Remote Ischemic Preconditioning
What is it and can it protect against spinal cord ischemia?
Thomas L. Forbes, MD

Spinal Cord Ischemia
- Endovascular Era – TEVAR
  - Incidence 2-12%
  - Risk is relative to the extent and location of the excluded aorta
- Much effort over the past 2 years has been directed towards
  - Understanding pathophysiology
  - Developing preventive strategies
  - Developing treatment algorithms

STRATEGIES FOR SPINAL CORD PROTECTION
• Decreased spinal cord metabolism (oxygen demand)
  -- hypothermia (systemic and local)
  -- avoidance of hyperglycemia
  -- pharmacologic approaches (eg. Barbiturates)
• Increased spinal perfusion (oxygen supply)
  -- heparin
  -- reattachment of critical intercostal arteries
  -- left heart bypass
  -- CSF drainage
  -- Avoid hypotension
  -- Ischemic Preconditioning?
What is Ischemic Preconditioning?

- First described in 1986 in myocardium
- Tissues exposed to brief periods of ischemia and then reperfusion develop resistance to subsequent more severe ischemic insults
- Stimulus transmitted through humoral, neurogenic and systemic inflammatory mediators to direct, or remote, target cells
- Upregulation of intracellular ATP K+ dependent channels that inhibit cell death

Ischemic Preconditioning

Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium

Charles E. Murry, B.S., Robert B. Jennings, M.D., and Keith A. Reiner, M.D., Ph.D.

- Reduction in infarct size was independent of collateral flow

Direct Ischemic Preconditioning

Staged endovascular repair of thoracoabdominal aortic aneurysms limits incidence and severity of spinal cord ischemia.

O’Callaghan A, Mastroiacco TM, Eggleton MU

- Table:

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<thead>
<tr>
<th>Patient cohort</th>
<th>Single-Stage Repair</th>
<th>Two-Stage Repair</th>
<th>P-Value</th>
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<tbody>
<tr>
<td>SCI complications</td>
<td>97.5%</td>
<td>11.7%</td>
<td>0.03</td>
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<tr>
<td>Mortality</td>
<td>18.8%</td>
<td>0</td>
<td>0.52</td>
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Direct Ischemic Preconditioning

First-in-man endovascular preconditioning of the paraspinal collateral network by segmental artery coil embolization to prevent ischemic spinal cord injury

Crown R. E., MD, MS; Giannotta DL, MD, MS; Mithoefer W, MD, MS; and Tice AL, MD, MS

- Preconditioning of collateral network with preoperative selective segmental artery endovascular coil embolization
- Case 1: selective lumbar artery embolization 4-weeks before open repair of TAAA
- Case 2: selective lumbar artery embolization 8-weeks before EV repair of TAAA
Remote Ischemic Preconditioning & Spinal Cord

Remote ischemic preconditioning protects the spinal cord against ischemic insult: An experimental study in a porcine model

- **RCT using porcine model**
- Hindlimb ischemia RIPC
- SC ischemia thru subclavian and segmental artery at the level of the diaphragm
- MEPs

Mechanisms of RIPC

RIPC causes initial oxidative stress, which seems to protect the spinal cord either via neural, humoral, or systemic (immunological) pathways

**Mechanisms of RIPC**

- Tissues exposed to brief periods of ischemia and then reperfusion develop resistance to subsequent more severe ischemic insults
- Short periods of non-lethal ischemia followed by reperfusion of tissue or organ prepare remote tissue or organ to resist a subsequent more severe ischemia-reperfusion injury

**Mechanisms of RIPC**

- Direct
  - Tissues exposed to brief periods of ischemia and then reperfusion develop resistance to subsequent more severe ischemic insults
- Remote
  - Short periods of non-lethal ischemia followed by reperfusion of tissue or organ prepare remote tissue or organ to resist a subsequent more severe ischemia-reperfusion injury
Remote Ischemic Preconditioning
• Despite promising evidence from experimental studies, the clinical effects of RIPC have been controversial
  – Heterogeneity of inclusion and exclusion criteria
  – Confounding factors such as comedication, anesthesia, comorbidities

Remote ischemic preconditioning and thoracoabdominal aneurysm repair: Can an arm save a cord (or legs)?
Mariel Orenstein, MD, MSc; Thomas J. Lindsay, MD(M), MSc; and Thomas L. Forbes, MD
• Only current ongoing RIPC & SC RCT is with cervical decompression
• Pilot study with open and endovascular TAAA repair