Ultrasound contrast agents to facilitate sonothrombolysis in patients with acute myocardial infarction

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Primary objective: Can application of diagnostic ultrasound and microbubbles enhance epicardial coronary recanalization with a lower and safer dose of a thrombolytic agent such as alteplase 50mg when combined with normal care consisting of prasugrel...

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

Summary

ID

NL-OMON39042

Source
ToetsingOnline

Brief title
Sonolysis study

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
acute myocardial infarction

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: KNAW / ICIN

Intervention

Keyword: acute myocardial infarction, sonothrombolysis

Outcome measures

Primary outcome

* The effect of sonothrombolysis on the TIMI flow before primary PCI between

the two patient groups.

Secondary outcome

* Cardiac function on follow-up, based on echocardiographic and MRI data.

Enzymatic curves

Study description

Background summary

The optimal treatment strategy in patients with acute ST-elevated myocardial infarction (STEMI) is immediate restoration of epicardial coronary blood flow. Thrombolytic therapy is the most widely used therapy, however, important limitations are a relatively low recanalization rate, and hemorrhagic complications. Currently, primary percutaneous coronary intervention (PCI) is the treatment of choice in STEMI patients, however, its widespread use is hampered by limited availability of specialized facilities and trained staff. Therefore, there is a need for simpler and low-risk methods for effective recanalization of thrombosed arteries that can be initiated early in the disease process.
In this respect, the application of ultrasound, and ultrasound in combination with thrombolytic agents have been investigated and were found to enhance thrombus dissolution in vitro and in vivo. Recently, in vivo studies using thrombo-occlusive canine and rabbit models demonstrated that ultrasound contrast agents (UCAs) enhance this thrombus dissolving effect of ultrasound, resulting in higher recanalization rates of occluded arteries. We hypothesize that under influence of ultrasound, UCAs enhance dissolution of thrombus in patients with acute ST-elevation myocardial infarction premedicated with a low dose of alteplase, prasugrel, aspirin and heparin.

Study objective

Primary objective:
Can application of diagnostic ultrasound and microbubbles enhance epicardial coronary recanalization with a lower and safer dose of a thrombolytic agent such as alteplase 50mg when combined with normal care consisting of prasugrel, aspirin and heparin?

Secondary objectives:
* To investigate whether ultrasound in combination with UCAs has a beneficial effect on echocardiographic and enzymatic infarct size in patients with acute myocardial infarction pretreated with a low dose of alteplase, prasugrel, aspirin and heparin

Study design

Randomized controlled single blinded multi-center study.

Intervention

Immediately before treatment with primary PCI, patients presenting with an STEMI will be randomized to undergo intravenous infusion of an UCA and diagnostic ultrasound or saline, both for 15 minutes

Study burden and risks

Visits: This study requires four additional visits to the hospital, all other measurements will be performed in the periprocedural period.
Blood samples: No additional measurements beside normal care.
Coronary angiography: During or immediately after ultrasound application, the patient is catheterized and a diagnostic angiogram, and if needed primary PCI, is performed. At the beginning of the procedure, an intravenous bolus of heparin (5000 IU) is given. Angiography is performed by manual injection through the contrast-filled guiding catheter, synchronized to an acoustic heart beat signal, to enable measurement of the TIMI frame count and myocardial blush grade prior to the start of the procedure (20).
Echocardiography: Resting echocardiography is performed minimally 24 hours after primary PCI for assessment of global and regional wall motion. In short, parasternal long axi, parasternal short axis, and three standard apical views will be acquired. Three-dimensional echocardiography is performed with the HP Ie33. Echocardiography will be repeated 6 weeks after presentation.
MRI: Patients are studied on a clinical 1.5 Tesla scanner within 2 to 9 days after primary PCI, and for 4-month follow up. In short, the following parameters are assessed.
Functional Imaging: ECG-gated cine SSFP (Steady State Free Precession) MR images are obtained during repeated breath-holds in the three standard long axis views (four-, three- and two-chamber view). Additional short axis slices are acquired covering the entire left ventricle, to examine regional and global

left ventricular function.
Perfusion Imaging: During i.v. injection of Gd-DTPA first-pass perfusion imaging is performed with a saturation-recovery gradient-echo pulse sequence. Delayed contrast-enhanced images are acquired 10 minutes post-contrast with an inversion-recovery gradient-echo pulse sequence to identify the location and extent of myocardial infarction. The data are obtained with slice locations identical to the functional images.

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

* age 18-80 years
* acute onset (< 6 hours)
* sum ST elevation > 6mm + V3R > 1mm in case of an inferior infarction

* diagnosed with STEMI according to the criteria of the ACC (19)
* initial oral informed consent

Exclusion criteria

* previous myocardial infarction
* clinical instability
* pregnancy / breast feeding
* known pulmonary hypertension (>90 mmHg)
* known allergy to ultrasound contrast agents
* any reason judged by the investigators to hamper inclusion
* Contraindications to alteplase

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-03-2008
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	28-06-2013
Application type:	First submission
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
ISRCTN	ISRCTN32486185
CCMO	NL40613.029.13