

Remote Ischemic Preconditioning: During STEMI and before PCI

Hans Erik Bøtker, MD, Ph.D., FESC, FACC

Professor of Cardiovascular Medicine

Aarhus University Hospital Skejby

Denmark

Concept of remote preconditioning

Local
remote

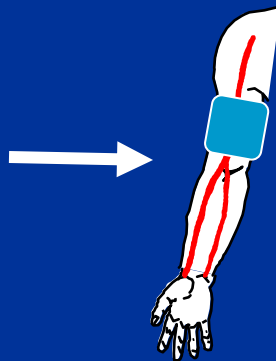


Occlusion
of CX
Infarct size
in LAD



Przyklenk, Kloner et al. *Circulation* 1993;87:893-9

Distant
remote



Four cycles of 5
minutes of limb
ischemia induced by
blood pressure cuff
inflation (200 mm Hg)

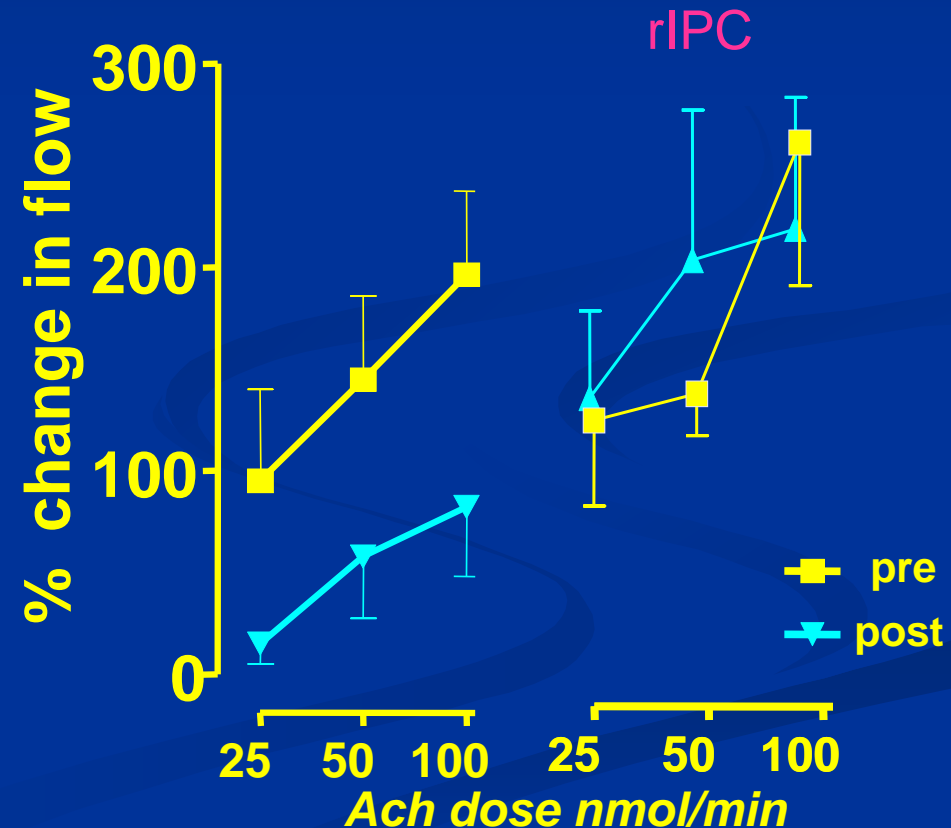
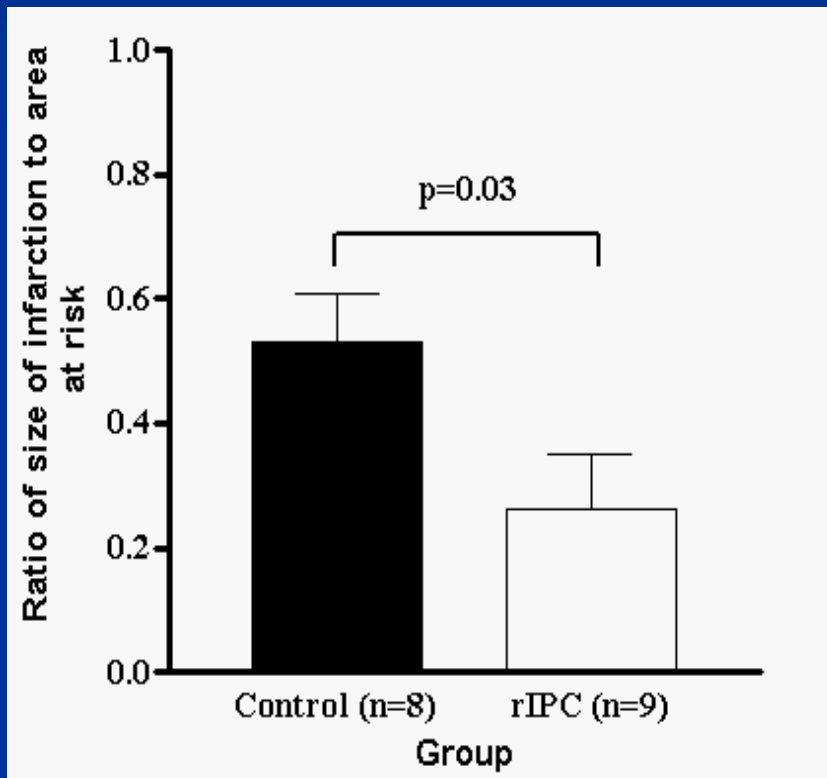


Brinbaum, Dale, Kloner. *Circulation* 1997; 96: 1641-6
Kharbanda et al. *Circulation* 2002;106:2881-3

Activation of endogenous cardioprotection: Remote Preconditioning by limb ischaemia

Animal Infarction model

Human forearm model



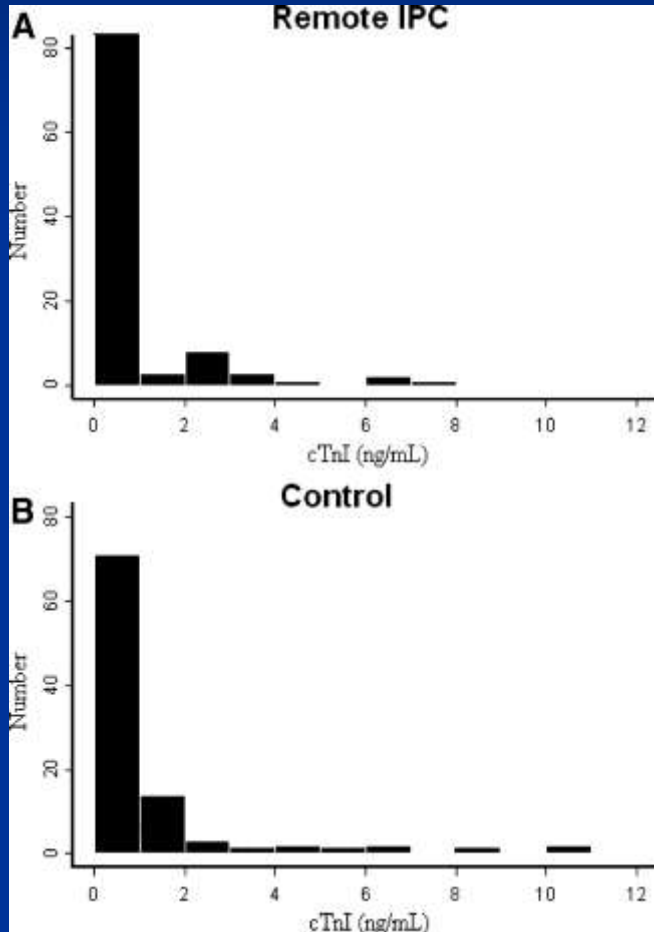
Early translational studies

	Patient group	Stimulus	Outcomes	N
Cheung (2006) ²	Paediatric cardiac surgery	Upper-limb ischaemia (4 cycles of 5 min)	Reduced troponin; reduced inotrope score; reduced airway resistance	37
Hausenloy (2007) ²³	CABG	Upper-limb ischaemia (3 cycles of 5 min)	Reduced troponin	57
Ali (2007) ²⁴	AAA surgery	Lower-limb ischaemia (2 cycles of 10 min)	Reduced troponin I; reduced perioperative MI; preserved renal function	82
Hoole (2009) ²⁵	Elective coronary angioplasty	Upper-limb ischaemia (3 cycles of 5 min)	Reduced troponin I; reduced MACCE	242
Venugopal (2009) ²⁶	CABG (cold-blood cardioplegia)	Upper-limb ischaemia (3 cycles of 5 min)	Reduced troponin	45
Thielmann (2010)	CABG with crystalloid cardioplegic arrest	Upper-limb ischaemia (3 cycles of 5 min)	Reduced troponin	53

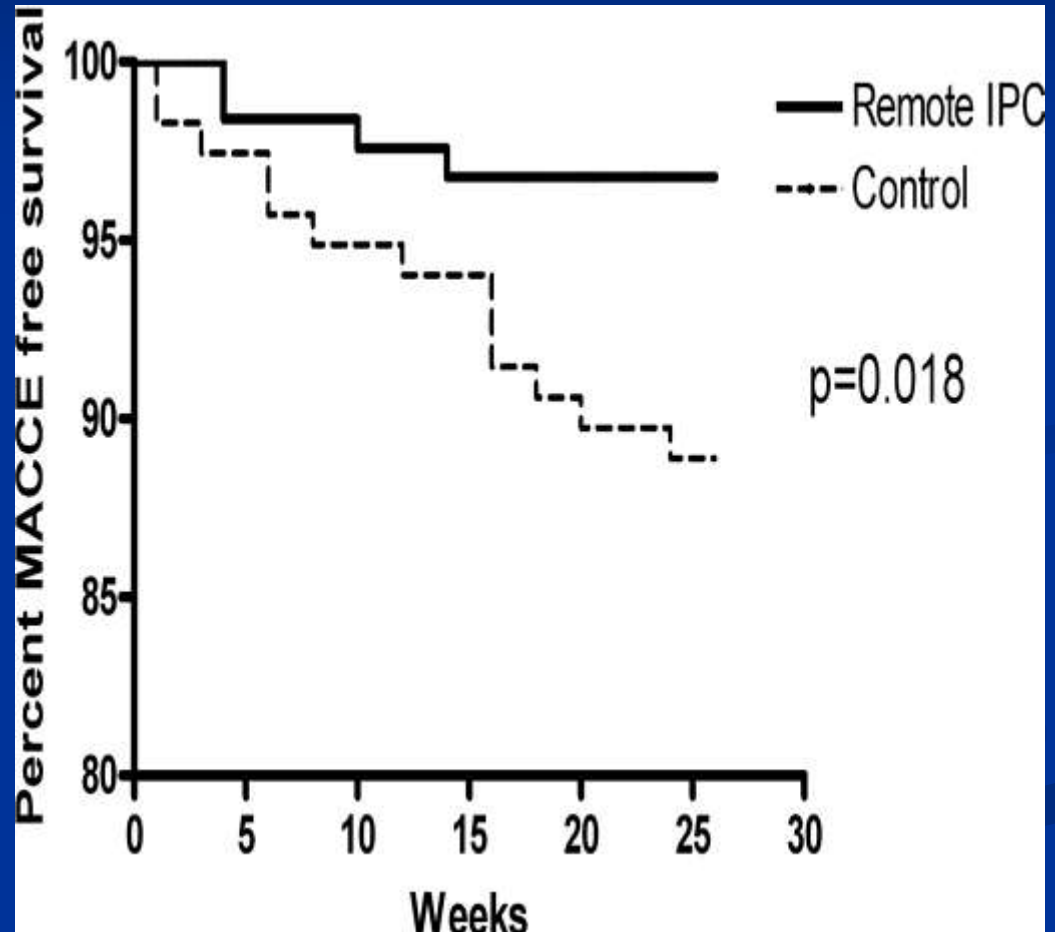
Predictable ischemia

Predictable ischemia: PCI

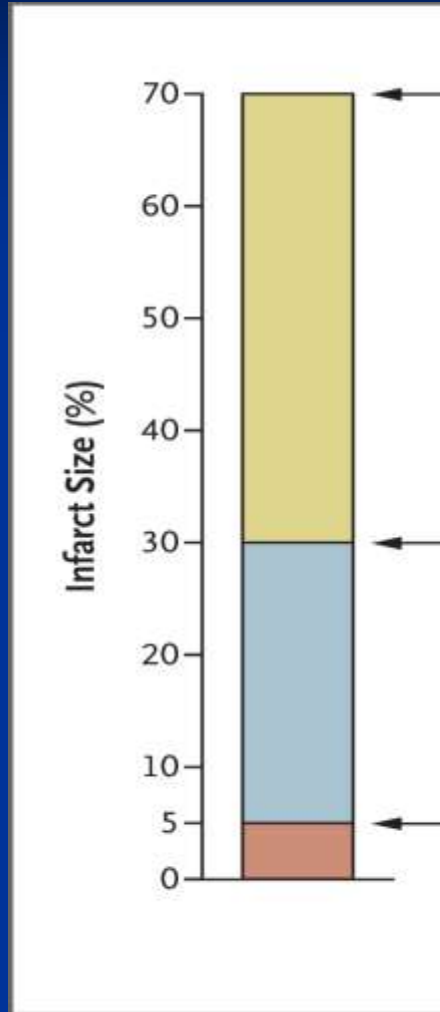
Distribution of 24-hour cTnI in patients after PCI



Kaplan-Meier graph of the MACCE rate at 6 months after PCI in 201 patients



Unpredictable ischemia



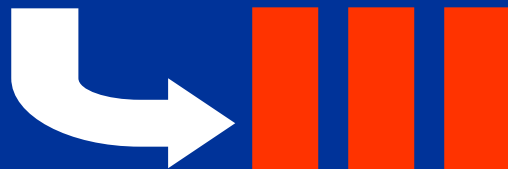
Myocardial infarction
without reperfusion

Myocardial infarction
with reperfusion

Myocardial infarction
with reperfusion and
cardioprotection



The challenge in unpredictable ischemia



Per(i)conditioning (rIPerC) → unpredictable ischaemia

rIPerC during transfer to primary PCI



ECG

Randomization



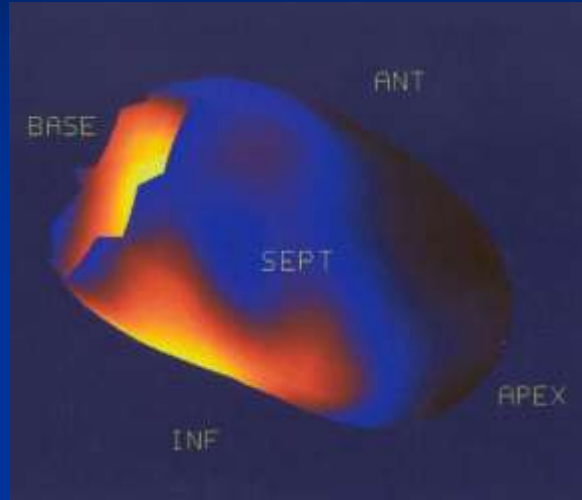
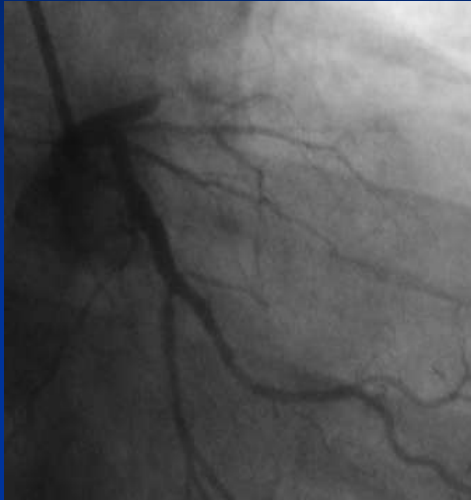
Patient



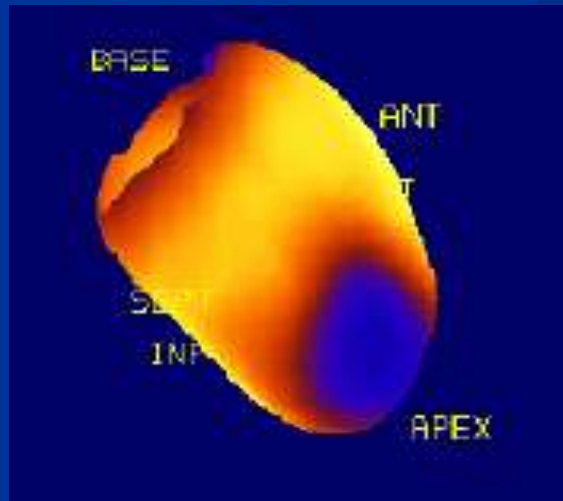
Ambulance



Primary Endpoint: Myocardial Salvage Index



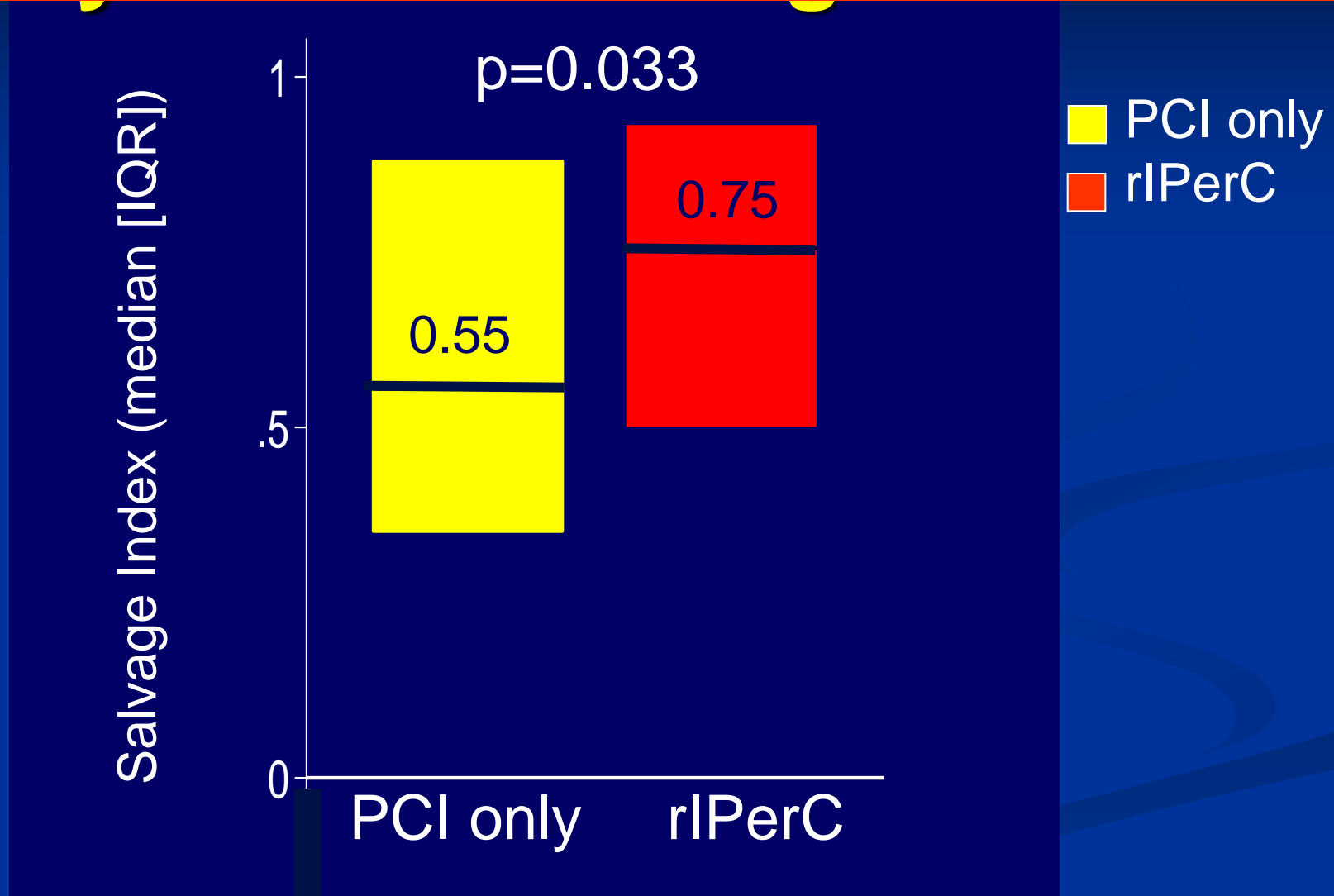
Acute scan:
Area-at-risk
(AAR)



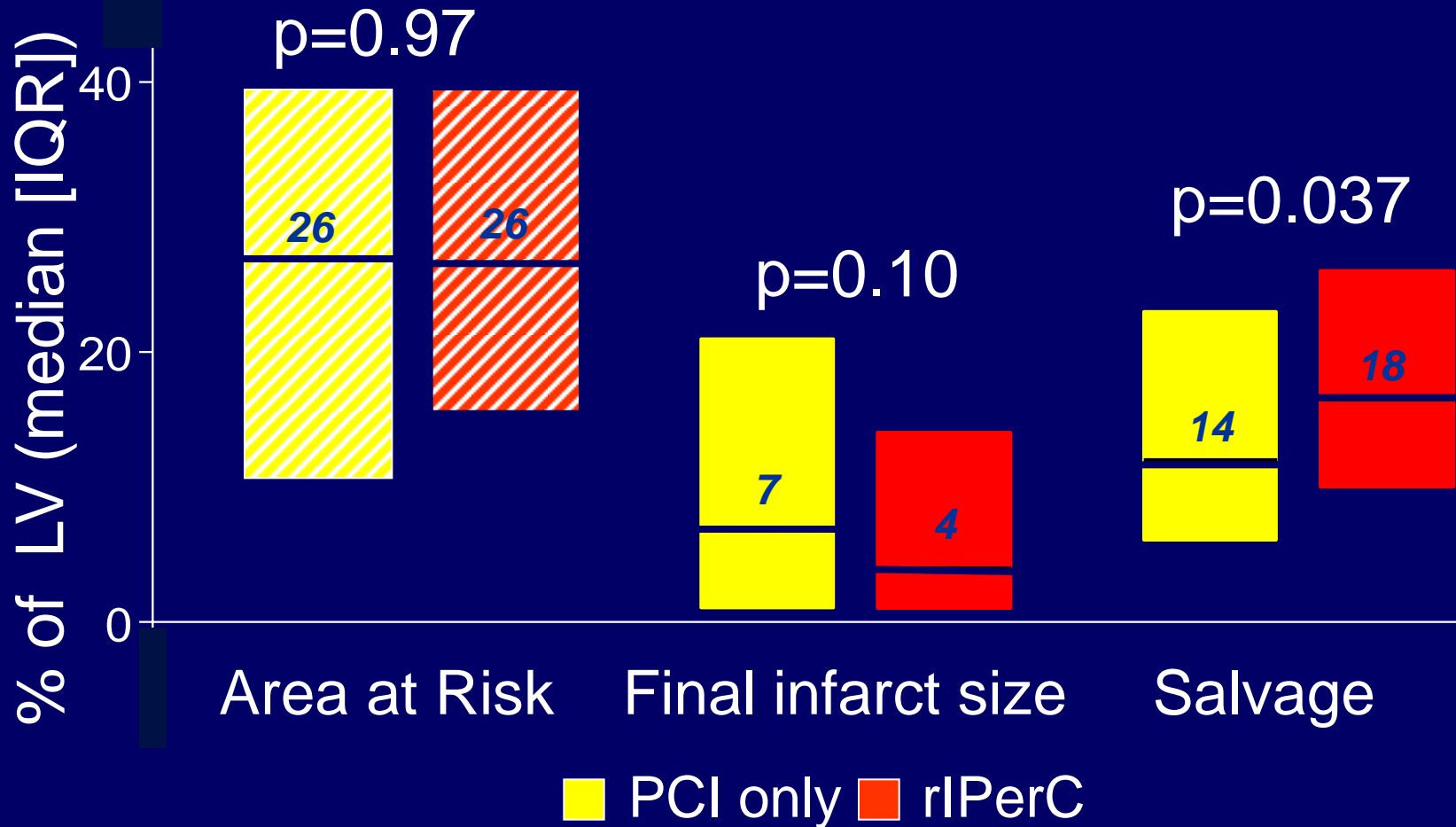
**Salvage index =
(AAR-FIS)/AAR**

One month scan:
Final infarct size
(FIS)

Primary Endpoint: Myocardial Salvage Index

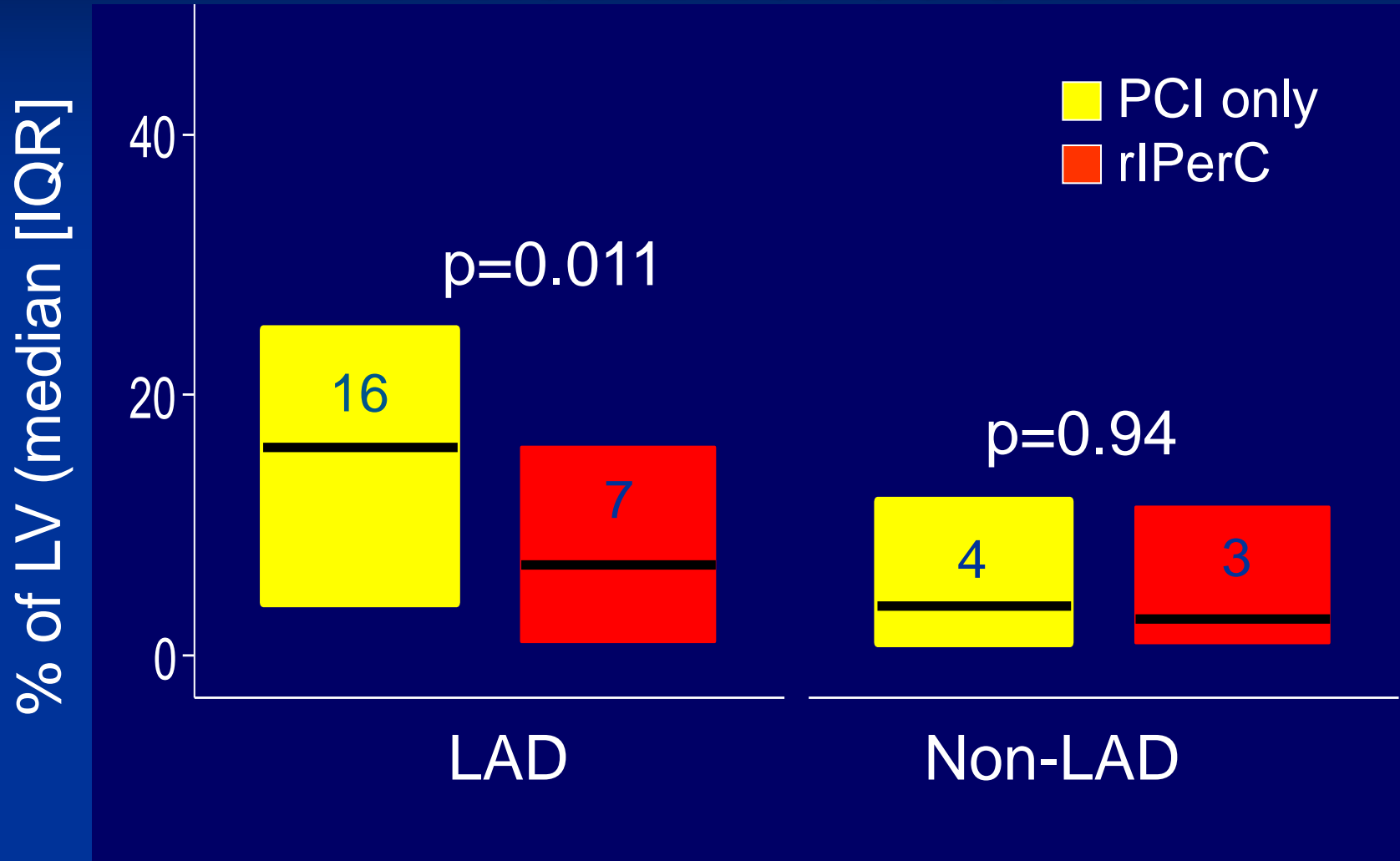


Scintigraphic Data

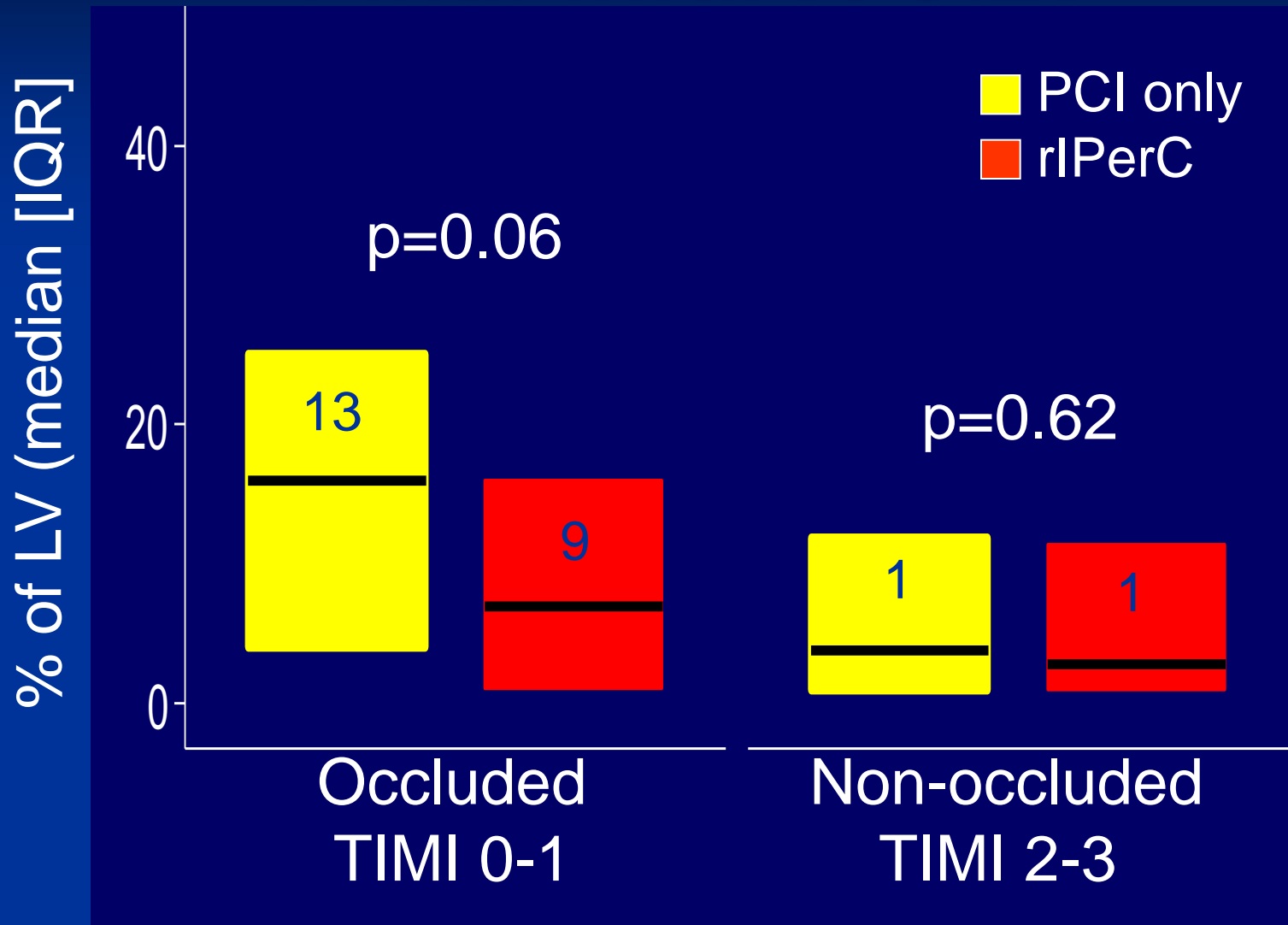


Infarct Location

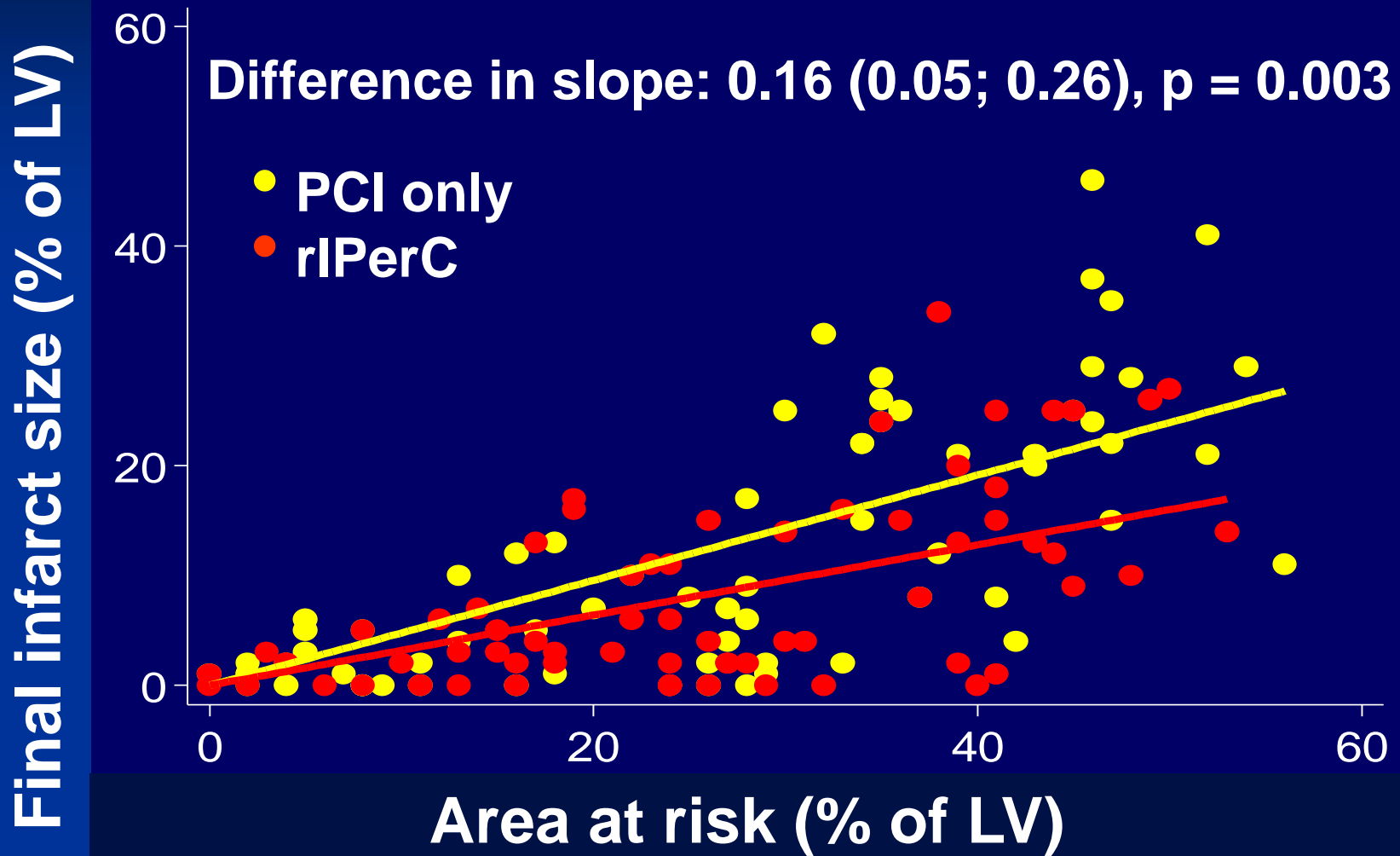
Final Infarct Size



Vessel patency and Final Infarct Size



Relation Between AAR and FIS



Clinical Endpoints and Echocardiography (30-d)

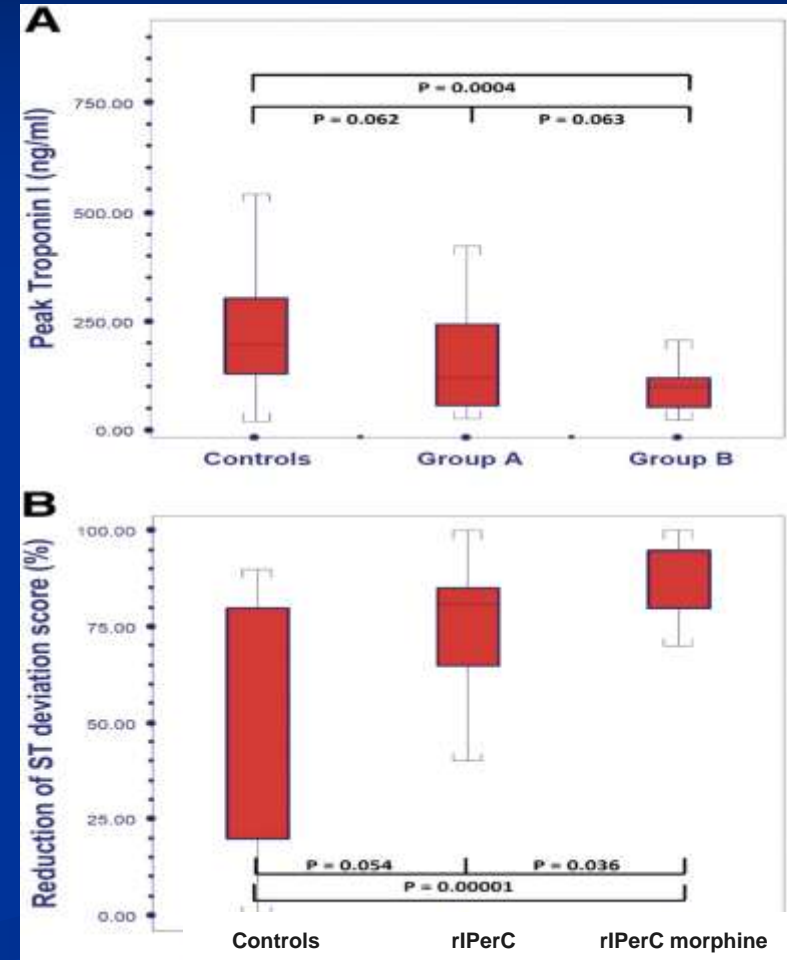
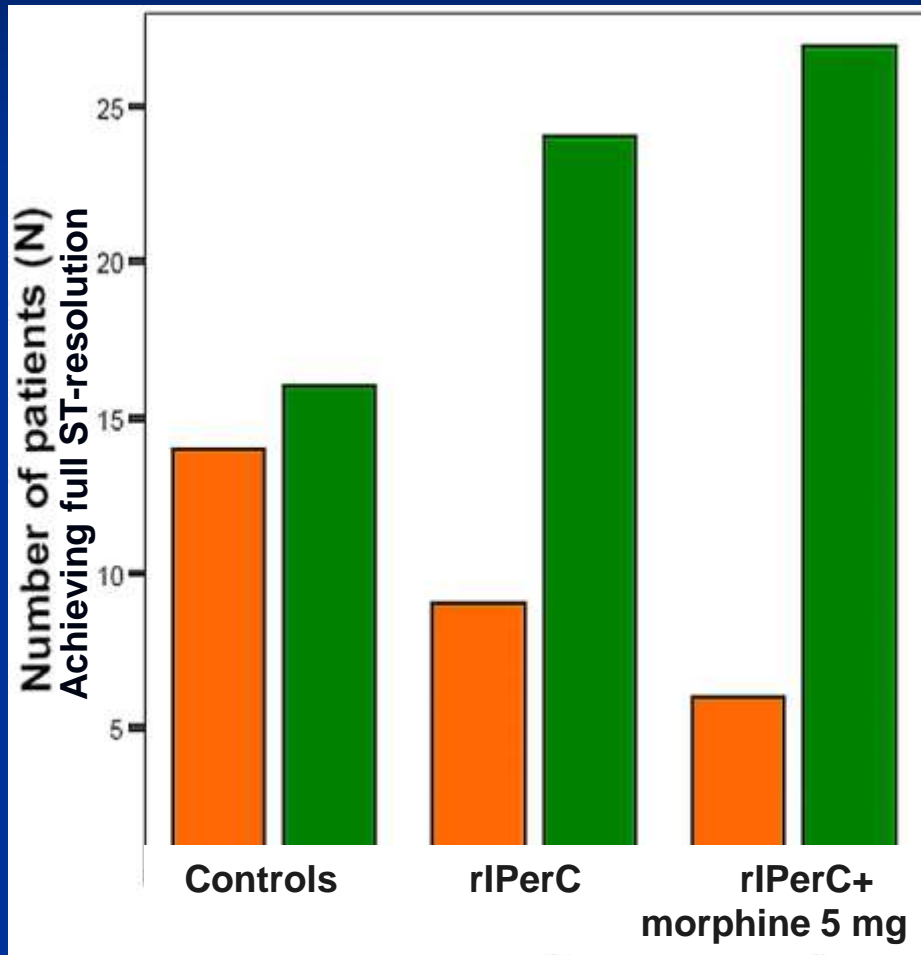
	PCI only (n=125)	riPerC (n=126)	P Value
MACE	3/1/0	3/1/0	1.0
LVEF %	53 [45; 58]	53 [47; 58]	0.73
- LAD	47 [38; 54]	51 [43; 60]	0.18
- Non-LAD	55 [49; 58]	53 [47; 58]	0.39

MACE: (death/reMI/stroke),

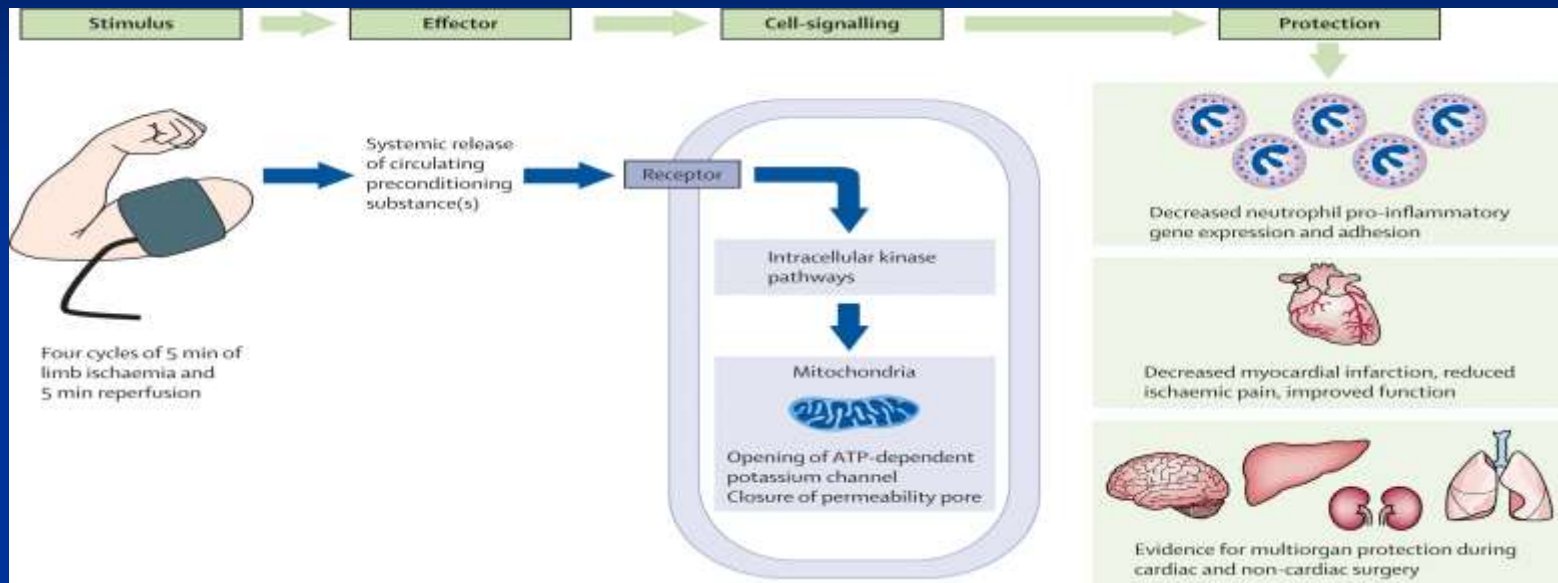
LVEF: Left ventricular ejection fraction estimated by Echocardiography, [median, IQR]

Conditioning and drug treatment

Enhancement by morphine (n=96)



Remote conditioning as an established treatment



- Clinical outcome trials
- Dose/timing of RIPC
- Relation to comorbidity, age and drug treatment
- Other areas – stroke – AAA - transplantation
- Methods – AAR - collaterals

- Mechanisms
- Signalling pathways
- Why are we not conditioned all the time?
- Can we amplify the protection? Combination of conditioning? Drugs?

Conclusions

- Remote ischemic conditioning is feasible
- Remote ischemic conditioning reduces lethal reperfusion injury in predictable as well as unpredictable ischemia
- Widespread use must await demonstration of a clinical benefit in large scale studies and a better understanding of underlying mechanisms