Journal of Cardiology 66 (2015) 91–96

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Review

Remote ischemic conditioning: Current clinical perspectives

Sophie Le Page (MD), Fabrice Prunier (MD, PhD)*

L'UNAM Université, Université d'Angers, EA 3860 Cardioprotection, Remodelage et Thrombose, CHU Angers, Service de Cardiologie, Angers, France

ARTICLE INFO

Article history:
Received 7 December 2014
Accepted 16 January 2015
Available online 2 March 2015

Keywords:
Cardioprotection
Ischemia-reperfusion injury
Conditioning

ABSTRACT

Remote ischemic conditioning (RIC) constitutes a promising method in which a tissue or organ is exposed to intermittent ischemia/reperfusion periods enabling it to provide protection to a distant target organ. RIC has been tested in various clinical settings through its simple application by means of intermittent inflation of a blood pressure cuff placed on a limb, primarily evaluating its potential abilities to decrease myocardial injury biomarkers. Its use on other organs, such as the kidneys or brain, has recently been a topic of research. To date, no study has yet been powerful enough to reach a conclusion on the potential benefit of RIC on clinical outcomes. The future role of RIC in the clinical arena could be clarified by the large phase III trials currently underway targeting major outcomes as primary endpoints.

Contents

Introduction

While restoring blood flow in a heart that is undergoing ischemia is paramount to improving clinical outcome, the reperfusion process itself can paradoxically induce irreversible cellular damage, referred

* Corresponding author at: Université Angers, "Cardioprotection, Remodelage, Thrombose", EA 3860, rue Haute de Reculée, FR-49045, Angers, France.
Tel.: +33 0241 355 147; fax: +33 0241 354 004.
E-mail address: FaPrunier@chu-angers.fr (F. Prunier).

http://dx.doi.org/10.1016/j.jjcc.2015.01.009
0914-5087/

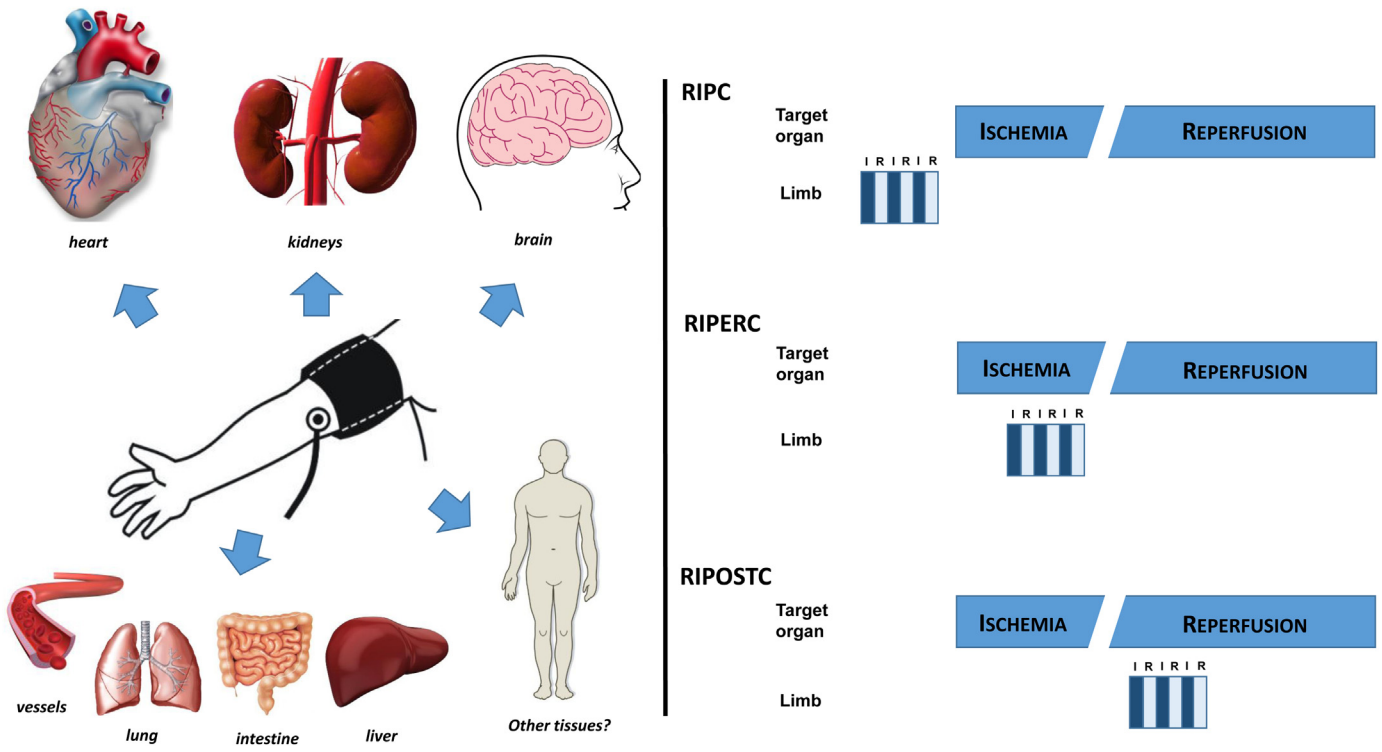

Fig. 1. Schematic representation of the targets of remote ischemic conditioning (RIC). This figure shows the potential targets of RIC in the ischemia/reperfusion context. Cycles of brief inflation/deflation of a cuff placed on limb can be performed before ischemia (remote ischemic preconditioning, RIPC), during ischemia (remote ischemic preconditioning, RIPerC), or after blood flow restoration (remote ischemic postconditioning, RIPostC). I, ischemia induced by the blood pressure cuff inflation; R, reperfusion by deflation of the blood pressure cuff.

to as myocardial reperfusion injury [1]. This phenomenon has been observed in several clinical settings, including cardiac surgery [coronary artery bypass grafting (CABG), valvular replacement, congenital heart repair], major vascular surgery (aortic aneurism repair, carotid endarterectomy), percutaneous coronary intervention (PCI), and organ transplantation. Despite the numerous improvements that have been made in modern management strategies for at-risk patients to reduce ischemia-related cardiac damage, limiting myocardial reperfusion injury remains a challenge.

In 1986, Murry et al. described local ischemic preconditioning (IPC) as a cardioprotective technique [2]. IPC consists of four cycles of 5 minutes (min) of ischemia and 5 min reperfusion of the circumflex artery before placing a sustained ligature, and the technique was found to significantly reduce myocardial damage in dogs. Some years later, Zhao et al. reported similar beneficial effects when applying transient brief episodes of ischemia at the time of reperfusion [3]. This ischemic postconditioning (IPostC) technique has proven successful in patients with acute myocardial infarction. Staat et al. were the first to report that four cycles of 1-min inflation and 1-min deflation of an angioplasty balloon, initiated within 1 min of reopening the culprit coronary artery, reduced infarct size by 34% [4]. Most of the clinical trials published on this subject have demonstrated that IPostC can mitigate infarct size [5]. Nevertheless, both IPC and IPostC require invasive procedures that may present high risk in a clinical situation. Remote ischemic conditioning (RIC) therefore represents a particularly attractive alternative. First assessed within the heart by Przyklenk et al. in 1993 [6], RIC is a conditioning strategy in which an organ or tissue other than the target is exposed to brief periods of I/R for conditioning. Given that it allows invasive procedures to be avoided, the RIC technique using transient limb ischemia as a stimulus has emerged as an intelligent strategy choice for a wide range of clinical scenarios involving potential ischemia-reperfusion insult [7].

In this review, we present an overview of RIC-induced effects and clinical perspectives in the heart and other organs.

RIC stimulus in humans

RIC offers a simple application consisting of intermittent inflation of a blood pressure cuff or tourniquet placed on an upper or lower limb. As with other strategies tested in local ischemic conditioning, there have been various different RIC regimens reported, as presented in Fig. 1. RIC stimulus can be applied prior to the intervention at risk (remote preconditioning, RIPC), during ischemia (remote perconditioning, RIPerC), or after blood flow restoration (remote postconditioning, RIPostC).

Clinical applications of RIC

Given how simple RIC is to perform, numerous clinical trials have been launched to measure RIC-induced effects on myocardial injury and, more recently, on the occurrence of cardiovascular events.

RIC in cardiac surgery

The first attempt to translate RIC experimental findings to the clinical arena was made by Gunaydin et al. in 2000, involving eight patients undergoing scheduled CABG [8]. Their results were mitigated due to the trial being clearly underpowered. Since then, numerous trials involving cardiac surgery patients have been conducted, as summarized in Online Table 1.

RIC in pediatric surgery

Cheung et al. produced successful results in 2006 when evaluating RIC in 37 children undergoing congenital heart repair [9]. Myocardial injury, assessed by troponin I release, was found to be reduced after remote preconditioning of a lower limb applied in