MICROVASCULAR RECOVERY USING CONTRAST ULTRASOUND IN ST-ELEVATION MYOCARDIAL INFARCTION - AMBULANCE PILOT STUDY

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Primary objectives: 1. Safety 2. Practical feasibility Secondary objectives: 1. angiographic patency rate before PCI 2. Cumulative ST-segment resolution. 3. myocardial infarct characteristics 4. Myocardial perfusion on contrast echocardiography 5....

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

Summary

ID

NL-OMON49044

Source
ToetsingOnline

Brief title
MRUSMI - Ambulance

Condition

- Coronary artery disorders

Synonym
myocardial infarction and microcirculation

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Donatie Howard Foundation aan VUmc

Intervention

Keyword: Ambulance, Microvascular obstruction, Myocardial infarction, Sonothrombolysis

Outcome measures

Primary outcome

- Safety, assessed by the occurrence of ventricular arrhythmias defined as sustained ventricular tachycardia and/or ventricular fibrillation and the occurrence of shock defined as a systolic blood pressure (SBP) <100mmHg in combination with tachycardia (HR > 100/min), after initiation of sonothrombolysis and before percutaneous coronary intervention.
- Technical feasibility will be assessed by extent of sonothrombolysis completion during ambulance transfer and quality of the images. Sonothrombolysis completion will be measured by counting the number of applied high MI impulses and quality of the images will be assessed by counting the amount of visible segments during sonothrombolysis.

Secondary outcome

- Cumulative ST-elevation resolution
- Angiographic patency rate on coronary angiography
- Myocardial infarct size by delayed enhancement imaging, as well as the salvageability index, defined as the difference between extent of delayed enhancement by Gd MRI and the T2 weighted double or triple inversion spin echo assessment of risk area, divided by the area at risk. Presence and extent of myocardial injury. Scar size, LVEF and other quantitative assessments as function of LV mass/volume.

- Frequency of left ventricular remodeling

- Myocardial perfusion on follow up contrast enhanced echocardiography

- Maximum CPK and troponin

- Occurrence of adverse events (AEs), serious adverse events (SAEs), suspected unexpected serious adverse reactions (SUSARs) and six month event free survival. AE is defined as any untoward medical occurrence in the patient during the intervention period (one hour after sonothrombolysis initiation), whether or not considered causally related to the intervention. SAE is defined as any untoward medical occurrence that at any dose results in a life-threatening situation or death, or requires (prolongation of) hospitalization or results in a persistent or significant disability during 6 month follow up. SUSARs are defined as the occurrence of hypotension, ventricular rhythm disorders, cardiac arrest and/or anaphylaxis within one hour after sonothrombolysis initiation. Six-month event free survival is calculated from treatment initiation to six months afterwards, where events include death, congestive heart failure, life threatening arrhythmias, recurrence of ACS and need for prophylactic defibrillator.

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. Also, peripheral microvascular obstruction often occurs, as part of the microvascular injury pathway. Additional drugs can be administered in this case, but detection of this obstruction is difficult, even with intracoronary measurements using specialized wires. A method by which this microvascular obstruction might be visualized is with ultrasound echocardiography and ultrasound contrast agents (UCAs). Besides the added diagnostic value of ultrasound contrast agents, the application of ultrasound and UCAs with and without thrombolytic agents have been investigated and were found to enhance thrombus dissolution in vitro and in vivo (sonothrombolysis). Pilot studies also demonstrated that ultrasound and microbubbles might have a beneficial effect on the microcirculation in humans. We consider the duration of patient stay in the ambulance as a window of opportunity for the prePCI treatment. Therefore the aim of this pilot study is to examine the safety, feasibility and efficacy of pre-hospital (ambulance) sonothrombolysis for STEMI patients.

Study objective

Primary objectives: 1. Safety 2. Practical feasibility
Secondary objectives: 1. angiographic patency rate before PCI 2. Cumulative ST-segment resolution. 3. myocardial infarct characteristics 4. Myocardial perfusion on contrast echocardiography 5. left ventricular remodeling 6. maximum CPK/troponin levels

Study design

The MRUSMI Ambulance Trial will be a single center safety and feasibility pilot study, comparing prehospital sonothrombolysis and post-PCI sonothrombolysis versus standard care in STEMI patients. There will be no control group in this study. Instead we will use the patients randomized to the control group from the MRUSMI post-PCI study, to set our results in perspective. The study will be carried out in one of the ambulances of the ambulance station in Zaandam and in the Amsterdam UMC - Location VUmc. A mobile echocardiography device will be installed in the ambulance and vials of ultrasound contrast agents (Luminity ®) and the vial activator (shaker) will be present in the ambulance. Education of all emergency and ambulance staff in the ambulance post in Zaandam will be required prior to study initiation, to ensure all eligible subjects are allowed to participate and no delays in conventional therapy administration occur as a consequence of participation. Ambulance staff will be trained to perform parasternal short axis contrast ultrasound echocardiography and a physician researcher will accompany ambulance personnel while including the first few patients. Patients with STEMI who meet the inclusion criteria will be asked by the physician researcher (and later on the ambulance personnel) to participate in the MRUSMI ambulance study. This will only be asked if confirmation of STEMI has taken place via Lifenet (system in which the ambulance ECG is faxed to the hospital and interpreted by a physician, the physician confirms the STEMI ECG

and allows for the ambulance to bring the patient to the catheterization laboratory). Obtaining informed consent in this way will ensure the subject is receiving adequate information about the research protocol and yet treatment in a timely fashion.
The patient will be informed about the study orally, as in the MRUSMI post PCI trial:

*Beste mevrouw/ meneer,
Wij doen onderzoek naar een extra behandeling met echogeluid en microbellen bij patiënten met een hartinfarct. Wij willen onderzoeken of deze behandeling een beschermend effect heeft op de kleine vaten van het hart. De behandeling bestaat uit het toedienen van microbelletjes via het infuus en het gelijktijdig maken van een echo van het hart. Deze behandeling vindt nu plaats en duurt ongeveer tot aankomst in het ziekenhuis. Het onderzoek geen significante risico*s.

Na de behandeling krijgt u van ons een brief met nadere informatie en kunt u deze rustig doornemen en vragen stellen indien nodig.

Zou u willen meedoen met het onderzoek?*

If oral informed consent is given, the intervention will be given approximately 30 minutes or until arrival at the hospital.The system utilized in the ambulance will be the CX 50 Portable ultrasound system (Philips Healthcare) operating at 1.8 MHz using the low MI mode with intermittent high MI impulses. Upon arrival in the hospital standard care procedures will be performed (CAG + PCI). After PCI, patients will be informed about the study and will be given opportunity to ask about the protocol and to give written informed consent. There will be no active randomization, instead patient outcomes will be compared with the outcomes of the control group of the MRUSMI trial. Note that all patients receive sonothrombolysis in the ambulance. The follow up examinations are contrast enhanced echocardiography at 3-4 months, CMR at week 1 and after 6-8 weeks.

Intervention

Sonothrombolysis: contrast enhanced echocardiography with intermittent high MI impulses (see above)

Study burden and risks

Use of ultrasound contrast agent with very small risk of allergic reaction and reperfusion rhytm disturbances. The study will be performed in a safe environment in the ambulance and on the coronary care unit. Instable patients (cardiogenic shock etc.) will be excluded
An extra MRI will be made and an extra contrast echocardiography.

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 presenting with STEMI with:, - >= 2mm ST-segment elevation in 2 anterior or lateral leads; or
- >= 1 mm ST-segment elevation in 2 inferior leads
- >= 1mm ST-segment elevation in lateral leads (I, aVL, V5, V6)
AND
- Within 12 hours of symptom onset
- Age >= 30 years
- Adequate apical and/or parasternal images by echocardiography

Exclusion criteria

- Previous coronary bypass surgery
- Cardiogenic shock
- Known or suspected hypersensitivity to ultrasound contrast agent used for the study
- Known bleeding diathesis or contraindication to glycoprotein IIB/IIIA inhibitors, anticoagulants or aspirin
- Known large right to left intracardiac shunts

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-08-2020
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Ultrasound probe and machine
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Luminity/Definity
Generic name:	perflutren-containing lipid microspheres
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	31-01-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-02-2020
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
EudraCT	EUCTR2019-001883-31-NL
CCMO	NL69980.029.19