The effect of proactive versus reactive treatment of hypotension on postoperative disability and outcome

Gepubliceerd: 22-03-2021 Laatst bijgewerkt: 18-08-2022

The hypothesis of this study is that a proactive strategy keeps the blood pressure at a safe margin and avoids dropping below the minimal acceptable threshold of a MAP of 65 mmHg. This proactive strategy may improve postoperative disability and...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25882

Bron
NTR

Verkorte titel
PRETREAT

Aandoening

Intraoperative hypotension, postoperative disability and outcome

Ondersteuning

Primaire sponsor: University Medical Center Utrecht, The Netherlands
Overige ondersteuning: ZonMW Goed Gebruik Geneesmiddelen

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary outcome is disability at six months after surgery, measured by the 12-item World Health Organization Disability Assessment Score (WHODAS) 2.0 scale. The WHODAS scale records difficulties experienced in different functional domains including, cognition, mobility, self-care, getting along, life activities and participation during the previous 30 days. Disability is defined as a decrement in each functioning domain corresponding to score between 0% and 100%, in which no disability stands for a score of 0% and full disability represents a score of 100%, including death. The WHODAS 2.0 is easy to use and patient centered. In a validation study including non-cardiac surgical patients, the WHODAS 2.0 has been found to be a clinically acceptable, valid, reliable and responsive instrument for measuring postoperative disability. Moreover, as multiple organ systems are susceptible to low organ perfusion, the primary endpoint of the study should reflect the variation in possible adverse effects of IOH, not only a specific organ injury due to possible hypoperfusion. Hence, the primary endpoint is measured with the 12-item WHODAS 2.0 scale. The primary endpoint will be collected using Castor EDC.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
Over 1.4 million surgical procedures are performed every year in the Netherlands, of which one million under general or regional anaesthesia. Unfortunately, surgery is not without complications. A risk factor for complications that commonly occurs during surgery under anaesthesia is low blood pressure (hypotension). Anaesthesiologists have been using cardiovascular drugs since the emergence of large-scale anaesthesia to treat hypotension, but despite those efforts, in more than 75% of surgical procedures (approximately 750.000 procedures per year) patients have one or more episodes of hypotension (a Mean Arterial Pressure (MAP) below 65 mmHg). Patients with more and greater blood pressure fluctuations have a greater chance of their blood pressure dropping below the currently advocated minimal acceptable threshold of a MAP of 65 mmHg.
A stricter blood pressure management to prevent hypotension in a larger population is not straightforward. Applying the right drug in an appropriate amount at an appropriate time is surprisingly challenging.
The current paradigm of blood pressure management is predominantly reactive: blood pressure is treated when it approaches a specified minimally acceptable threshold (for example MAP 65) or when it is rapidly dropping. From a risk perspective it makes more sense to shift the paradigm to a proactive approach: setting higher blood pressure thresholds so that the anaesthesiologist will intervene earlier to keep the blood pressure at a certain margin above the specified blood pressure threshold. Patients at greater risk of severe blood pressure fluctuations need to be kept at a higher target blood pressure to keep them above the threshold. This requires a strategy that allows the anaesthesia team to keep their patients’ blood pressures at the appropriate level.

Objective:

The aim of this adaptive multicentre randomized controlled trial is to maintain patients at a target blood pressure level with a sufficient margin from a minimal acceptable blood pressure threshold of a MAP of 65 mmHg to reduce the incidence of hypotension. We will investigate whether a proactive blood pressure management approach improves functional disability at six months compared to the reactive blood pressure management approach, i.e. care as usual, in adult patients after elective noncardiac surgery.

Study design:
A multicentre adaptive randomized controlled trial. Patients will be either randomized to the intervention (proactive blood pressure management strategy) or care-as-usual (predominantly reactive blood pressure management strategy).The proactive blood pressure management strategy will be evaluated and further revised in adaptation cycles of three weeks. At three and six months into the trial, the need for continuing the adaptation cycles will be reflected. When the intervention has a successful impact on the clinical process and no or little further progress is expected, the adaptation cycles will end and only the evaluation of the effect of the treatment strategies will continue.

Study population:
Adult patients scheduled for elective non-cardiac surgery under general anaesthesia or central neuraxial anaesthesia with a scheduled postoperative hospital stay of at least one night– i.e. inpatients – will be considered eligible for inclusion.

Intervention:
The intervention is the proactive risk based blood pressure management strategy that keeps the blood pressure at a set margin and avoids dropping below the minimal acceptable threshold of a MAP of 65 mmHg.The proactive strategy consists of two components: 1) a target blood pressure that provides a sufficient margin, based on the individual risk on developing hypotension; and 2) a clinical guideline with suggestions how to keep patients at their target blood pressure.
Patients with a high likelihood of intraoperative hypotension (IOH; MAP < 65 mmHg) should require larger margins and thus higher target blood pressures compared to those with a low likelihood to develop IOH. Therefore patients will be divided into low-, intermediate- and high-risk groups based on their IOH likelihood, with resulting blood pressure targets of MAP 70, 80, and 90 mmHg respectively.

Main study parameters/endpoints:
The primary outcome of the study is functional disability at six months after surgery, measured with the 12-item World Health Organization Disability Assessment Score (WHODAS) 2.0, which reflects difficulties experienced in different functional domains (cognition, mobility, self-care, getting along, life activities and participation in the previous 30 days).
Three levels of secondary outcomes can be distinguished: 1) at the level of changes in the behavior of the anaesthesia team; 2) the change in blood pressures and prevention of hypotension; and 3) the impact on patient outcome. The behavioral impact is measured through changes in blood pressure interventions, e.g. dosages of cardiovascular drugs, time to first intervention after a blood pressure dropped below a particular threshold. At the blood pressure level, the incidences, depths and durations of both intraoperative hypotension and

hypertension will be evaluated. At the patient outcome level, disability (WHODAS 2.0) and quality of life (EQ-5D-5L) at 30 days postoperatively, quality of life measured (EQ-5D-5L) 6 months postoperatively, and all-cause mortality within 6 months will be studied. In addition, short term effects – i.e. the effects on a patient's hospital – will be evaluated, e.g. in-hospital mortality, the incidence of several complications, length of hospital stay and estimated intraoperative blood loss. See 'data collection' under the section 'secondary endpoints' for specified time points.

Doel van het onderzoek

The hypothesis of this study is that a proactive strategy keeps the blood pressure at a safe margin and avoids dropping below the minimal acceptable threshold of a MAP of 65 mmHg. This proactive strategy may improve postoperative disability and outcome in patients undergoing surgery compared to a reactive approach (i.e. care-as-usual).

Onderzoeksopzet

All required data are routinely collected within the current standards of care. The data will be extracted from the electronic patient record systems through the enterprise data warehouse from each centre. During the adaption cycles of the trial (first six months of the trial), all determinants, process level and behavioural level parameters will be extracted from the electronic patient record system every three weeks. During the rest of the trial this data will be extracted every year. For the full duration of the trial, we will extract data on cardiology consultation and/or ECG examination within 24 hours after surgery, and in-hospital mortality from the electronic patient record system every three weeks. We will review the medical charts of patients who received cardiology consultation and/or ECG examination to detect new onset atrial fibrillation and/or new onset heart failure and/or ischemia. Every year all other patient level parameters will be extracted from the electronic patient record system.

Onderzoeksproduct en/of interventie

The proactive strategy consists of two components: 1) a target blood pressure that provides a sufficient safety margin above the minimal acceptable threshold of a MAP of 65 mmHg; 2) a guideline with suggestions how to keep patients at their target blood pressure.
Patients with a high likelihood of IOH require larger safety margins and thus higher target blood pressures compared to those with a low IOH likelihood. In the current literature, no comprehensive list of risk factors is available for this purpose. Hence, using combined historic data from the UMC Utrecht and the Amsterdam AMC, risk factors for the development of intraoperatieve hypotension were identified. Based on their hypotension risk – i.e. their individual predicted risk – patients will be divided into low-, intermediate- and high-risk strata, with resulting blood pressure targets of MAP 70, 80, and 90 mmHg respectively. The guideline with suggestions how to keep patients at their target blood pressure will have the same core components for all centers, i.e. each center will use the class of drugs that are indicated for the cause of hypotension. The actual drug used may differ between centers and hence the guideline will be adapted to local practices. This way our risk based intervention strategy will have the highest chance of success of widespread implementation in the

Netherlands. The attending anesthesiologist can make patient-specific adjustments to the intervention strategy. The aim of the guidelines is only to reach the target blood pressure, not to make specific treatment decisions. Adjustments that the anesthesiologist can make include adjusting the target blood pressure or use a different vasopressor dosing regimen. Interventions are already documented in the electronic patient record, and the anesthesia team will further be encouraged to document reasons for making patient-specific adjustments.

Contactpersonen

Publiek

UMC Utrecht
Teus Kappen

088-7577076

Wetenschappelijk

UMC Utrecht
Teus Kappen

088-7577076

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Adult ≥18 years or older
• Elective, non-cardiac surgery under general anaesthesia or central neuraxial anaesthesia
• Expected hospital stay of at least one night after surgery

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation

in this study:
• Low risk surgery: Opthalmic surgery, endoscopic gastrointestinal procedures, (interventional) radiologic procedures, obstetric procedure
• Organ transplantation
• Procedures with a scheduled surgical time of less than 30 minutes
• Participation in another clinical trial that is interfering with the procedures and outcomes of the PRETREAT trial
• Patients unable to fully comply to study needs (e.g. legally incapable patients or patients unable to communicate in Dutch or English).
• Patients with an American Society of Anaesthesiologists (ASA) Physical status 5

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	14-06-2021
Aantal proefpersonen:	5000
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Positief advies

Datum:	22-03-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9391
Ander register	METC Utrecht : 20-749

Resultaten

Samenvatting resultaten
N/A