Remote ischaemic preconditioning

Full citation	**Ali ZA, Callaghan CJ, Lim E et al. (2007) Remote ischemic preconditioning reduces myocardial and renal injury after elective abdominal aortic aneurysm repair: a randomized controlled trial. Circulation 116, I98-105**
Study details	Study type: randomised, double-blind trial Location(s): UK Aim(s): to investigate the potential of RIPC on myocardial and renal protection after elective open AAA repair Study dates: February 2003 and December 2005 Follow-up: 7 days Sources of funding: Cambridge University Hospitals NHS Foundation Trust
Participants	Population: patients with AAAs undergoing elective open surgical repair Sample size: 82; 93% (76/82) male Inclusion criteria: patients referred for primary elective open AAA repair were included. No additional information was provided Exclusion criteria: over 90 years of age, needed concomitant procedures other than AAA repair, history of an acute coronary syndrome or myocardial infraction within 3 months, or taking sulfonylurea oral hypoglycaemic agents or nicorandil drug therapy Baseline characteristics: • Mean age: RIPC group, 74 years; control group, 75 years • Sex: RIPC group, 93% male; control group, 93% male • Mean aneurysm size: not reported • History of angina: RIPC group, 24%; control group, 27% • History of hypertension: RIPC group, 51%; control group, 63% • History of diabetes: RIPC group, 5%; control group, 5% • History of hypercholesterolaemia: RIPC group, 39%; control group, 46%
Intervention	Lower limb RIPC: This involved sequential cross-clamping of the common iliac arteries with 10 minutes ischaemia, followed by 10 minutes of reperfusion (RIPC stimulus). In order to reduce the risk of trash foot, sequential cross-clamping was performed to minimise repeat clamping of a single iliac artery. To prevent prolonged operating times, surgeons used a standardised approach whereby the iliac vessels were dissected before the neck of the aneurysm. The right iliac vessel was cross-clamped for 10 minutes followed by reperfusion during which time the left iliac was prepared. The cross-clamp was then placed to the left iliac vessel for 10 minutes and subsequently released, providing a total of 20 minutes of lower limb ischemia. During this time, the remainder of the operative dissection was carried out until the surgeon was prepared to cross-clamp the aorta before opening the aneurysm sac.
Comparison	Conventional open surgical repair without RIPC

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Outcomes measures	Outcomes included length of stay, mortality, myocardial injury, myocardial infarction, renal impairment, and adverse events.
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Patients were randomized by a computer-generated list in randomly sequenced blocks of 5, 6, 8, or 12. 2. Allocation concealment (selection bias): Low risk – Treatment allocations were concealed using numbered, sealed, opaque envelopes. 3. Blinding of participants and personnel (performance bias): Low risk – Patients and data collectors not present in the operating room were blinded of treatment allocations. 4. Blinding of outcome assessment (detection bias): Low risk – Results were compared and analysed by 2 blinded groups of assessors, labelled A and B. 5. Incomplete outcome data (attrition bias): Low risk – No losses to follow-up were reported and all participants were included in the analyses. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified Overall risk of bias: Low Directness: directly applicable

Full citation	**Li C, Li YS, Xu M et al. (2013) Limb remote ischemic preconditioning for intestinal and pulmonary protection during elective open infrarenal abdominal aortic aneurysm repair: a randomized controlled trial. Anesthesiology 118, 842-52**
Study details	Study type: randomised, double-blind trial Location(s): China Aim(s): to assess whether limb RIPC would reduce intestinal and pulmonary injuries in patients undergoing open surgical repair of infrarenal AAAs Study dates: January 2008 to June 2011 Follow-up: 24 hours Sources of funding: Sun Yat-Sen University hospital (self-funded)
Participants	Population: patients with AAAs undergoing elective open surgical repair. Sample size: 62; 90.1% (55/61) male Inclusion criteria: patients less than 80 years who were due to receive open surgical repair. No additional information was provided Exclusion criteria: infarction within 3 months, angina pain within 48 hours of surgery, ejection fraction less than 40%, poor pulmonary function (PaO2 < 60 mmHg), COPD, history of inflammatory bowel disease, history of diarrhoea within 1 week of surgery, or intestinal chronic inflammatory disease Baseline characteristics: • Mean age: RIPC group, 62 years; control group, 67 years • Sex: RIPC group, 93% male; control group, 84% male • Mean aneurysm size: RIPC group, 72 mm; control group, 69 mm • Hypertension: RIPC group, 77%; control group, 58% • Diabetes: RIPC group, 45%; control group, 29% • Previous myocardial infarction: RIPC group, 16%; control group, 26%
Intervention	Upper limb RIPC: A blood pressure cuff was placed on the left upper arm and 3 inflating–deflating cycles were performed. Each cycle consisted of 5 minutes of inflation to 200 mmHg followed by 5 minutes of reperfusion by deflating the cuff. All procedures were consistently performed by the same surgeon.
Comparison	Sham RIPC: an uninflated cuff was placed on the left upper arm for 30 min.
Outcomes measures	The primary outcomes were haemodynamic data and variables reflecting lung function. Secondary outcomes included mortality, ventilator support time, ICU- and hospital-free days; new arrhythmia, perioperative myocardial infarction, diagnosis of congestive heart failure, symptoms and signs of pulmonary congestion, neurologic events, upper limb ischemia requiring intervention,

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	intestinal injury markers, markers of oxidative stress and systemic inflammatory response, and scores of the severity of intestinal and pulmonary injury.
Risk of bias assessment (using Cochrane risk of bias)	1. Random sequence generation (selection bias): Low risk – randomisation was performed by an independent person using a computer random number generator with a 1:1 allocation using blocks of varying sizes. 2. Allocation concealment (selection bias): Low risk – Allocation details were stored in numbered, sealed, and opaque envelopes. Treatment allocation was revealed by anaesthetists opening the envelope on the morning of surgery. 3. Blinding of participants and personnel (performance bias): Low risk – Patients, investigators, surgeons, critical care teams, and individuals participating in data analysis were all blinded to group allocations. 4. Blinding of outcome assessment (detection bias): Low risk – as stated above. 5. Incomplete outcome data (attrition bias): Low risk – No losses to follow-up were reported and all participants were included in the analyses. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Mouton R, Pollock J, Soar J et al. (2015) Remote ischaemic preconditioning versus sham procedure for abdominal aortic aneurysm repair: an external feasibility randomized controlled trial. Trials 16, 377**
Study details	Study type: randomised, double-blind trial Location(s): UK Aim(s): to investigate whether RIPC could be successfully introduced in elective AAA repair Study dates: January 2010 to December 2012 Follow-up: 48 hours Sources of funding: the National Institute of Health Research and the North Bristol NHS Trust
Participants	Population: patients with AAAs undergoing elective EVAR or open surgical repair. Sample size: 69; sex-specific proportions were not reported. Inclusion criteria: patients referred for a primary elective AAA repair (EVAR or open surgery) were included. No additional information was provided Exclusion criteria: patients taking sulphonylurea oral hypoglycaemic drugs or nicorandil were excluded Baseline characteristics: • Mean age: RIPC group, 72 years; control group, 72 years • Sex: not reported • Mean aneurysm size: not reported • Hypertension: RIPC group, 77%; control group, 71% • Ischaemic heart disease: RIPC group, 38%; control group, 26% • Cerebrovascular disease: RIPC group, 18%; control group, 20% • Congestive heart failure: RIPC group, 15%; control group, 3%
Intervention	Upper limb RIPC: A blood pressure cuff was placed on the upper arm (side not specified) and three 10-minute cycles of conditioning were performed. Each cycle consisted of 5 minutes of ischaemia (inflation of a blood pressure cuff to 40 mmHg above the patient's systolic blood pressure) followed by 5 minutes of reperfusion.
Comparison	Sham RIPC: a pressure cuff was inflated for the same periods as the RIPC intervention but only to 40 mmHg.
Outcomes measures	Outcomes included acute kidney injury scores as classified by the acute injury network (AKIN), mortality, myocardial infarction, new postoperative ECG changes, new arrhythmia, troponin T levels above 14 ng/L, and adverse events.
Risk of bias assessment (using	1. Random sequence generation (selection bias): Low risk – Randomisation was performed with a 1:1 allocation, using computer-generated randomisation sequences of varying block sizes and stratified by type of surgery. 2. Allocation concealment (selection bias): Low risk – Allocations were concealed and accessed via a secure password protected.

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Cochrane risk of bias tool)	website and were concealed until sufficient information to uniquely identify the individual had been entered. 3. Blinding of participants and personnel (performance bias): Low risk – With the exception of the in-theatre anaesthetic team who administered the intervention, everyone (participants, surgeons, nursing staff and research nurses) was blinded to the intervention received. 4. Blinding of outcome assessment (detection bias): Low risk – as stated above. 5. Incomplete outcome data (attrition bias): Low risk – All loses to follow-up were adequately explained. Furthermore analyses were performed using an intention to treat approach. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Murphy N, Vijayan A, Frohlich S et al. (2014) Remote ischemic preconditioning does not affect the incidence of acute kidney injury after elective abdominal aortic aneurysm repair. Journal of cardiothoracic and vascular anaesthesia 28, 1285-92**
Study details	Study type: randomised, double-blind trial Location(s): UK Aim(s): to assess the effects of RIPC on renal outcome in patients with AAAs having elective open surgical repair. Study dates: September 2009 to December 2012 Follow-up: 3 days Sources of funding: not reported
Participants	Population: patients with AAAs undergoing elective open surgical repair Sample size: 62; 85.5% (53/62) male Inclusion criteria: adults with AAAs referred for primary elective open surgical repair were included. No additional information was provided Exclusion criteria: myocardial infarction within 2 weeks of surgery, history of upper limb vascular insufficiency, kidney disease requiring renal replacement, or AAAs requiring emergency AAA repair Baseline characteristics: • Median age: RIPC group, 75 years; control group, 69 years • Sex: RIPC group, 94% male; control group, 77% male • Mean aneurysm size: not reported • Previous myocardial infarction: RIPC group, 22%; control group, 13% • Angina: RIPC group, 13%; control group, 16% • Hypertension: RIPC group, 64%; control group, 52% • Hypercholesterolemia: RIPC group, 23%; control group, 16% • Chronic kidney disease: RIPC group, 61%; control group, 55%
Intervention	Upper limb RIPC: A blood pressure cuff was placed on the upper arm (side not specified) and three 10-minute cycles of conditioning were performed. Each cycle consisted of 5 minutes of ischaemia (inflation of a blood pressure cuff to 100 mmHg above the patient's systolic blood pressure) followed by 5 minutes of reperfusion.
Comparison	Sham RIPC: method not specified
Outcomes measures	Outcomes included mortality, kidney injury (measured by creatinine levels and AKIN scores), myocardial infarction, and length of hospital stay.

Full citation	**Murphy N, Vijayan A, Frohlich S et al. (2014) Remote ischemic preconditioning does not affect the incidence of acute kidney injury after elective abdominal aortic aneurysm repair. Journal of cardiothoracic and vascular anaesthesia 28, 1285-92**
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Patients were assigned randomly, using a random number computer generator in a 1:1 ratio for parallel arms 2. Allocation concealment (selection bias): Unclear risk – Allocations were concealed using sealed envelopes. No further details were provided. 3. Blinding of participants and personnel (performance bias): Low risk – Authors do not explicitly state that participants were blinded to group allocations. However, the trial is described as a double-blind trial and it is unlikely that patients would have been aware what was being done to them while under general anaesthesia. 4. Blinding of outcome assessment (detection bias): Low risk – Study investigators, attending anaesthetists and surgical staff were blinded to treatment assignments. 5. Incomplete outcome data (attrition bias): Low risk – Authors presented results based using an intention-to treat approach and presented final follow up results. All participants were accounted for. 6. Selective reporting (reporting bias): Low risk – All relevant outcomes were reported appropriately. 7. Other bias: Low risk – none identified. Overall risk of bias: Low Directness: directly applicable

Full citation	**Walsh SR, Boyle JR, Tang TY et al. (2009) Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 16, 680-9**
Study details	Study type: randomised, non-blinded trial Location(s): UK Aim(s): to determine whether RIPC reduces renal damage in patients with AAAs having elective open surgical repair Study dates: February 2006 to October 2007 Follow-up: 48 hours Sources of funding: The Mouton Charitable Foundation
Participants	Population: patients with AAAs undergoing elective open surgical repair Sample size: 40 men Inclusion criteria: patients with AAAs and no history of acute renal failure, no history of renal replacement therapy, no previous renal transplant, no history of renal disease, serum creatinine values less than 1.5 mg/dL and a serum urea values less than 20 mmol/L were included Exclusion criteria: a history of previous EVAR, a history of a lower limb amputation, or patients scheduled to receive suprarenal aneurysm repairs Baseline characteristics: • Mean age: RIPC group, 74 years; control group, 76 years • Sex: 100% in both arms • Mean aneurysm size: RIPC group, 60.7 mm; control group, 63.9 mm • Diabetes: RIPC group, 17%; control group, 9% • Previous myocardial infarction: RIPC group, 33%; control group, 18% • Angina: RIPC group, 28%; control group, 18% • COPD: RIPC group, 17%; control group, 18% • Hypertension: RIPC group, 44%; control group, 55%
Intervention	Lower limb RIPC: A cross-clamp was applied to the right common iliac artery for 10 minutes. Subsequently, the right iliac territory was reperfused and the clamp was applied to the left common iliac artery. Once each common iliac artery territory had undergone one 10-minute cycle of ischemia followed by 10 minutes of reperfusion, the aorta was cross-clamped and the aneurysm sac was opened.
Comparison	Conventional open surgical repair without RIPC

Full citation	**Walsh SR, Boyle JR, Tang TY et al. (2009) Remote ischemic preconditioning for renal and cardiac protection during endovascular aneurysm repair: a randomized controlled trial. Journal of endovascular therapy : an official journal of the International Society of Endovascular Specialists 16, 680-9**
Outcomes measures	The primary outcome measure was renal function (measured by urine output, urine retinal binding protein, and creatinine levels). Secondary outcomes included 30-day mortality, myocardial infarction, arrhythmia, congestive heart failure, pneumonia, renal failure, lower limb ischaemia requiring intervention, and postoperative length of stay.
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Low risk – Participants were randomised in blocks of 4 using computer-generated sequences. 2. Allocation concealment (selection bias): Low risk – Group allocations were concealed with sealed, opaque, envelopes which were opened on the day of surgery 3. Blinding of participants and personnel (performance bias): Unclear risk – It was unclear whether participants were blinded to treatment allocations. This was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): High risk – Outcome assessors were not blinded of treatment allocations 5. Incomplete outcome data (attrition bias): Low risk – No losses to follow-up were reported in either treatment arm. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Moderate Directness: directly applicable

Full citation	**Walsh SR, Sadat U, Boyle JR et al. (2010) Remote ischemic preconditioning for renal protection during elective open infrarenal abdominal aortic aneurysm repair: randomized controlled trial. Vascular and endovascular surgery 44, 334-40**
Study details	Study type: randomised, non-blinded trial Location(s): UK Aim(s): to determine whether RIPC reduces renal and cardiac damage in patients with AAAs having elective open surgical repair. Study dates: November 2006 to January 2008 Follow-up: 48 hours Sources of funding: The Mouton Charitable Foundation
Participants	Population: patients with AAAs undergoing elective EVAR Sample size: 40; 85% (34/40) male Inclusion criteria: patients with AAAs and no history of acute renal failure, no history of renal replacement therapy, no previous renal transplant, no history of renal disease, serum creatinine values less than 1.5 mg/dL and a serum urea values less than 20 mmol/L were included Exclusion criteria: a history of previous EVAR, a history of a lower limb amputation, or patients scheduled to receive fenestrated or branched aneurysm repairs Baseline characteristics: • Median age: RIPC group, 75 years; control group, 72 years • Sex: RIPC group, 72% male; control group, 100% male • Mean aneurysm size: RIPC group, 67.8 mm; control group, 77.4 mm • Diabetes: RIPC group, 4.5%; control group, 0% • Previous myocardial infarction: RIPC group, 18%; control group, 22% • Angina: RIPC group, 4.5%; control group, 16% • COPD: RIPC group, 4.5%; control group, 5.5% • Hypertension: RIPC group, 54%; control group, 88%
Intervention	Lower limb RIPC: Ischaemia was induced by placing an inflatable tourniquet around the thigh and inflating it until there was no audible doppler signal in either pedal artery. After 10 minutes the cuff was deflated and the procedure was repeated on the other leg.
Comparison	Conventional open surgical repair without RIPC
Outcomes measures	The primary outcome measure was renal function (measured by urine output, urine retinal binding protein, and serum creatinine levels). Secondary outcomes included serum troponin levels and the incidence of major adverse cardiac events (cardiac arrest, cardiac death, cardiac failure, unstable angina, or myocardial infarction).

Full citation	**Walsh SR, Sadat U, Boyle JR et al. (2010) Remote ischemic preconditioning for renal protection during elective open infrarenal abdominal aortic aneurysm repair: randomized controlled trial. Vascular and endovascular surgery 44, 334-40**
Risk of bias assessment (using Cochrane risk of bias tool)	1. Random sequence generation (selection bias): Unclear risk – Participants were randomised in blocks of 4 using computer-generated sequences. 2. Allocation concealment (selection bias): Low risk – Group allocations were concealed with sealed, opaque, envelopes which were opened on the day of surgery. 3. Blinding of participants and personnel (performance bias): Unclear risk – It was unclear whether participants were blinded to treatment allocations. This was unlikely to bias results as objective outcomes were measured. 4. Blinding of outcome assessment (detection bias): High risk – Outcome assessors were not blinded of treatment allocations 5. Incomplete outcome data (attrition bias): Low risk – Authors presented results based using an intention-to treat approach and presented final follow up results. All participants were accounted for. 6. Selective reporting (reporting bias): Low risk – All pre-specified outcomes were reported 7. Other bias: Low risk – none identified Overall risk of bias: Moderate Directness: directly applicable