The ERICCA trial

Effect of Remote Ischemic preConditioning on clinical outcomes in patients undergoing Coronary Artery bypass graft surgery:
A multi-center double-blind randomized controlled clinical trial

British Heart Foundation

Efficacy and Mechanism Evaluation programme

MRC Medical Research Council

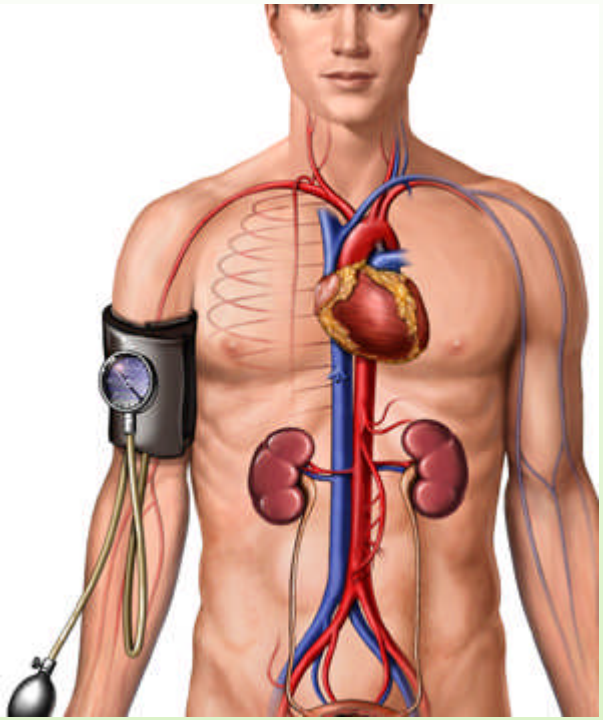
NHS National Institute for Health Research

Rationale

- Higher risk patients undergoing cardiac surgery
- Need for novel cardioprotective strategies
- Remote ischemic conditioning (RIC) can reduce peri-operative myocardial injury (PMI)
- *Can RIC improve long-term clinical outcomes?*

Remote ischemic conditioning

- Cycles of brief ischemia/ reperfusion can protect the heart and other organs
- Simple, non-invasive, low-cost intervention
- RIC potentially reduces PMI by 30 - 40%



1612 patients via 29 UK centres

CABG ± valve on-pump blood cardioplegia / Euroscore ≥ 5

RIC
4 x 5 min cuff inflations / deflations

Sham RIC
4 x 5 min simulated cuff inflations / deflations

Follow-up at one year

Recruitment completed March 2014

Primary combined endpoint

At one year post-randomization

- Cardiovascular death
- MI
- Stroke
- Coronary revascularization

Secondary endpoints

- 30 day MACCE
- Peri-operative myocardial injury
- Inotrope score
- Acute Kidney Injury
- Length of ITU/ Hospital stay

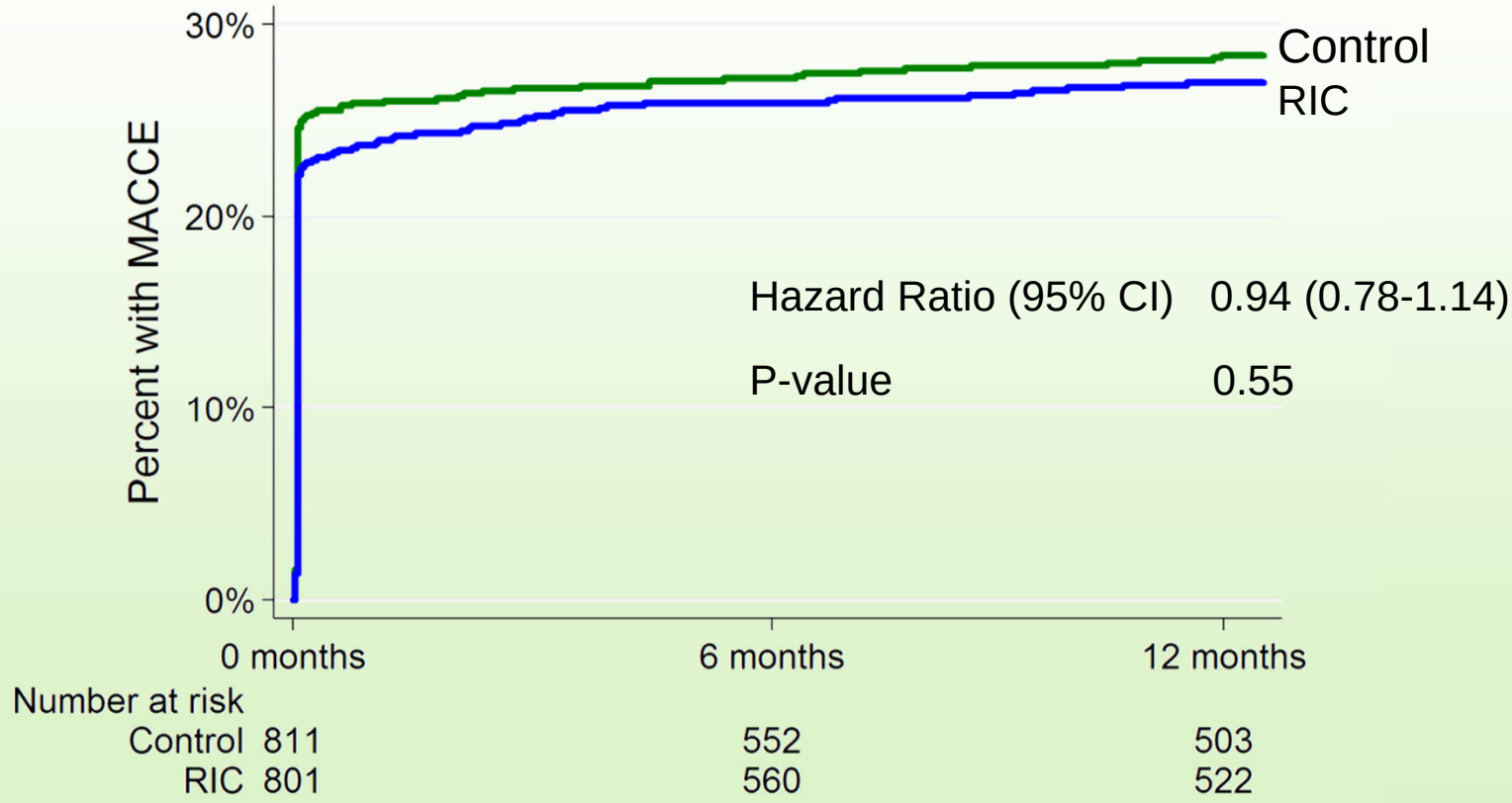
Baseline characteristics

Characteristic	Control N=811	RIC N=801
Male	586 (72%)	556 (69%)
Age (years)	76 (SD 7)	76 (SD 6)
Additive Euroscore	6.7 (SD 1.7)	6.6 (SD 1.6)
LVEF (%)	52 (SD 12)	52 (SD 13)
Diabetes	211 (26%)	203 (25%)
High cholesterol	554 (68%)	570 (71%)
Hypertension	599 (74%)	602 (75%)
Beta-blocker	471 (58%)	479 (60%)
Nitrates	223 (27%)	221 (28%)
Cholesterol-lowering	668 (82%)	641 (80%)
ACE-I	391 (48%)	428 (53%)

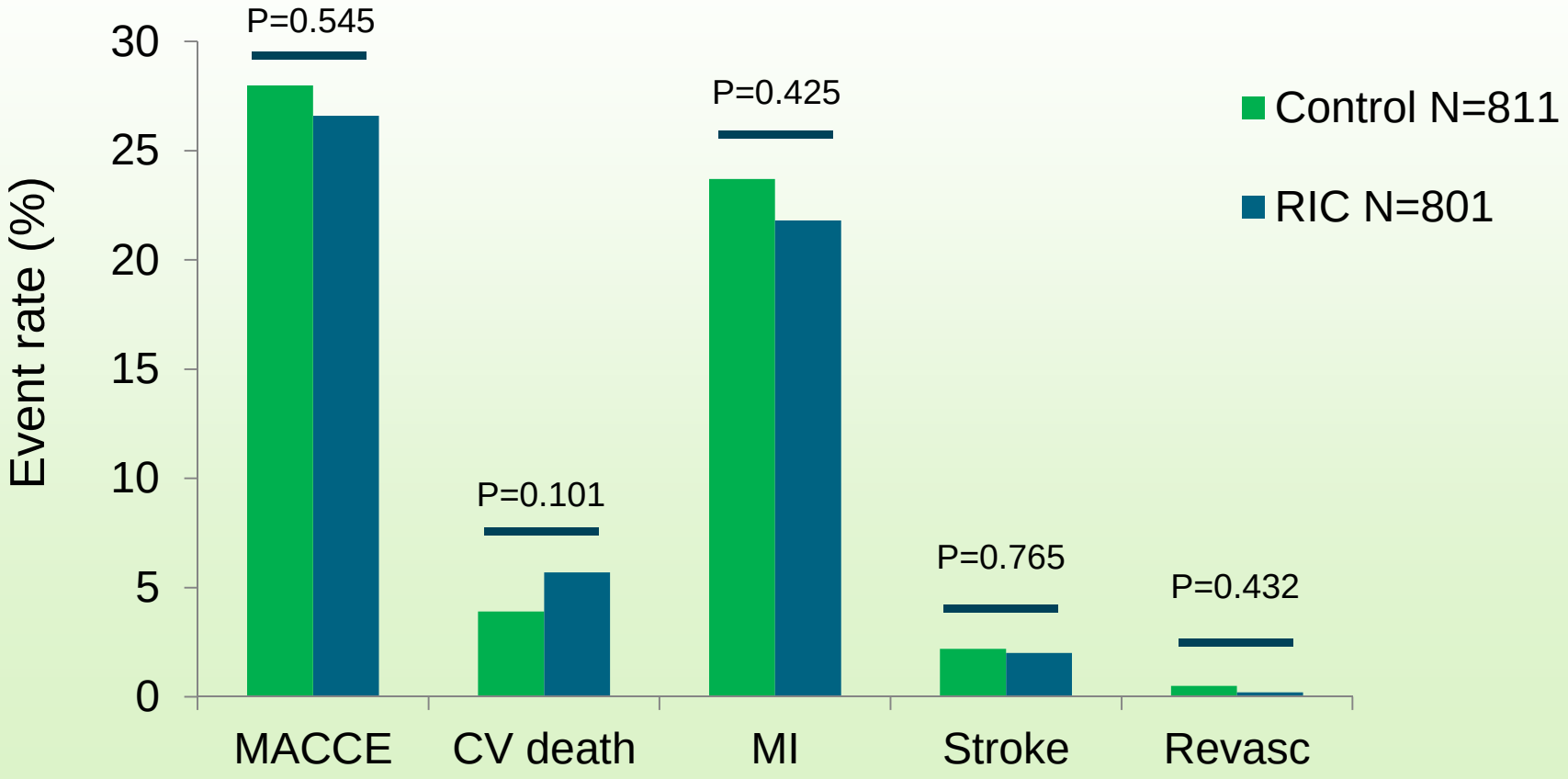
Surgery characteristics

Characteristic	Control N=811	RIC N=801
CABG + valve surgery	406 (51%)	371 (47%)
Cardiopulmonary bypass time (min)	112 (SD 50)	112 (SD 51)
Cross-clamp time (min)	76 (SD 40)	74 (SD39)
Volatile anesthesia (Isoflurane/Sevoflurane)	321 (40%)	324 (41%)
Propofol	706 (87%)	721 (90%)
IV Nitrates	230 (28%)	233 (29%)
Fentanyl	660 (81%)	658 (82%)
Morphine	236 (29%)	241 (30%)

Primary combined endpoint



Primary combined endpoint



Primary combined endpoint

Endpoint	Control N=811		RIC N=801		P-value
	N	%	N	%	
MACCE	227	28.0	213	26.6	0.55
CV Death	32	3.9	46	5.7	0.10
MI	192	23.7	175	21.8	0.43
Stroke	18	2.2	16	2.0	0.77
Revasc	4	0.5	2	0.2	0.43

Secondary endpoints

Endpoint	Control		RIC		P-value
	Med	IQR	Med	IQR	
Peri-operative myocardial injury (72 hr AUC hsTrop-T)	**35,730 N=369**	**22,812-57,207**	**30,500 N=366**	**20,481-54,186**	**0.039**
Inotrope score	**5.6 N=793**	**0.0 -15.5**	**6.0 N=772**	**0.0-14.9**	**0.98**
ITU stay	**3 N=793**	**1-5**	**3 N=779**	**1-4**	**0.22**
Hospital stay	**10 N=793**	**7-17**	**10 N=779**	**7-16**	**0.19**

Secondary endpoints

Endpoint	Control N=772		RIC N=749		P-value
	N	%	N	%	
AKI	293	38	287	38	0.98
Stage 1	226	29.3	230	30.7	
Stage 2	44	15.7	38	5.1	
Stage 3	23	3.0	19	2.5	

Discussion

- Multiple causes of PMI
- Co-morbidities and concomitant medication can affect RIC
- Some neutral small clinical studies
- PMI as a surrogate marker of cardioprotection

Conclusions

- RIC did not improve long-term clinical outcomes in high-risk patients undergoing on-pump cardiac bypass surgery with blood cardioplegia
- In other settings of ischemia/reperfusion injury such as STEMI (CONDI2/ERIC-PPCI) and organ transplantation (REPAIR) the effect of RIC on major clinical outcomes remains to be investigated

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Trial Steering Committee

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Chair: Rajesh Kharbanda

End-point Validation Committee

Chair: Simon Kendall

Recruiting Centres

All patients, research nurses and staff

British Heart Foundation

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