2$ (ETCO$_2$) was measured with the aid of a side-stream infrared CO$_2$ analyzer (model 200; Instrumentation Laboratories, Lexington, MA). ETCO$_2$ and conventional lead II electrocardiogram were continuously monitored. The animals were able to breathe room air spontaneously.

A polyethylene catheter (PE-50; Becton Dickinson, Franklin Lakes, NJ) was advanced into the descending aorta from the surgically exposed left femoral artery for the measurement of aortic pressure and blood gas. Another PE-50 catheter was advanced into the right atrium through the left external jugular vein for the measurement of right atrial pressure. Aortic and right atrial pressures were measured with reference to the mid-chest with high-sensitivity transducers (model 42584-01; Abbott Critical Care Systems, North Chicago, IL). A 3F PE catheter (model C-PMS-301J; Cook Critical Care, Bloomington, IN) was advanced through the right external jugular vein into the right atrium. A precurved guidewire supplied with the catheter was then advanced through the catheter into the right ventricle for the induction of ventricular fibrillation (VF). All the catheters were flushed intermittently with saline containing 2.5 IU/mL of crystalline bovine heparin. A thermocouple microprobe, 10 cm in length and 0.5 mm in diameter (9030-12-D-34; Columbus Instruments, Columbus, OH), was inserted into the left femoral vein for the measurement of blood temperature. The temperature was maintained at 37°C ± 0.2°C with the aid of a cooling blanket or infrared surface heating lamps.

Experimental Procedures
Forty-five minutes prior to inducing VF, baseline measurements were obtained. The animals were then randomized with the Sealed Envelope Method into one of the four groups: 1) RPC initiated 40 minutes before the induction of VF, 2) RpostC1 initiated coincident with the start of CPR, 3) RpostC2 initiated 5 minutes after successful resuscitation, or 4) sham control.

Four cycles of remote ischemia were performed in the RPC, RpostC1, and RpostC2 groups. Each cycle of remote ischemia was performed by 5 minutes of left upper and right lower limb ischemia followed by reperfusion for 5 minutes. Limb ischemia was performed by placing a thin elastic tourniquet around the upper third of the limb in a tight position to stop the arterial blood supply. During the ischemic period, the skin color changed to cyanosis; after recirculation, the skin color returned to rose. For the animals randomized in the control group, the tourniquet was placed around the limb but not tightened.

Ten minutes prior to inducing VF, the animals were mechanically ventilated with a tidal volume of 0.60 mL/100 g of body weight, a frequency of 100 breaths/min, and an $\text{FiO}_2$ of 0.21. VF was electrically induced with a progressive increase in
60-Hz current to a maximum of 3.5 mA delivered to the right ventricular endocardium. The current flow was continued for 3 minutes to prevent spontaneous defibrillation. Mechanical ventilation was discontinued after onset of VF. Precordial compression was initiated after 6 minutes of untreated VF with a pneumatically driven mechanical chest compressor. Coincident with the start of precordial compression, the animals were mechanically ventilated at a frequency of 100 breaths/min and with FiO2 of 1.0. Precordial compression was maintained at a rate of 200/min and synchronized to provide a compression/ventilation ratio of 2:1 with equal compression-relaxation. The depth of compression was initially adjusted to maintain a coronary perfusion pressure (CPP) at 22 ± 2 mm Hg. Resuscitation was attempted with up to three 2-J countershocks after 8 minutes of CPR. If ROSC was not achieved, a 30-second interval of CPR was performed prior to attempting a subsequent sequence of shocks. This procedure was repeated for a maximum of three cycles. ROSC was defined as the return of supraventricular rhythm, with a mean aortic pressure of greater than 50 mm Hg for a minimum of 5 minutes. Following ROSC, mechanical ventilation was continued with 100% oxygen for 1 hour, 50% for the 2nd hour, and 21% thereafter. After the experiment, all catheters including the endotracheal tube were removed. The rats were then returned to their cages equipped with a heated pet mat (Allied Precision Industries, Elburn, IL) to maintain the temperature of the cage at 24–26°C. All the animals were closely observed for an additional 68 hours, after which they were euthanized with an intraperitoneal injection of sodium pentobarbital (150 mg/kg). At necropsy, the organs were inspected for gross abnormalities, including evidence of traumatic injuries consequent to cannulation, airway management, or precordial compression.

**Measurements**

Aortic and right atrial pressures, electrocardiogram, and endtidal PCO2 values were continuously recorded on a PC-based data-acquisition system supported by WINDAQ software (DATAQ, Akron, OH). CPP was calculated as the difference between decompression diastolic aortic and time-coincident right atrial pressure measured at the end of each minute of precordial compression. Myocardial function was noninvasively measured at baseline and hourly after resuscitation for a total of 4 hours with a Philips ultrasound system (Model HD11XE; Philips, Andover, MA), using a 12.5-Hz transducer. All measurements, including cardiac output (CO), ejection fraction (EF), and myocardial performance index (MPI), were reviewed and confirmed separately by two investigators. CO and EF served as quantitative measurements of myocardial contractile function, and MPI was obtained as both systolic and diastolic function (19). Aortic blood pH, PCO2, PO2, hemoglobin, and lactate concentrations were measured at baseline and at 4 hours postresuscitation on 200 μL aliquots of blood with a Stat Profile pHOx Plus L analyzer (Model PHOXplusL; Nova Biomedical Corporation, Waltham, MA). Neurologic function was evaluated according to the method of neurologic deficit score (NDS) at 24-hour intervals for a total of 72 hours. The neurologic deficits were scored from 0 (no observed neurologic deficit) to 500 (death or brain death) (20). NDS was examined and confirmed by two investigators who were blinded to the study. Survival time was recorded in the animals with ROSC.

**Statistical Analysis**

Continuous variables were presented as mean ± SD when data were normally distributed or as a median (25th, 75th percentiles) when data were not normally distributed. Normal distribution was confirmed with the Kolmogorov-Smirnov test. Variables were compared with one-way analysis of variance (ANOVA) or the Kruskal-Wallis test for nonparametric data. Comparisons between time-based measurements within each group were performed with repeated-measures ANOVA. If there was a significant difference in the overall comparison of groups, comparisons between any other two groups were made by the Bonferroni test. For the comparison of categorical variables, such as ROSC and survival rate, the Fisher exact test was used. A p value of less than 0.05 was considered significant.

**RESULTS**

Thirty-two rats were used for this study, four of which were excluded because of instrumentation or technical errors. Consequently, 28 studies were performed and completed. Baseline hemodynamics, myocardial function, and blood analytical measurements did not differ among the four groups (Table 1). There was no difference among the groups in the amount of electric current that was required for inducing VF. During CPR, CPP was maintained at an even level, and no significant difference was observed among the four groups (Table 2). The rate of ROSC, duration of CPR, and number of shocks that were required for establishing ROSC were better in the RPC group than the other three groups although statistically insignificantly different (Table 3).

Postresuscitation myocardial function, as evaluated by the changes of CO, EF, and MPI, was significantly impaired in all animals when compared to the baseline value. However, in animals treated with remote ischemic pre- and postconditioning, myocardial function was gradually improved following 4 hours of postresuscitation observation and significantly better than the control group. At the end of 4-hour postresuscitation, CO recovered to within 90% of baseline in the RpostC1 group and also within 85% of baseline in both the RPC and RpostC2 groups. Meanwhile, EF recovered to within 84% of baseline in all three groups. The improvement in myocardial function in both the RpostC1 and RpostC2 groups was equal and also similar to that in the RPC group even though the protection was provided after ischemia and reperfusion (Figs. 1–3).

A significant volume of urine output and lower levels of arterial lactate were observed at 4-hour postresuscitation in the RPC, RpostC1, and RpostC2 groups when compared with the control group (Table 3).

The same duration of survival of 72 hours was achieved in all animals treated with remote ischemic pre- and postconditioning in the three groups, which was significantly longer than the control group with an average duration of 34 ± 25 hours.
In addition, the survival rate at 72-hour postresuscitation was statistically insignificantly different among the RPC, RpostC1, and RpostC2 groups and was significantly greater than that in the control group (Table 4).

In the control group, two rats died at 24-hour postresuscitation, accompanied with one more the following 24 hours and another rat in the next 24 hours. Consequently, only one rat survived for 72 hours, with good neurologic function in this group. All the resuscitated rats in the remaining three groups obtained good neurologic function during the 72 hours of postresuscitation observation. In addition, each rat in the two RpostC groups completely recovered without neurologic deficit at 48-hour postresuscitation; three in the RpostC2 group, two in the RpostC1 group, and one in the RPC group obtained complete recovery at 72 hours (Fig. 4). Finally, the NDSs at 24-, 48-, and 72-hour postresuscitation were statistically insignificantly different among the three groups with remote ischemic pre- and postconditioning and were significantly better than that in the control group (Fig. 5).

At necropsy, no significant abnormalities were observed on gross examination in all animals.

**TABLE 1. Baseline Characteristics of All Groups**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control</th>
<th>Remote Ischemic Preconditioning</th>
<th>Remote Ischemic Postconditioning 1</th>
<th>Remote Ischemic Postconditioning 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (g)</td>
<td>513±11</td>
<td>510±17</td>
<td>512±12</td>
<td>512±15</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>357±18</td>
<td>353±18</td>
<td>354±18</td>
<td>347±17</td>
</tr>
<tr>
<td>Mean aortic pressure (mm Hg)</td>
<td>139±8</td>
<td>136±6</td>
<td>133±5</td>
<td>134±4</td>
</tr>
<tr>
<td>Right atrial blood pressure (mm Hg)</td>
<td>1.1±0.4</td>
<td>1.1±0.3</td>
<td>1.1±0.2</td>
<td>1.2±0.2</td>
</tr>
<tr>
<td>End-tidal $\text{CO}_2$ (mm Hg)</td>
<td>41±1</td>
<td>40±1</td>
<td>41±1</td>
<td>41±1</td>
</tr>
<tr>
<td>Cardiac output (mL/min)</td>
<td>104±6</td>
<td>107±4</td>
<td>105±3</td>
<td>106±6</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>70±2</td>
<td>69±3</td>
<td>70±1</td>
<td>70±4</td>
</tr>
<tr>
<td>Myocardial performance index</td>
<td>0.69±0.05</td>
<td>0.69±0.05</td>
<td>0.68±0.07</td>
<td>0.68±0.06</td>
</tr>
<tr>
<td>Arterial lactate (mmol/L)</td>
<td>0.9±0.3</td>
<td>0.8±0.3</td>
<td>0.8±0.2</td>
<td>0.9±0.3</td>
</tr>
</tbody>
</table>

Values are presented as mean ± so.

**TABLE 2. Coronary Perfusion Pressure During Cardiopulmonary Resuscitation**

<table>
<thead>
<tr>
<th>CPP</th>
<th>Control</th>
<th>Remote Ischemic Preconditioning</th>
<th>Remote Ischemic Postconditioning 1</th>
<th>Remote Ischemic Postconditioning 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPP in PC1 (mm Hg)</td>
<td>23.6±0.6</td>
<td>23.3±1.1</td>
<td>23.3±0.9</td>
<td>23.3±0.7</td>
</tr>
<tr>
<td>CPP in PC4 (mm Hg)</td>
<td>23.3±0.7</td>
<td>23.4±0.4</td>
<td>23.4±0.6</td>
<td>23.3±0.6</td>
</tr>
<tr>
<td>CPP in PC8 (mm Hg)</td>
<td>23.7±0.5</td>
<td>23.3±0.6</td>
<td>23.7±0.6</td>
<td>23.3±0.5</td>
</tr>
</tbody>
</table>

CPP = coronary perfusion pressure, PC$n$ indicates n min after precordial compression. Values are presented as mean ± so.

**TABLE 3. Cardiopulmonary Resuscitation Outcomes, Urine Output, and Arterial Lactate**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control</th>
<th>Remote Ischemic Preconditioning</th>
<th>Remote Ischemic Postconditioning 1</th>
<th>Remote Ischemic Postconditioning 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Return of spontaneous circulation</td>
<td>5/7</td>
<td>7/7</td>
<td>5/7</td>
<td>5/7</td>
</tr>
<tr>
<td>Duration of cardiopulmonary resuscitation (min)</td>
<td>8.4±0.7</td>
<td>8.0±0.0</td>
<td>8.6±0.7</td>
<td>8.5±0.7</td>
</tr>
<tr>
<td>No. of shocks</td>
<td>3.4±2.6</td>
<td>1.0±0.6</td>
<td>2.4±1.9</td>
<td>3.3±2.3</td>
</tr>
<tr>
<td>PR 4-hr urine output (mL)</td>
<td>1.0±1.0</td>
<td>2.8±0.4$^a$</td>
<td>3.0±0.3$^b$</td>
<td>2.9±0.6$^b$</td>
</tr>
<tr>
<td>PR 4-hr arterial lactate (mmol/L)</td>
<td>2.2±0.6</td>
<td>1.2±0.3$^a$</td>
<td>1.0±0.1$^b$</td>
<td>1.1±0.3$^b$</td>
</tr>
</tbody>
</table>

PR = postresuscitation.

$^a p < 0.01$ versus control group.

$^b p < 0.05$ versus control group.

Values are presented as mean ± so.
DISCUSSION

The present study demonstrated that RpostC was successfully induced by repeated and transient limb ischemia in a rat model of CA and resuscitation. Consequently, RpostC initiated during CPR or after successful resuscitation significantly attenuated postresuscitation myocardial and cerebral dysfunction and improved the duration of survival when compared with the control group. No adverse effect was observed after limb ischemic conditioning. In addition, equal postresuscitation myocardial and cerebral function were achieved in both the RpostC groups when compared with the RPC group although their CPR outcomes were worse than the RPC group.

Despite improved training, new guidelines, and the establishment of medical emergency outreach teams, CA outcomes have improved only slightly (1, 21). The disappointing outcomes of CPR are largely related to the high in-hospital mortality following successful resuscitation, mainly caused by postresuscitation myocardial and cerebral dysfunction (8). Recently, Segal et al (13) demonstrated that ischemic postconditioning induced by intermittent mechanical chest compressions improved post-CPR cardiac and cerebral function in a pig model. However, it is difficult to control the interruptions in the actual clinical setting and is not recommended by current guidelines (13). Cour et al (22) demonstrated that the inhibition of the mitochondrial permeability transition pore with cyclosporine A attenuated post-CPR myocardial dysfunction and improved short-term survival in a rabbit model. Consequently, the drug is expensive and its benefits and usage require further investigation. An alternative and feasible approach would be to add an active protection of the vital organs during CA and resuscitation. This can potentially be done through RpostC for CA victims.

To date, the optimal algorithms for remote ischemic conditioning for the therapeutic use have not been adequately addressed. First, no insights have been obtained regarding the optimal remote stimulus in terms of the number of cycles of brief IR or the duration of each episode. Second, there is no information as to whether the outcome is superior with arm versus leg ischemia applied at two or more sites instead of one (23). In this study, we applied remote ischemic conditioning by four cycles of 5 minutes of limb ischemia and then 5 minutes of reperfusion following the popular choice by other groups. In an attempt to achieve the optimal efficacy of remote stimulus, we used the arm and leg together as the sites for ischemic conditioning. Considering the feasible timing for RpostC in the clinical setting, we implemented RpostC either during CPR or after successful resuscitation.

Currently, no investigation has reported the protective effects produced by RpostC in a CA model. Previous evidences on
organ protection induced by regional and remote ischemic postconditioning were mainly focused on animal models of regional cardiac IR injury, which indicated that the time window of intervention may occur in the protective effects. However, the conclusions from these studies may have no relevance to that in a CA model. Previously, Yang et al (24) demonstrated that direct myocardial postconditioning starting 30 seconds after reperfusion significantly decreased infarction by 55.9%, whereas myocardial protection was no longer evident when starting postconditioning 10 minutes after reperfusion in a rabbit model. Subsequently, Kin et al (25) demonstrated that the first minute of reperfusion was critical to cardioprotection induced by direct myocardial postconditioning and the protective effects were lost with postconditioning delayed 1 minute after reperfusion in a rat model. Recently, Basalay et al (26) demonstrated that remote ischemic conditioning via femoral artery provided a similar degree of cardioprotection when applied 25 minutes prior to myocardial ischemia, 10 or 25 minutes after the onset of ischemia, or 10 minutes after the onset of reperfusion in a rat model. However, the cardioprotection disappeared when remote ischemic conditioning was applied 30 minutes after reperfusion.

In the present study, we used a rat model of CA and resuscitation and demonstrated that ischemic postconditioning via remote limbs produced significant myocardial and cerebral protection even if it was applied 5 minutes after successful resuscitation. In addition, when IPC via the remote limbs was applied prior to CA, better CPR outcomes were achieved, for example, best ROSC, decreased duration of CPR, and energy requirement for defibrillation. These results were consistent with our previous study, which demonstrated that IPC improved the outcomes of CPR (11). However, RpostC delivered after CA still provided equal postresuscitation myocardial and cerebral protection when compared with the RPC group in this study.

Despite the evidence of myocardial and cerebral protection with remote ischemic conditioning are compelling, the protective mechanisms are still unclear. The investigations for the evidence and potential mechanism for organ protection induced by emerging RpostC are rare and only applied in the models of IR injury of regional organs. An early study demonstrated that RpostC significantly decreased myocardial infarction; the potential mechanism of protection might be involved in reduced oxygen radical–induced injury and improved antioxidant action (15). Recently, Wang et al (16) demonstrated that RpostC alleviated focal cerebral IR injury through reactive oxygen species–mediated inhibition of endogenous δ protein kinase C activation signaling cascade. Peng et al (17) demonstrated that RpostC protected global cerebral IR injury by up-regulating endothelial nitric oxide synthase through the phosphatidylinositol-3 kinase/Akt pathway. In the clinical setting, Loukogeorgakis et al (27) first demonstrated that RpostC was successfully induced in humans and, furthermore,
provided the effective protection for endothelial IR injury by \( K_{ATP} \) channel activation. Subsequently, Botker et al (28) applied RpostC to the adult patients with acute myocardial infarction and found that RpostC significantly increased myocardial salvage after percutaneous coronary intervention and also partly decreased the infarction size. Recently, Rentoukas et al (29) observed that RpostC was helpful to ST-segment resolution and troponin I recovery after percutaneous coronary intervention, and this cardioprotective effect of RpostC can be enhanced by opioid receptor activation.

There were limitations in this study. First, although myocardial and cerebral function were preserved by RpostC in this model of CA and resuscitation, the potential mechanisms for organ protection were not explored in the study. Second, cardiac and cerebral protection induced by RpostC were only evaluated by organ function in a short observation period in this study. A longer observation period is needed in a future study. In addition, the levels of serum biomarkers and the severity of apoptosis of myocardial cells and neurons would be necessarily increased to comprehensively evaluate organ protection induced by RpostC. Further clinical studies are also required to confirm the effectiveness of RpostC in the clinical setting.

CONCLUSION

RpostC, initiated during CPR or after successful resuscitation, significantly attenuated postresuscitation myocardial and cerebral dysfunction and improved the duration of survival in a rat model of CA and resuscitation.

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REFERENCES