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Exploration of the Application of Remote Ischemic Conditioning in Nursing of Cardiac Arrest

Yi-maizi Xu[1], Mingyue Yang[1], Fangchi Liu[1], Chao Zhang[1], Yimeng Yan[1], Zhixian Feng[2]*

[1]Hangzhou Normal University School of Nursing, Hangzhou 311121, Zhejiang, China
[2]Affiliated Shulan (HangZhou) Hospital, Shulan International Medical College, Zhejiang Shuren University, Hangzhou 310022, Zhejiang, China

***Corresponding author:** *Zhixian Feng, 1833898759@qq.com*

Abstract: Cardiac arrest (CA) is a major global public health challenge, and its high morbidity and low survival rate pose severe tests for emergency and critical care. Although modern CPR techniques significantly improve the immediate resuscitation success rate in CA patients, poor outcomes such as neurological impairment still significantly increase the long-term care burden and reduce the quality of survival. In recent years, the application of remote ischemic conditioning (RIC) has attracted much attention in the field of cardiac arrest through its unique myocardial-nerve dual protection mechanism against the heart. This paper summarizes the conceptual connotation, physiological mechanism, operation method, and its application progress in CA and explores the potential of this technology in the field of CA care in order to provide reference for the research and application of RIC in the field of emergency care.

Keywords: Remote ischemic conditioning; Cardiac arrest; Nursing; Review

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1. Introduction

Cardiac arrest (CA) is one of the main causes of death and disability worldwide, and its morbidity and mortality remain high [1]. Although the continuous development of emergency techniques such as cardiopulmonary resuscitation (CPR) has improved the survival rate of patients with cardiac arrest, the long-term prognosis is still not ideal, and survivors are often accompanied by different degrees of neurological dysfunction [2]. Therefore, it is of great significance in clinical and nursing work to explore effective adjuvant therapy to improve the survival rate and neurological prognosis of patients with CA. In recent years, remote ischemic conditioning (RIC), as an innovative therapeutic strategy, has been extensively and deeply studied for its mechanism of reducing reperfusion injury [3]. This strategy shows good protective effect in many ischemic diseases and provides a new research direction for the treatment of cardiac arrest in the clinic. This review focuses on reviewing the concept,

physiological mechanism, operation methods, and application progress of RIC in CA. By analyzing the existing research, it explores the potential of this technology in the field of CA nursing in order to provide a reference for clinical practice and future research of nursing practice in CA.

2. Remote ischemic conditioning

2.1. The concept of remote ischemic conditioning

RIC refers to the application of transient non-fatal ischemia-reperfusion stimulation on distant organs or tissues of the body (usually selected limbs), thus activating the endogenous protective mechanism, and significantly improving the tolerance of important organs such as heart, brain, liver, kidney, and skin to the subsequent severe ischemic and hypoxic injury [4]. As early as 1986, Murry first confirmed that intermittent reperfusion could prevent myocardial ischemic injury in animal experiments . Subsequent studies have gradually confirmed that this method is suitable for many important organs, such as kidney, liver, lung, gastrointestinal tract and skin [3]. Depending on the timing of intervention (pre, during, and post-ischemia), RIC can be divided into three categories: remote ischemic preconditioning(RIPC), perconditioning, and remote ischemic postconditioning (RIPostC)[4].

2.2. Physiological mechanisms of remote ischemic conditioning

The exact mechanism of RIC is not completely clear, but it has obvious similarities with ischemic regulation [5]. Several studies have shown that remote ischemic conditioning (RIC) induces the release of biologically active substances such as adenosine, nitric oxide, bradykinin, and norepinephrine. These substances exert their protective effects through multiple mechanisms, including neural regulation, humoral regulation, modulation of inflammatory responses, and activation of intracellular signaling pathways. These interconnected pathways work synergistically to transmit protective signals to target organs, resulting in a systemic protective effect [6, 7]. Common molecular mechanism of RIC: (1) Release of vasoactive substances to enhance cell membrane stability [7]; (2) Activation of mitochondrial K + -ATP channels to regulate neurotransmitter release [8]; (3) Activate eNOS, produce nitric oxide and reduce free radical release [9]; (4) Regulate immune cell and cytokine levels and suppress inflammatory responses [10]; (5) Enhance antioxidant capacity and reduce oxidative stress and inflammatory responses [11]; (6) Inhibit the ER stress pathway and prevent excessive autophagy activation [12]. The protective effect of RIC has obvious time window characteristics: the first stage occurs immediately after RIC treatment for 2 to 3 h; the second stage occurs for 12 to 24 h after RIC treatment, lasting for 48 to 96 h or even longer [13].

2.3. Implementation of remote ischemic conditioning

At present, the specific treatment scheme of RIC has not yet reached a unified consensus. The commonly used clinical operation scheme is as follows: fixing the cuff on the upper arm (bilateral or unilateral), rapidly inflating and pressurizing with a pressure of 200mmHg, releasing the pressure after 3–5 minutes, and pressurizing again after 5 minutes. This is an ischemia-reperfusion cycle, and one treatment lasts for 4–5 cycles, about 30–45 minutes [14, 15]. In clinical practice, the intervention of upper limb forearm ischemia is the most commonly used, and the simultaneous intervention of both limbs is more commonly used than unilateral intervention, and the protective effect is stronger [16, 17]. In terms of treatment cycle, there are differences among different studies. Some clinical studies adopt a single treatment, and long-term treatment schemes include 1–2 times a day for 1–4 weeks, or even extended to 3–12 months [7, 14]. Although there are differences in the treatment cycle and parameter setting,

existing studies have confirmed that various schemes can achieve certain organ protection effects.

3. The current situation of cardiac arrest

3.1. Definition and classification

CA refers to the sudden stop of cardiac mechanical activity, accompanied by the disappearance of pulse and circulatory signs, which can be divided into out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA) according to the location of the event [18]. In the out-of-hospital environment, OHCA patients are much more difficult to get professional first aid in time than IHCA patients, and the overall CA patients' condition progresses rapidly, which can cause irreversible damage to multiple organs in a short time.

3.2. Morbidity and mortality rates

It is reported that the mortality rate of CA is extremely high, ranging from 78% to 85% [19]. Among them, the incidence of OHCA is about 53–62/100,000. Because of its difficulty in treatment, the mortality rate is close to 90%, and only about 10% of patients can survive and leave the hospital [20, 21]. Statistics show that 1.5–1.7 cases of IHCA will occur in every 1000 hospitalized patients, and about a quarter (25.8%) of the patients can be discharged alive after rescue [18]. After the occurrence of CA, the reperfusion injury (RI) may be caused by the resumption of perfusion. RI can lead to endothelial dysfunction, impaired oxygen and glucose metabolism, intracellular calcium influx, coagulation and platelet dysfunction, microvascular obstruction, myocardial dysfunction and arrhythmia, which seriously affects the prognosis of patients [22]. Given the high lethality of CA, the clinical treatment must race against time. The core goal is to quickly restore effective circulation, optimize organ perfusion, and maximize the protection of neurological function while improving the survival rate. This puts high demands on emergency treatment, which also means that nurses shoulder an extremely critical and arduous mission.

3.3. Cause of disease

The etiology of CA is mainly divided into cardiogenic and non-cardiogenic [23]. The cardiac causes include ischemic heart disease, non-atherosclerotic coronary disease, fatal arrhythmia without ischemic heart disease, cardiomyopathy, valvular heart disease, etc. Non-cardiac causes include trauma, malignant tumor, non-traumatic bleeding, asphyxia, lack of oxygen, drug overdose, septic shock, and many other factors.

4. Progress in the application of remote ischemic conditioning in cardiac arrest

4.1. Intervention approach of RIC in CA

RIC mainly adopts two intervention strategies in the treatment of CA: RIPC and RIPostC (usually 3–4 cycles of 5-min ischemia/ 5-min reperfusion with sphygmomanometer cuff on both upper limbs at a pressure of 200mmHg), which play a protective role in the heart through different time windows and molecular mechanisms [24, 25]. RIPC is suitable for foreseeable ischemic events [26]. From the time sequence characteristics of nursing implementation, RIPC is more suitable for preventive intervention of foreseeable ischemic events, such as elective heart surgery and other clinical scenarios. Its protective mechanism involves inducing myocardial cells to release endogenous substances such as acetylcholine and adenosine in advance and finally triggering mitochondrial ROS- protein kinase-transcription factor cascade reaction by activating the downstream signal pathway of membrane receptors [27].

However, the application of this technique in sudden cardiac arrest has obvious limitations [28]. In contrast,

RIPostC shows a wider application prospect in emergency nursing practice. It is an intervention measure implemented immediately after cardiac arrest and cardiopulmonary resuscitation, which not only retains some protective mechanisms of RIPC (such as adenosine receptor activation), but also alleviates reperfusion injury through unique ways such as delaying pH recovery and inhibiting mPTP opening [29, 30]. The existing research confirmed that RIPostC can not only effectively alleviate myocardial injury, but also significantly improve the prognosis of neurological function after cardiac arrest [31]. RIC is simple to operate, low-cost, safe and non-invasive. At the same time, it will not hinder the reperfusion treatment, and it shows good therapeutic effect in the protection of heart and brain, which provides a solid foundation for its popularization and application in the field of emergency medicine [32].

From the point of view of nursing operation, RIC's operation process is simple, the intervention process is completely non-invasive, it will not cause additional harm to patients, the implementation cost is low, and it has high health economic value. The implementation of this technology does not affect the development of emergency nursing measures such as routine cardiopulmonary resuscitation and advanced life support, and this compatibility makes it have unique application value in emergency nursing.

4.2. RIC in animal CA

At present, RIC has played a good therapeutic role in many animal experiments. In the pig model of cardiac arrest, the application of RIC after resuscitation can effectively reduce the degree of myocardial injury [33]. Another pig model experiment showed that RIpostC intervention significantly improved the prognosis of post-cardiac arrest syndrome (PCAS) in pig model [34]. The rat model of cardiac arrest confirmed that RIC intervention can reduce nerve injury and neuronal cell death, exert neuroprotective effect and improve brain function after resuscitation [28, 35]. In addition, in another study on rat model, RIC can effectively protect the brain from ischemic injury after asphyxial cardiac arrest [36]. These animal experimental results provide important mechanism evidence for the potential application value of RIC in cardiac arrest nursing.

4.3. RIC in clinical CA

Clinical evidence shows that, RIC is very likely to bring clinical benefits to patients with heart diseases [37]. Previous studies have confirmed that it is not only safe and feasible to apply RIC to the care of patients with CA resuscitation when OHCA patients are transported to the emergency room, but also can significantly improve the clinical prognosis of patients [3]. In patients with ST-segment elevation myocardial infarction (STEMI) complicated with cardiogenic shock or cardiac arrest, RIC intervention before percutaneous coronary intervention (PCI) can significantly reduce the risk of adverse cardiac events for 90 days [38]. In cardiovascular surgery, preoperative application of RIPC can effectively improve the mitochondrial function and contraction function of atrial myocardium in patients with ischemic cardiac arrest, and provide significant cardiac protection for surgical patients [39]. Although the study confirmed the protective effect of RIC on the myocardium and nerves of CA, the research data of RIC in the clinical field and nursing field of cardiac arrest are still limited. The answers to these key questions need to be carried out in large-scale, multi-center randomized controlled clinical trials in the future to provide more reliable evidence-based medical evidence. Future nursing research should also pay attention to the key issues such as the integration strategy of RIC and existing advanced life support processes.

4.4. Risk assessment of the RIC in the CA

As a non-invasive and simple treatment method, it shows good patient tolerance in clinic, but its application in patients with cardiac arrest still needs to pay attention to related adverse reactions and contraindications. The existing clinical evidence shows that RIC may cause local reactions such as arm pain, skin redness, swelling, skin petechiae and local edema, as well as general symptoms such as dizziness and finger numbness [40, 41]. When the lower limb is used as the treatment site, it is necessary to pay special attention to the risks of deep venous thrombosis and venous reflux disorder [42]. In addition, the contraindications of RIC include: soft tissue or vascular injury, intracranial hemorrhage, hemorrhagic disease or bleeding tendency, history of atrial fibrillation or myocardial infarction, severe vascular disease, uncontrolled hypertension (systolic blood pressure ≥ 180–200mmHg) and injury or infection at the operation site [43, 44]. Therefore, before implementing RIC, nurses should make a comprehensive evaluation, strictly grasp the indications and contraindications, and at the same time, make emergency plans, so as to identify and deal with possible complications in time and ensure the safety and effectiveness of treatment.

5. Enlightenment of the application of remote ischemic regulation in nursing care of cardiac arrest

5.1. The potential of RIC to improve the prognosis of CA

(1) Reducing reperfusion injury

Based on the mechanism of RIC, the endogenous protective mechanism induced by RIC is expected to significantly reduce the reperfusion injury of CA patients after reperfusion. It may promote the recovery of cardiac function by alleviating myocardial ischemia-reperfusion injury, improving myocardial microcirculation and reducing myocardial cell apoptosis [45]. For example, in some animal studies, it was confirmed that patients treated with RIC after resuscitation showed better left ventricular systolic function and more significant improvement of myocardial zymogram, which provided a strong experimental basis for RIC in reducing the nursing of heart reperfusion injury [33, 46].

(2) Neurological protection

After cardiac arrest, patients are often accompanied by different degrees of neurological dysfunction. RIC may effectively improve the prognosis of neurological function by regulating the level of oxidative stress, inhibiting neuroinflammatory reaction and promoting synaptic remodeling [47]. In addition, the systemic endogenous protective mechanism triggered by RIC can also be applied to the cerebrovascular system, so it is expected to improve the ischemia and hypoxia of the brain and have a positive impact on the prognosis of patients' neurological function. The existing animal studies show that RIC may improve the neurological function score after cardiac arrest, improve the brain function after resuscitation and prolong the survival time [31]. Although there is no direct clinical evidence to support it at present, based on the results of animal experiments, the physiological characteristics of cerebral vessels, and the mechanism of RIC, this speculation has high rationality and potential application value.

5.2. Potential of RIC with CA rehabilitation therapy

For surviving patients with cardiac arrest, rehabilitation therapy is of great significance to their functional recovery. RIC can continue to play a role in the rehabilitation stage, organically combined with rehabilitation training, and can promote the further recovery of patients' cardiac and neurological functions. Previous studies have shown that

the application of RIC technology in the recovery period after stroke can help the rehabilitation of neurological function [48]. This gives an important enlightenment to the patients who are recovering from cardiac arrest. Nurses can combine the existing clinical evidence to further explore the intervention effect of RIC in the rehabilitation treatment of patients with cardiac arrest, so as to help better improve the rehabilitation effect of patients and improve their quality of life.

5.3. RIC may optimize emergency nursing practice

RIC is feasible to be integrated into the emergency nursing process of patients with cardiac arrest. When the patient has cardiac arrest, the nursing staff can quickly prepare for RIC treatment of the patient's limbs while taking routine first aid measures such as cardiopulmonary resuscitation, to improve the treatment efficiency. This process integration makes full use of RIC's characteristics of simple operation and less trauma, and will not interfere with key emergency measures such as cardiopulmonary resuscitation, which provides a new idea for optimizing the emergency nursing process of cardiac arrest. During the implementation of RIC, nurses need to closely monitor patients' vital signs and limb peripheral circulation. Because RIC may cause patients with short-term limb pain, numbness and other discomfort symptoms, nurses should give psychological comfort and detailed explanation in time to relieve patients' tension. At the same time, the patient's reaction to RIC should be closely observed, such as whether there are abnormal situations such as blood pressure fluctuation and arrhythmia, to adjust the RIC scheme in time or take corresponding treatment measures. Through strict condition monitoring and evaluation, the safe and effective implementation of RIC in cardiac arrest nursing can be ensured.

6. Application challenges of RIC in CA

Because the research data of RIC in CA clinical field and nursing field are still limited, the practical application effect and safety of the above enlightenment need to be tested by large-scale clinical trials. This limits the popularization and application of RIC in the field of cardiac arrest nursing to some extent. RIC is a relatively new intervention strategy in the treatment of CA, but the nurses in the emergency center have a serious lack of understanding of its mechanism, operation method and application value in CA nursing. In the future, clinical and nursing researchers can carry out more related clinical trials, more comprehensively and accurately verify the application effect and safety of RIC in CA nursing, as well as provide solid data support for its promotion in the field of first aid.

7. Conclusion

As an innovative treatment strategy, RIC has shown remarkable clinical potential in the field of CA treatment. Although the research data of RIC in the field of CA nursing is limited at present, through the analysis of the research results of RIC in CA treatment, it can be inferred from the theoretical level that RIC has significant potential application value in improving the prognosis of patients with cardiac arrest and optimizing emergency nursing practice. These characteristics make RIC an important part of CA emergency care program and provide new treatment options for improving patients' survival rate and quality of life. However, in the actual application process, there are indeed many challenges, and it is necessary for researchers to continue in-depth research and gradually solve these problems in order to promote the application of RIC in CA emergency care.

Disclosure statement

The authors declare no conflict of interest.

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