Ischemic Remote Conditioning: An interesting concept or a clinical reality

Terence Valenzuela MD MPH
stolen from
Christopher Caldaron, MD
We cause/treat Ischemia-Reperfusion injury

Ischemia

Reperfusion

Cardioplegia

MI

Angioplasty

Inflammation

Dysfunction

Apoptosis

Necrosis
Reperfusion Injury

Ischemia/reperfusion >> injury

Major cause of morbidity

Strategy:

• Avoid it

• Modify the body’s response
Brief and repeated cycles of Ischemia and Reperfusion can protect ischemic myocardium from injury by preserving mitochondria and ameliorating damage from oxygen radicals and other biochemical intracellular changes during ischemia and reperfusion.
Remote IPC

- *Stimulus* organ (can be an arm) is preconditioned
- Confers protection on a distant *target* organ
Remote ischemic preconditioning

Kharbanda, Neilsen & Redington. Lancet 2009
Remote Ischemic preconditioning (rIPC) elaborates
A Transferable Blood Borne Effector

Preserves Mitochondrial structure and function

Preserves Cardiac performance
Does It Pick Up Peanuts?
333 consecutive adult patients with a suspected first acute myocardial infarction were randomly assigned to receive primary percutaneous coronary intervention

With (n=166 patients) versus Without (n=167) remote conditioning (intermittent arm ischemia through four cycles of 5-min inflation and 5-min deflation of a blood-pressure cuff).
Patients received remote conditioning during transport to hospital, and primary percutaneous coronary intervention in hospital.

The primary endpoint was myocardial salvage index at 30 days after primary percutaneous coronary intervention.

Measured by myocardial perfusion imaging as the proportion of the area at risk salvaged by treatment.
Ischemia

Acute coronary arterial occlusion

Region of perfusion defect

"Area at Risk"

Reperfusion < 20 min

Reperfusion 2-4 hr

Permanent occlusion

Normal

Ischemic

Viable, with post-ischemic dysfunction

Necrotic, with hemorrhage and contraction bands

Necrotic
Remote conditioning group

Median salvage index: 0.75 (IQR 0.50–0.93, n=73)
Mean salvage index: 0.69 (SD 0.27)

Control group

Median salvage index: 0.55 (IQR 0.35–0.88, n=69)
Mean salvage index: 0.57 (SD 0.26)
Windows of clinical opportunity

Remote

Ischemia

Reperfusion

Timing modes
Elective Coronary Angioplasty

Cardiac Remote Ischemic Preconditioning in Coronary Stenting (CRISP Stent) Study
A Prospective, Randomized Control Trial

Stephen P. Hoole, MA, MRCP; Patrick M. Heck, MA, MRCP; Linda Sharples, PhD; Sadia N. Khan, MA, MRCP; Rudolf Duehmke, MRCP; Cameron G. Densem, MD, MRCP; Sarah C. Clarke, MD, FRCP; Leonard M. Shapiro, MD, FRCP; Peter M. Schofield, MD, FRCP; Michael O’Sullivan, PhD, MRCP; David P. Dutka, MD, FRCP

RIPC associated with:

**Diminished cTnl** \( p=0.04 \)
**Diminished chest pain** \( p=0.01 \)
**Diminished ST segment deviation** \( p=0.0006 \)
**Diminished MACCE at 6 months** \( p=0.018 \)

Conclusion—Remote IPC reduces ischemic chest discomfort during PCI, attenuates procedure-related cTnl release, and appears to reduce subsequent cardiovascular events. (Circulation. 2009;119:820-827.)
Neuroprotection:

RIPC: Pre- and Per-Conditioning

>> Diminished stroke
>> Clinically feasible
>> Per- is superior

*Hahn et al. Stroke 2011*
Remote ischemic conditioning

Summary

- Diminishes myocardial infarction (Pre-/Per-/Post-)
- Diminishes stroke (Pre-/Per-)
- Transferrable protection (Factor –X)
- Modifies post-op dysfunction and multi-organ injury
- Chronic RIPC can favorably modify post-infarct remodeling
Attractive Features

- More RCT’s in progress
- Grounded in thousands of lab studies
- "Grass roots’ movement
  - No big pharma or device manufacturers driving research
  - Broad effort to translate to the bedside
  - No reported adverse events
  - Inexpensive

Botker HE et al Remote Ischemic Conditioning as a complement to angioplasty, and effect on myocardial salvage in patients with acute myocardial infarction: a randomised trial *Lancet* 2010; 375: 727–34