A clinical study to investigate the effects of remote ischemic preconditioning on cardiac mitochondrial hexokinase in CABG patients

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The aim of this clinical study is to investigate whether RIPC induced cardioprotection is associated with an increased amount of mitochondrial HK (mtHK) in the heart.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON36080

Source
ToetsingOnline

Brief title
mtHK after RIPC in CABG patients

Condition

- Coronary artery disorders
- Cardiac therapeutic procedures

Synonym
cardiovascular disease - heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Hartstichting

Intervention

Keyword: coronary artery bypass, cytokines, Hexokinase, Ischemic Preconditioning

Outcome measures

Primary outcome

Main study parameters are the HK mitochondrial binding ratio and

cardioprotection, evaluated by plasma cardiac troponin T (cTnT) values.

Secondary outcome

Secondary parameters are cytokine (IL-6, IL-10 and TNF-a) levels and inotropic

score. Furthermore CRP will be determined at the same time points as cTnT.

Study description

Background summary

Recent clinical data showed that remote ischemic preconditioning (RIPC) attenuates myocardial damage in cardiac surgery. Although the exact mechanism of RIPC, as well as clinical preconditioning (IPC), is not clear, several pathways have been demonstrated to play a role in cardioprotection. There is evidence that translocation of the glyocolytic enzyme hexokinase II (HKII) to the mitochondria by activation of IPC-associated survival signalling protects the heart against ischemia reperfusion injury. We want to investigate whether RIPC induced cardioprotection is associated with an increased amount of mitochondrial HK (mtHK). Furthermore, the promising role of cytokine IL-6 and CRP release in RIPC will be studied.

Study objective

The aim of this clinical study is to investigate whether RIPC induced cardioprotection is associated with an increased amount of mitochondrial HK (mtHK) in the heart.

Study design

Single centre, randomized, double blind, prospective study.

Intervention

The RIPC protocol exists of 3*5 minutes of limb ischemia, induced by blood pressure cuff inflation of the left upper arm. The first group will receive this treatment after induction of anaesthesia, but before start of surgery (RIPC). A second group will not receive RIPC and will serve as control group.

Study burden and risks

Patients will undergo 3*5 min of limb ischemia during surgery. This protocol has been used safely in previous studies, and, with exception of one study, showed preconditioning in patients undergoing CABG surgery. Possible benefits of RIPC are a reduced release of troponin after surgery, which correlated well with myocardial damage. Previous studies showed no adverse effects or harm of this protocol. A tissue sample of the myocardium is taken during placement of the cardiopulmonary bypass, ensuring that only tissue necessary for correct placement of the cannula for extracorporeal circulation will be removed. Additional blood samples (3 mL) will be taken before RIPC, 3 min after RIPC and at 24 and 48 h after surgery for cTnT and cytokine determination.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients who have to undergo first time elective on-pump CABG without valve surgery
- older than 18 years

Exclusion criteria

- Diabetes or representing with hyperglycaemia (glucose > 8mM)
- increased preoperative cardiac troponin T values
- Unstable angina or angina within 48 hours before infarction
- Concomitant procedures
- Ejection fraction < 40%
- severe COPD
- SaO2 < 90% at room temperature
- Peripheral vascular disease affecting the upper limbs
- Nicorandil use
- Pre-/peri-operative morphin use
- women

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Primary purpose: Basic science

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	05-03-2012
Enrollment:	46
Type:	Actual

Ethics review

Approved WMO Date:	20-05-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-12-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL35879.018.11