Effect of a machine learning-derived early warning system for hypotension vs standard care on depth and duration of intra- and postoperative hypotension in elective cardiac surgery - The HYPE-2 Randomized Clinical Trial

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Does HPI with diagnostic guidance affect severity of hypotension (defined as MAP

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51117

Source
ToetsingOnline

Brief title
HYPE-2

Condition

- Other condition

Synonym
Hypotension, low blood pressure

Health condition

Hemodynamiek, intraoperatief en tijdens intensive care opname

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Edwards lifesciences,Edwards Lifesciences;Irvine CA;USA

Intervention

Keyword: Cardiac surgery, Hypotension, Intesive care, Machine learning

Outcome measures

Primary outcome

The overall TWA of hypotension during both the off-pump phases of on-pump CABG surgery and the mechanically ventilated phase of post-operative ICU admission (or 8 hours maximum)

Secondary outcome

All secondary objectives will be analyzed for the overall duration of both the off-pump phases of on-pump CABG surgery and the mechanically ventilated phase of post-operative ICU admission (or 8 hours maximum):

• Incidence of hypotension

• Time spent in hypotension

• The percentage of time in hypotension

• The area under the curve (AUC) of a MAP <*65*mmHg

• The above-mentioned parameters including TWA will also be assessed for hypertension and for the HPI alarms. For hypertension and HPI alarm the area above the curve (AAT) will be calculated instead of the AUC, see Figure 6.

• Treatment choice (i.e., vasopressors, blood transfusions, fluids, inotropes,

position changes, decrease in anesthetics)

• Treatment dose

• Time to treatment. If an alarm or hypotensive event had more than 1 treatment, the time to first treatment will be used.

• Number of treatments

Exploratory outcomes

The above mentioned analyses will be repeated for specific time periods of the intervention phase including: the off-pump phases of on-pump CABG surgery; the pre-pump phase of on-pump CABG surgery; the post-pump phase of on-pump CABG surgery; the mechanically ventilated phase of post-operative ICU admission (or 8 hours maximum) and the fist hours after HPI and diagnostic guidance are disconnected?

In addition we will look the relation between TWA of hypotension and biomarker levels (CKMB, NT-proBNP, Lactate, Scvo2, Hematocrit and creatinine) and feasibility of working with the HPI and diagnostic guidance (assessment by number of- and reason for protocol deviation).

Study description

Background summary

Hypotension during cardiac surgery and post-operative intensive care unit (ICU) admission is associated with adverse outcomes. Yet, hypotension in the operating room (OR) and post-operative ICU admission is common. In a recent study performed in non-cardiac surgical patients in our center, we found that up to 60% of patients endured hypotension (defined as MAP below 65 mmHg) during anesthesia for an average of 10% of surgery time. The incidence of hypotension

in post cardiac surgery patients admitted to the Intensive Care Unit (ICU) of our center was, with 84%, even higher (unpublished data PHYSIC 1 study, conducted in the ICU of the Amsterdam UMC, location AMC). Hypotension is preventable, however, current management of hypotensive episodes is predominantly reactive and rather occurs with delay. Edwards Lifesciences (Irvine, CA) has developed an algorithm using continuous invasively-measured arterial waveforms to predict hypotension with high accuracy minutes before blood pressure actually decreases, the so called Hypotension Prediction Index (HPI). Two randomized controlled trials (RCT) in non-cardiac surgery have shown significant reduction in hypotension when HPI with diagnostic guidance was compared to standard care. No difference in median TWA of hypotension was found in another clinical RCT. However, in the latter, HPI with diagnostic guidance was associated with less hypotension when analysis was restricted to episodes during which clinicians intervened. Hence, poor protocol compliance in this trial is the most likely cause of the insignificant results. HPI has never been tested in cardiac surgery patients or patients admitted to the ICU. We hypothesize that the use of this algorithm will reduce hypotension as measured by the time weighted average (TWA) during the off-pump phase of on-pump coronary artery bypass graft (CABG) surgery (excluding cardiopulmonary bypassp pump time) and the mechanically ventilated duration of post-operative ICU admission.

Study objective

Does HPI with diagnostic guidance affect severity of hypotension (defined as MAP<65 mmHg) during both the off-pump phases of on-pump CABG surgery and the mechanically ventilated phase of post-operative ICU admission (or 8 hours maximum)?

Study design

This is a single center randomized controlled trial.

We will randomize the participants into two arms:

1) Treatment arm: HemoSphere Advanced Monitoring Platform (HemoSphere) with Acumen IQ sensor with HPI software. The treating cardiac anesthesiologist/anesthesia nurse (operating room) and critical care nurse/intensivist (intensive care) are trained to use Acumen IQ variables and HPI. Advanced hemodynamic variables provided by the HemoSphere include SVR, SVV, SV(I), CO/CI, dp/dt, Eadyn. The treating anesthesiologist, anesthesia nurse, intensivist and critical care nurse is provided with guidance by means of a flowchart suggesting when to treat and what the cause of hypotension is. Timing of treatment and choice of treatment is then left to the discretion of the attending anesthesiologist, anesthesia nurse or intensivist. In the ICU a nurse driven protocol will be provided, describing the suggested treatment per

cause of hypotension for the critical care nurses.

2) Conventional arm: Institutional Standard of Care with an intention to keep MAP equal to or above (>=) 65 mmHg. Standard hemodynamic monitoring for CABG patients during OR and ICU stay in our institutions includes: MAP, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate and pulse pressure variation (PPV). The HemoSphere with Acumen IQ sensor will be connected to collect data but the HemoSphere monitor will be covered completely for the treating physicians and nurses (anesthesiologist, anesthesia nurse, intensivist and critical care nurse). Timing and choice of treatment is conform current clinical practice (and thus left completely to the discretion of the attending anesthesiologist, anesthesia nurse, intensivist and critical care nurse).

Intervention

The intervention used in the treatment arm will consist of: HemoSphere with Acumen IQ variables including HPI and diagnostic guidance. HPI will be calculated via Acumen IQ sensor connected to the radial arterial line. The treating anesthesiologist, anesthesia nurse, intensivist and critical care nurse is trained to understand HemoSphere parameters and the meaning of HPI. The treating anesthesiologist, anesthesia nurse, intensivist and critical care nurse is provided with guidance concerning timing of treatment (HPI > 75) and the causes of hypotension. HPI values above 75 translate to a 75% of hypotension to occur in the following minutes. HPI values between 50-75 translates approximately to a 50-75% change of hypotension to occur in the following minutes. When HPI falls in the 50-75 range the study investigator starts diagnosing the cause of pending hypotension via the secondary screen. The secondary screen of the HemoSphere provides the investigator and treating anesthesiologist, anesthesia nurse, intensivist and critical care nurse with variables such as dp/dt, dynamic elastance, systemic vascular resistance as well as stroke volume, cardiac output and stroke volume variation. If HPI reaches >75, treatment is suggested to be started and the investigator informs the anesthesiologists of the most likely cause of hypotension. The anesthesiologist, anesthesia nurse and intensivist treat the patient based on these suggestions but may choose to deviate from the study protocol if deemed necessary in both timing as well as treatment. The critical care nurse also treats the patient based on these suggestions but treatment options are described in a nurse driven protocol. The critical care nurse may also choose to deviate from the study protocol if deemed necessary in both timing as well as treatment, but treatment options are limited to those described in the nurse driven protocol.

Study burden and risks

There are no additional risks associated with the use of the HemoSphere other

than described in the Instructions for Use. The study participants allocated to treatment according to de HPI algorithm will receive diligently titrated vasopressors, inotropes or fluids minutes before hypotension is predicted to occur. These treatment options are not different to conventional therapy. The anesthesiologist, anesthesia nurse, critical care nurse and intensivist treats the patient based on our suggestions but may choose to deviate from the study protocol if deemed necessary in both timing as well as treatment.
Theoretically, early treatment may lead to (transient) hypertension (MAP>100). However, no increase in TWA of time spent in hypertension (defined as MAP > 100mmHg) was observed in a RCT, comparing HPI with diagnostic guidance to standard care (Wijnberge, JAMA, 2020). In addition, no differences in the incidence of serious complications, including cardiac arrhythmia, was found. No other potential adverse events are expected from participation in this trials.

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

• Aged 18 years or older at inclusion
• Planned for elective on-pump CABG surgery or CABG with additional single heart valve surgery (e.g. valve repair or replacement)
• Planned to receive standard monitoring for cardiac surgery
• Target MAP of 65 mmHg or above during surgery (excluding pump time) and mechanically ventilated duration of ICU admission

Exclusion criteria

• Known cardiac shunts (significant)
• Severe cardiac arrhythmias (including but not limited to persistent atrial fibrillation prior to surgery)
• Expected to receive a hemodynamic assist device (e.g. intra-aortic balloon pump) during surgery
• Dialysis dependent kidney failure prior to surgery
• Planned to receive Perioperative Goal Directed Therapy (PGDT) other than standard intraoperative care
• Previous cardiac surgery in medical history

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2021
Enrollment:	130
Type:	Actual

Medical products/devices used

Generic name:	Hypotension prediction indicator (HPI) algorithm
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	26-04-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-07-2021
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

ID: 22510
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL76236.018.21
OMON	NL-OMON22510

Study results

Date completed:	17-03-2023
Actual enrolment:	142