Clinical Outcome and Cost-effectiveness of Reduced Noradrenaline by Using a Lower Blood Pressure Target in Patients with Cardiogenic Shock from Acute Myocardial Infarction: A Multicenter Randomized Trial

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This study has been transitioned to CTIS with ID 2024-510892-40-00 check the CTIS register for the current data. The objective of this study is to evaluate the (cost-)effectiveness of reduced noradrenaline in patients with CS by using a lower MAP...

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

Summary

ID

NL-OMON56427

Source
ToetsingOnline

Brief title
NORSHOCK

Condition

- Coronary artery disorders

Synonym
Cardiogenic shock, heart attack

Research involving

Human

Sponsors and support

Primary sponsor: Cardiologie
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMw

Intervention

Keyword: Infarction, Noradrenaline, Shock

Outcome measures

Primary outcome

Composite end-point of all-cause mortality and severe renal failure within 30

days.

Secondary outcome

All-cause mortality

Length of hospital stay

Length of ICU stay

Enzymatic infarctsize

Vascular complications

Arrhythmias

Neurological outcome

Study description

Background summary

Yearly around 6000 patients in the Netherlands suffer from cardiogenic shock (CS) due to acute myocardial infarction (AMI) and this number is increasing based on demographic developments. Mortality in CS is still as high as 50%. CS occurs after large AMI causing loss of function of the heart muscle. The poor pumping function leads to a state with low blood flow to end-organs with

subsequent multi-organ failure with
high mortality rates. Renal failure and subsequent renal replacement therapy occur due to low blood flow to the kidneys and is a surrogate marker for end-organ perfusion and a strong predictor for death in CS.

The first-line pharmacologic strategy in CS is noradrenaline, as recommended by scientific statements. Noradrenaline is a vasopressor drug routinely used in the treatment of CS, in the assumption that maintaining a mean arterial blood pressure (MAP) >= 65 mmHg will improve myocardial and organ (e.g.renal) blood flow. However, there is no evidence that noradrenaline improves patient outcomes. Firstly, pharmacologically induced improvement of blood pressure has not been associated with better survival. Secondly, there is no evidence that an increase in MAP, if achieved by noradrenaline, leads to greater myocardial and other end-organ blood flow. As a matter of fact, its vasoconstrictive properties reduce flow
to the microcirculation of the organs as can be frequently seen by discoloring of skin in patients treated with noradrenaline. And lastly, noradrenaline is associated with adverse events such as (supra-)ventricular arrhythmias that reduce the efficacy of the myocardial pumping function and increase the myocardial oxygen demand. This can lead to expansion of the myocardial infarction and worsening of the heart muscle function.

The current, scientifically weak recommendation for noradrenaline (Class IIb) is based on one study that compared noradrenaline with dopamine in a population with all types of shock. The overall trial was neutral and only in a small subgroup a trend was reported towards lower 28-day mortality and less arrhythmias in CS patients treated with noradrenaline. However, there are serious methodological concerns as randomization was not stratified and the test for subgroup differences suggests that the effect was likely based on chance. In light of the aforementioned limitations the optimal first-line treatment and MAP target in CS remains unclear.

Study objective

This study has been transitioned to CTIS with ID 2024-510892-40-00 check the CTIS register for the current data.

The objective of this study is to evaluate the (cost-)effectiveness of reduced noradrenaline in patients with CS by using a lower MAP target of >= 55 mmHg, compared to usual care. We hypothesize that reduced use of noradrenaline will improve overall survival and decrease renal failure requiring renal replacement therapy. A combined clinical endpoint of mortality and renal replacement therapy is an accepted endpoint for CS. The need for cost-effectiveness analysis relies on the fact that we expect that reduced use of noradrenaline is safe and effective and will therefore reduce costs.

Study design

An open label, multicenter randomized controlled trial to ensure level 1 evidence for superiority of the intervention. The usual care arm will provide a reliable basis for the cost-effectiveness analysis. Patients will be randomly assigned (1:1) to the intervention or usual care group.

Intervention

Reduced administration of noradrenaline by using a lower blood pressure target (mean arterial pressure >= 55 mmHg).

Study burden and risks

Patients included in this study will not be exposed to additional investigations that are not part of standard care. They are however requested to fill out questionnaires at four moments in time.
Patients in the interventional arm will be exposed to a lower blood pressure. In order to ensure safety, organ functions will be closely monitored. Patients in the ususal care arm might unnecassary be exposed to noradrenaline and its accompanying side-effects.

Contacts

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Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

'Planned early revascularization'
'Systolic blood pressure <90mmHg for > 30minutes, OR use of drugs to maintain SBP>90 mmHg at presentation before randomization'
'Signs of pulmonary congestion'
'4. Signs of impaired organ perfusion with at least one of the following criteria:
a) Altered mental status
b) Cold, clammy skin and extremities
c) Oliguria with urine output <30ml/hour
d) Serum lactate >2.0 mmol/L'

Exclusion criteria

'Resuscitation >30 minutes'
'No intrinsic heart action'
'Cerebral deficit with fixed dilated pupils (not drug-induced)'
'Mechanical cause of cardiogenic shock'
'Onset of shock >12 hours'
'Massive lung embolism'
'Shock due to other cause (bradycardia, sepsis, hypovolemia, etc.)'

Study design

Design

Study phase:	4
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-10-2022
Enrollment:	776
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Norepinephrine
Generic name:	Norepinephrine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	13-04-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2022
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-02-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	03-04-2023
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Approved WMO
Date: 06-04-2023

Application type: Amendment

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Approved WMO
Date: 21-07-2023

Application type: Amendment

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Approved WMO
Date: 25-07-2023

Application type: Amendment

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Approved WMO Date:	17-08-2023
Application type:	Amendment
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Approved WMO Date:	23-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	27-11-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO Date:	04-12-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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
EU-CTR	CTIS2024-510892-40-00
EudraCT	EUCTR2021-005551-36-NL
ClinicalTrials.gov	NCT05168462
CCMO	NL79416.018.21