# RIPC prior to cardiac surgery

*Dr Derek J Hausenloy*

BHF Senior Clinical Research Fellow
The Hatter Cardiovascular Institute,
University College London, UK.

Honorary Consultant Cardiologist
University College London Hospital, UK.

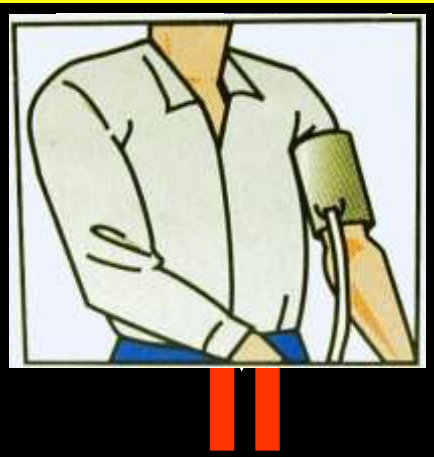
IC Therapeutics Meeting, Monday November 15th 2010.

# Background

- Novel cardioprotective strategies are required to improve clinical outcomes in CHD patients.
- Sicker patients are being operated on.
- CK-MB/Troponin release during CABG surgery linked to worse outcomes. Renal and cerebral outcomes.
- RIPC at proof-of-concept stage.
- Multicentre large randomized clinical trials needed.

# ‘Conditioning’ the heart *remotely*

**Remote Ischemic Preconditioning**



**CABG surgery**
**Cardiac transplant**
**PCI**

**Heart Ischemia**

**STEMI**

**Heart Reperfusion**

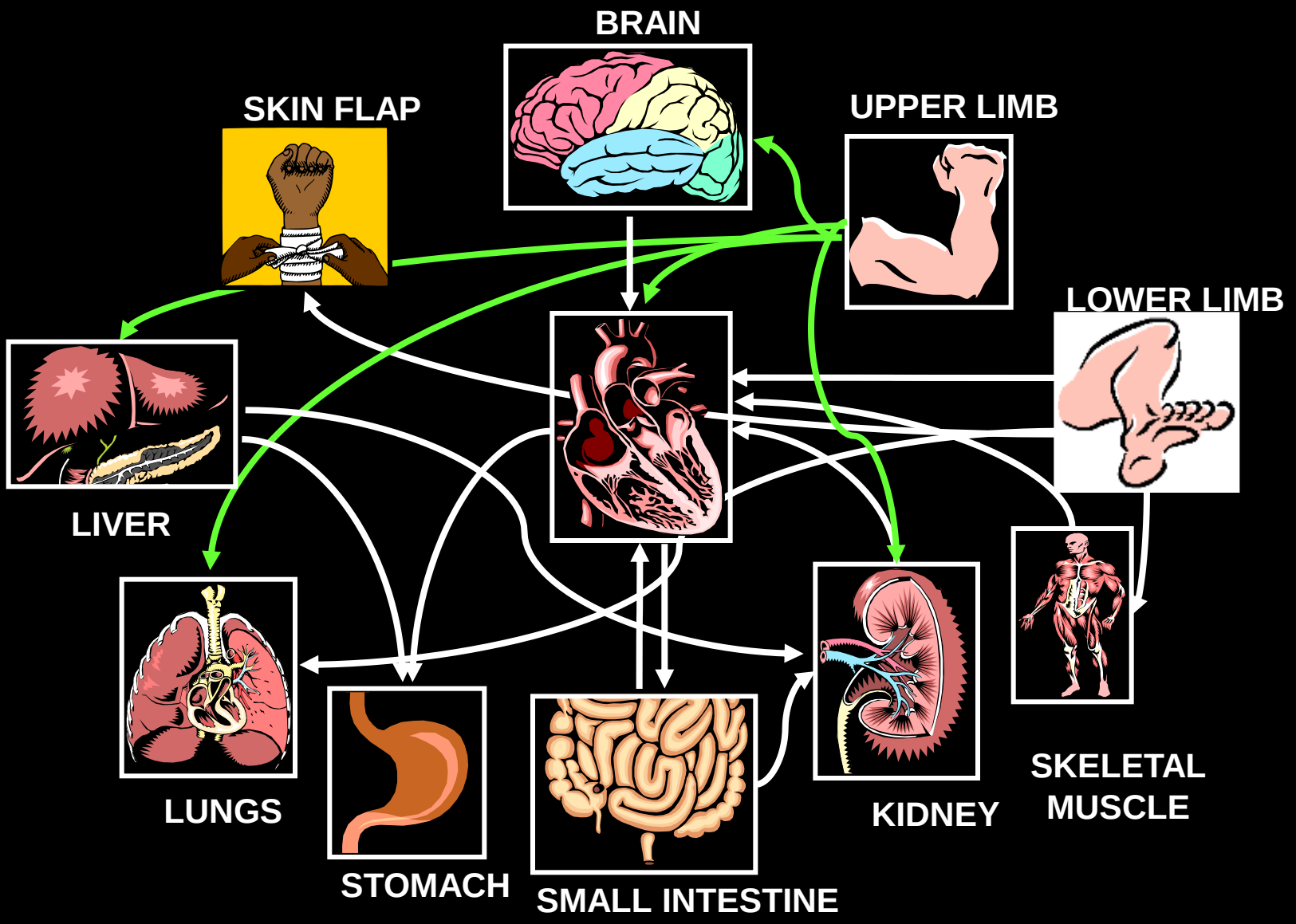
**CABG surgery**
**Cardiac transplant**
**Cardiac arrest**
**STEMI**

**No ‘Conditioning’**

**‘Conditioned’**

# From heart to inter-organ protection

Hausenloy & Yellon Cardiovasc Res 2008:79;377.



# RIPC in paediatric cardiac surgery

Cheung et al JACC 2006:47;2277.

- Complicated surgery with high morbidity.
- 37 children requiring corrective cardiac surgery.
- RIPC comprised inflation of cuff placed on lower limb to 15mmHg>SBP for 4x5 min.
- RIPC improved troponin-I, inotrope requirement and airway resistance.

# RIPC in CABG surgery

Hausenloy et al Lancet 2007:370;575.

- 57 adult CABG patients:
  RIPC- 3x5 min cuff inflation
  Control- 30 min deflated cuff
- RIPC reduced myocardial injury by 43%.
- However, mixture of ICCF and cardioplegia.

Time (h)

# RIPC in CABG patients (cardioplegia)

Venugopal et al Heart 2009 95(19):1567-71

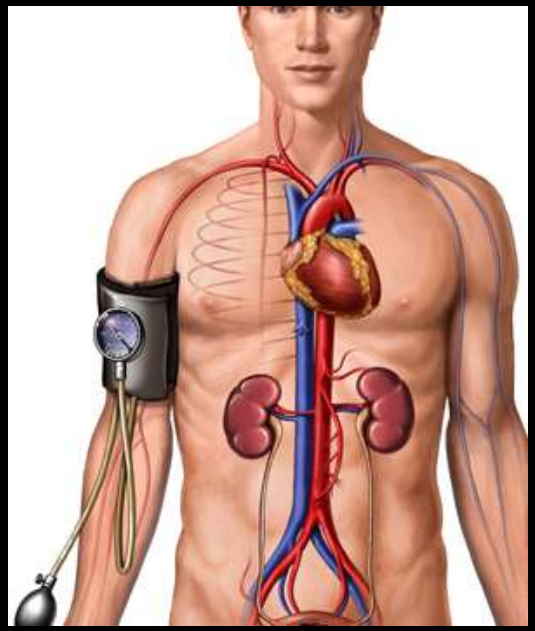
- Cardioplegia only patients.
- 36 adult CABG patients
  RIPC-3x5 min cuff inflation
  Control-30 min deflated cuff
- RIPC reduced myocardial injury by 39% (reduction in trop T AUC over 72 hrs).

# RIPC on renal outcomes

Venugopal et al Am J Kidney Dis. 2010 Oct 23. [Epub ahead of print]

- **A**cute kidney injury (AKI) affects up to 30% of patients undergoing cardiac surgery, with 1%-2% of patients going on to require dialysis therapy.
- 78 adult elective CABG patients randomised to:

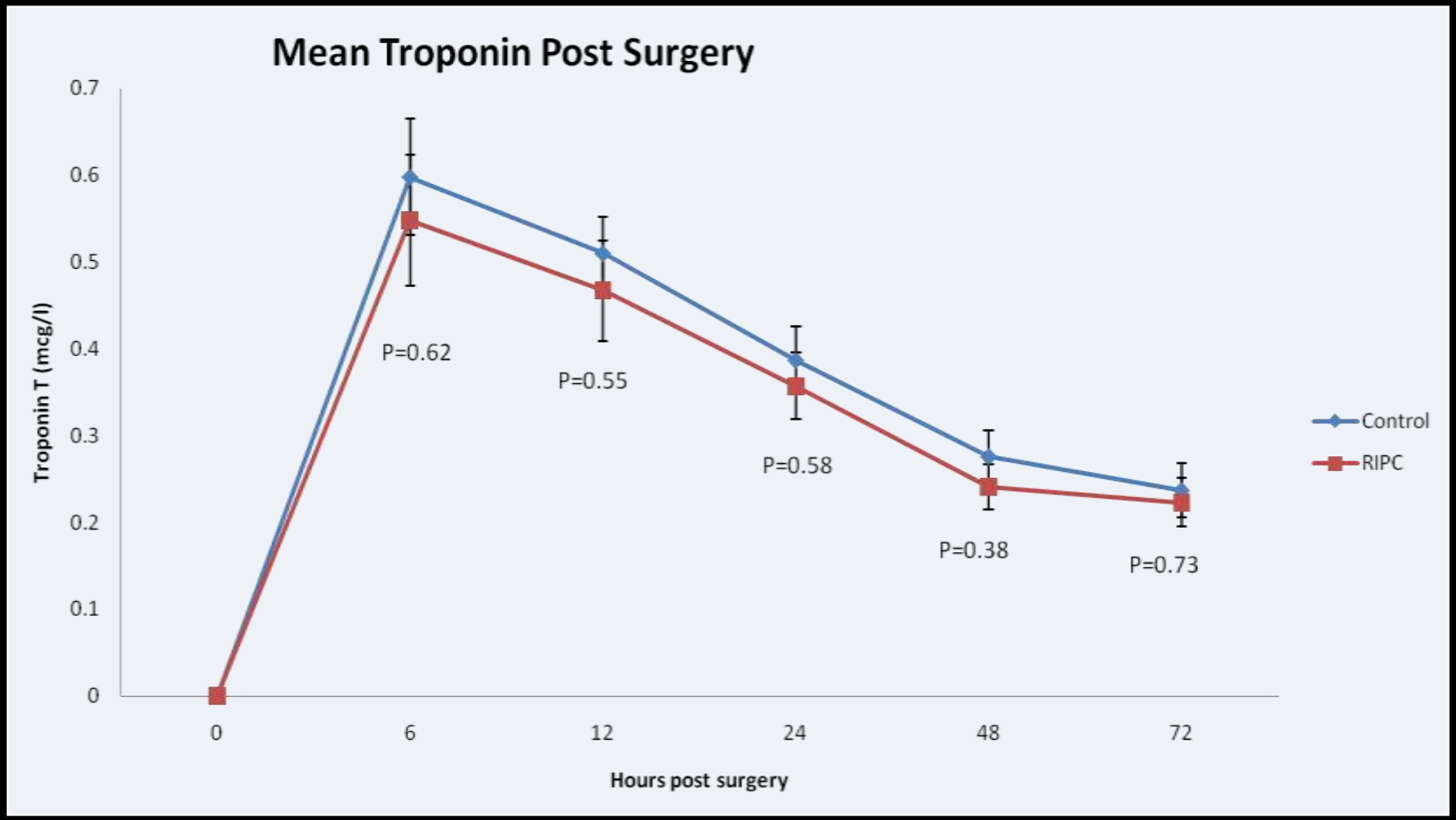
  RIPC-3x5 min cuff inflation Control-30 min deflated cuff
- RIPC reduced the development of AKI from 10/40 patients in control to 4/38 in RIPC-treated patients.



# RIPC in diabetic CABG patients

Babu et al Unpublished

- The diabetic heart is resistant to IPC.
- 55 adult diabetic CABG patients RIPC vs control.
- RIPC had no effect on myocardial injury .



# Summary of RIPC CABG studies

| Study | N | RIC | Pt | Cardio protect | Clamp time | CPB time | Result | Notes |
|---|---|---|---|---|---|---|---|---|
| Cheung et al 2006 | 37 | 4x5 min leg | Children | Cardio | 55,59 | 80,88 | ↓Trop I | |
| Hausenloy et al 2007 | 57 | 3x5 min arm | Adult CABG± valve | CCF and cardio | 45,36 | 80,75 | 43%↓ 72 hr AUC Trop T | |
| Venugopal et al 2009 | 45 | 3x5 min arm | Adult CABG± Valve | Cardio | 65,53 | 97,86 | 42%↓ 72 hr AUC Trop T | No diabetics |
| Gegouskov et al 2009 abstract | 40 | 3x5 min arm | Adult CABG± valve | Cardio | N/A | N/A | ↓6, 24, 48 hr CKMB and Trop T | |
| Thielmann et al 2010 | 53 | 3x5 min arm | Adult CABG | Cryst | 76,71 | 110,109 | 35%↓ 48 hr AUC Trop I | No diabetics |
| Rahman et al 2010 | 162 | 3x5 min arm | Elective urgent CABG | Cardio | 71, 76 | 96,100 | No difference in 48hr Trop T | IV GTN given to most patients. No diabetics. |
| Wagner et al 2010 | 101 | 3x5 min arm 18 hr pre | Elective CABG | Cryst | 51, 45 | 87,80 | ↓Trop I | |

# The ERICCA study

Effect of Remote Ischaemic Conditioning on clinical outcomes in patients undergoing Coronary Artery bypass graft surgery

Hypothesis: RIC improves clinical outcomes in patients (Euroscore>6) undergoing CABG surgery

Design: 11 centre 1610 patient randomised double-blinded RCT

Funding: £1.6 million NIHR/MRC/BHF- EME grant

Primary outcome: Death, MI, revascularisation, stroke at one year.

Secondary outcomes:

- Peri-operative myocardial injury (high-sens Trop-T)
- Peri-operative renal injury (AKI score, blood NGAL)
- Length of ITU/hospital stay and inotrope score
- SMWT, Quality of life, LV ejection fraction

# Why the discrepancy?

Patient selection:

- Routine versus urgent
- CABG±valve
- Diabetics

RIC stimulus:

- Arm versus leg
- Number of cycles
- Applied effectively

Cardiac surgery:

- Isoflurane
- IV GTN
- Cross-clamp and bypass times

# Conclusions

- Remote ischaemic preconditioning has emerged as a non-invasive virtually cost-free strategy for protecting the heart during CABG surgery- proof-of-concept.
- The optimal RIPC protocol and patient group remains to be determined.
- Large multi-centre clinical studies are required to determine whether any effect on clinical outcomes.

# Acknowledgements

Professor Derek Yellon
Dr Vinod Venugopal
Dr Girish Babu
Dr Edney Boston-Griffiths

Staff and patients at the Heart Hospital

British Heart Foundation