

# Remote Ischaemic Preconditioning for Heart Surgery (*RIPHeart-Study*)

- a prospective, randomized, double-blind, multicenter, clinical trial

German Research Foundation (DFG)/  
Federal Ministry of Education and Research  
→ Programme „Clinical Trials“ (ME 3559/1-1)

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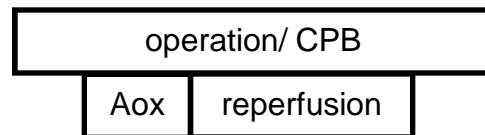


→ Clinical trials: CABG

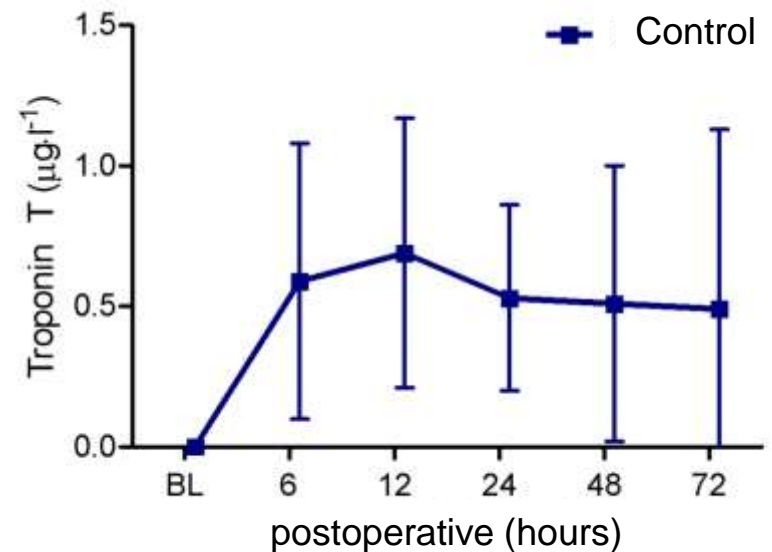
Effect of remote ischaemic preconditioning on myocardial injury in patients undergoing coronary artery bypass graft surgery: a randomised controlled trial

Derek J Hausenloy, Peter K Mwamure, Vinod Venugopal, Joanne Harris, Matthew Barnard, Ernie Grundy, Elizabeth Ashley, Sanjeev Vichare, Carmelo Di Salvo, Shyam Kolvekar, Martin Hayward, Bruce Keogh, Raymond J MacAllister, Derek M Yellon

- CABG (n=57)
- Control group (n=30)



Aox = aortic cross-clamping



**→ Primary endpoint****In-hospital ‚Composite outcome‘**

**1. Mortality:** Death from any cause

**2. Myocardial infarction (MI):**

≤ 72 h postop: „ESC/ACC/AHA“ MI type 5

- i) Troponin T ↑ >5 times the 99th percentile of the normal reference range and
- ii) new pathological Q-waves (or new LBBB) or ischemia (echo) or bypass occlusion.

from day 4: no pre-defined criteria in lokal study centers

**3. Stroke:**

In-hospital NIH-Stroke Scale (NIHSS) ≥ 4

**4. Acute kidney failure:**

≤ 48 h postoperative (= RIFLE – Injury, Failure, Loss):

- i) SCreat ≥2-fold
- ii) urine output ≤ 0,5 ml/kg/h x 12 hr

from day 3: renal replacement therapy

RIFLE= Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease

## → Secondary endpoints

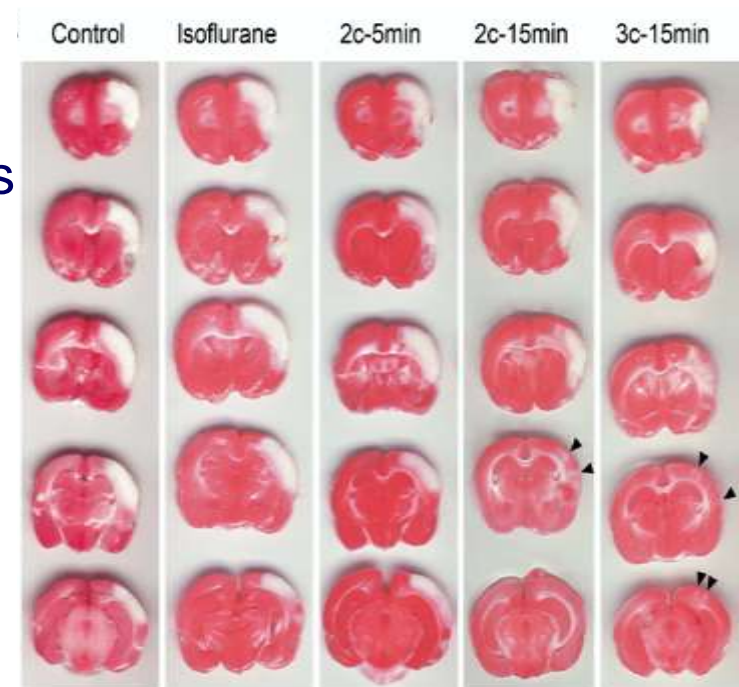
- Cumulative dosage of catecholamines <24hr
- Time of mechanical ventilation
- Length of ICU- and hospital stay
- Myocardial damage (troponin T) <48hr
- Renal dysfunction (creatinine) during hospital stay
- New onset of atrial fibrillation < 72hr
- Extracorporeal life support (ECLS) <30d

## → Postoperative cognitive dysfunction (POCD)

*Neuroscience* 151 (2008) 1099–1103

### LIMB REMOTE-PRECONDITIONING PROTECTS AGAINST FOCAL ISCHEMIA IN RATS AND CONTRADICTS THE DOGMA OF THERAPEUTIC TIME WINDOWS FOR PRECONDITIONING

- permanent lig. of A. cerebri media plus 30 min occl. of Aa. carotis communes
- RIPC via A. femoralis ischemia
- 2x5, 2x15, 3x15 min RIPC
- Infarct size



## → Postoperative cognitive dysfunction (POCD)

### Test battery (preop, 1wk, 3 months)

- Minimal mental state examination
- Rey's Auditory Verbal Learning Test
- PEGBOARD Test
- Trail Making Test
- Stroop Test
- Digit Span
- Symbol Digit Substitution Test
- Verbal Fluency Test
- Beck's Depression Index

→ Power analysis – In-hospital ,Composite outcome‘

Total 2008 (n=64,374)	CABG (n=45,514)	AVR (n=11,160)	CABG/AVR (n=7,700)
Mortality <sup>1</sup>	3.0%	3.3%	5.7%
Stroke	1.2%	1.3%	2.2%
Acute kidney failure <sup>1</sup>	3.2%	4.5%	7.3%
MI <sup>2-5</sup>	2.4% - 7.9% (median 4.7%)		
Composite	~12%	~14%	~20%

- Total event rate in the control group: ~ 12%
- Study aim: relative risk reduction by 1/3 to 8%
- n=931 per group (80% power,  $\alpha=0.05$ ); additional drop-outs of 10%
- **Sample size: 1035 patients per group**

→

1. [www.bqs-outcome.de](http://www.bqs-outcome.de) 2008
2. *J Cardiothorac Vasc Anesth.* 2007;21:502-511 (2,4-5,1%; n=1.853)
3. *N Engl J Med.* 2002;347:1309-1317 (2,8-5,4%; n=5.022)
4. *Eur Heart J.* 2008;29:1548-1559 (3,9-4,2%; n=14.330)
5. *J Thorac Cardiovasc Surg.* 2006;132:392-400 (6,2-7,9%; n=2.666)

**→ Inclusion criteria**

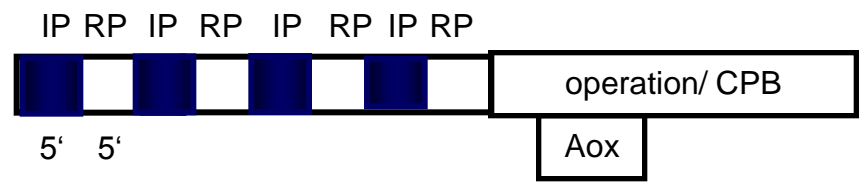
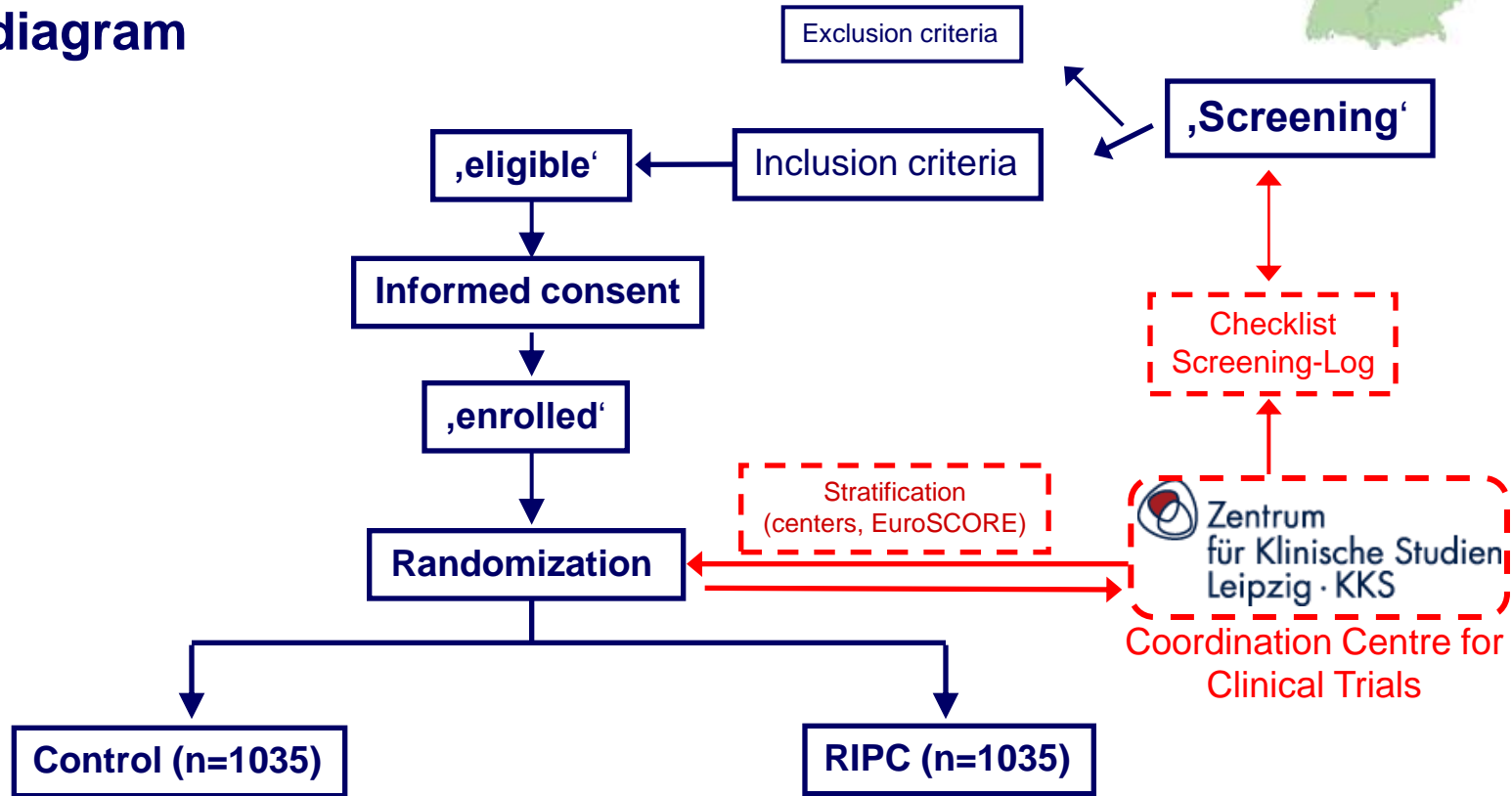
- Any elective cardiac surgery with use of CPB:
  - CABG
  - aortic valve surgery
  - mitral valve surgery
  - Ascending thoracic aorta replacement
  - Major cardiac procedure in addition to CABG
- age  $\geq 18$  yrs
- Informed consent

**→ Exclusion criteria**

1. **Severe kidney disease** (SCreat > 2.0 mg/dl)
2. **Severe liver disease** (INR >1.8/ Bilirubin > 150 µmol/l)
3. **Surgery**: Emergency; Off-pump; minimal-invasive; Arch/ descending aortic replacement; carotid endarterectomy
4. **Atrial fibrillation < 6 months**
5. **Severe lung diseases**
6. Heparin-induced thrombozytopenia type II
7. **Neurological disease** (e.g. M. Parkinson, Multiple Sklerose, Epilepsie, M. Alzheimer, Delir)
8. **Acute infection mit ABs**
9. **MI < 7 days, instable angina < 24 hr and pos. Troponin**
10. **Stroke < 2 months**
11. **Others**



**→ Flow diagram**



IP = ischemic preconditioning  
RP= reperfusion

Aox = aortic cross-clamping

→ Thanks!

