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Depth of anaesthesia related to the changes in patient body temperature during surgery requiring deep hypothermia

Submission date 05/01/2024	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 10/01/2024	**Overall study status** Completed	
Last Edited 05/03/2025	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Monitoring of anaesthetic depth and target-controlled infusion (TCI) of anaesthetics is common practice if not an outright recommended procedure. It can prevent the under or overdosing of anaesthetic drugs. However, the temperature is a critical factor that affects both the accuracy of anaesthesia depth monitoring and the validity of the models used to calculate TCI doses. Therefore, a study was designed in patients undergoing elective cardiopulmonary bypass surgery on extracorporeal circulation with deep hypothermia to obtain data about the relationship between plasma concentration of intravenous anaesthetics, anaesthesia depth monitor levels and stress response.

Who can participate?
Adult patients aged 18 years old and over indicated for elective pulmonary endarterectomy

What does the study involve?
The only intervention in the study protocol is repeated blood sampling before induction in anaesthesia, after induction in anaesthesia and during cooling and rewarming of the patient on cardiopulmonary bypass.

What are the possible benefits and risks of participating?
There is no benefit for individual participants. Generally, measuring plasma concentrations of anaesthetics and comparing them with depth of anaesthesia values and the preset TCI protocol will allow more accurate adjustment of anaesthetic doses and avoid adverse effects resulting from both underdosing and overdosing.

There is no additional invasive procedure necessary to sample the blood, therefore, there is no risk for the patients.

Where is the study run from?
General University Hospital in Prague (Czech Republic)

When is the study starting and how long is it expected to run for?
January 2023 to January 2026

Who is funding the study?
General University Hospital in Prague (Czech Republic)

Who is the main contact?
Assoc. Prof. Jan Kunstyr, Ph.D, jan.kunstyr@vfn.cz (Czech Republic)

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
160124

Study information

Scientific Title
Monitoring of the depth of anaesthesia in patients undergoing surgery on extracorporeal circulation with circulatory arrest in deep hypothermia

Study objectives
Monitoring of the depth of anaesthesia and target controlled infusion allow to prevent episodes of "awake" anaesthesia on the one hand and anaesthetic overdose on the other. The aim of our observational study is to evaluate the depth of anaesthesia monitored by processed EEG in relation to concentration of anaesthetics and stress response during surgery performed on the extracorporeal circulation in deep hypothermia with periods of circulatory arrest.

Ethics approval required

Ethics approval required

Ethics approval(s)
approved 21/09/2023, Ethics Committee of the General University Hospital in Prague (U Nemocnice 2, Praha 2, 12808, Czech Republic; +420224964131; eticka.komise@vfn.cz), ref: 144 /23 S-IV

Study design
Single-centre minimally invasive study

Primary study design
Interventional

Study type(s)
Prevention, Safety

Health condition(s) or problem(s) studied
Prevention of both awake anaesthesia and anaesthetic overdose in patients undergoing surgery in deep hypothermia

Interventions
This is a single centre minimally invasive study planned for 2 years that will include 30 patients undergoing surgery for extracorporeal circulation with deep hypothermia and circulatory arrest. The blood concentration of anaesthetics and stress response are the only planned interventions.

Patients enrolled in the study will undergo elective extracorporeal circulation surgery with deep hypothermia. Monitoring the depth of anaesthesia and target-controlled infusion of anaesthetics are standard parts of such cases. The only intervention required by the study design will be blood draws to determine plasma concentrations of anaesthetic agents and the body's stress response. These collections will be performed before induction of anaesthesia, after induction and after connection to the extracorporeal circulation each time the body temperature falls by 5 deg C until the target temperature is reached. Similarly, the same readings will be taken as the patient warms until normothermia is reached.

The primary outcome of our low-intervention study is to obtain data to elucidate the relationship between intravenous anaesthetic concentrations and stress response with anaesthesia depth monitor values in patients undergoing cardiac surgery on extracorporeal circulation in deep hypothermia. This should lead to more accurate dosing of these agents to reduce the risk of underdosing or, conversely, overdosing.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The following primary outcome measures will be assessed immediately before induction in general anaesthesia (norepinephrine only), 5 minutes after induction in general anaesthesia, and 5 minutes after the start of extracorporeal circulation, in 35, 30, 25, and 20 degrees of C respectively, in target temperature, between 2 periods of circulatory arrest, during rewarming in 20, 25, 30 and 35 degrees of C:
1. Plasma concentration of propofol, sufentanil and norepinephrine measured using sensitive UHPLC-MS/MS (ultra-high performance liquid chromatography-tandem mass spectrometry) with

isotopically labelled internal standards on the Shimadzu UHPLC Nexera X3 coupled with a Triple Quad 8045 tandem mass spectrometer with methodology validated following the European Medicines Agency (EMA) Guideline on bioanalytical method validation
2. Depth of anaesthesia level measured using the Masimo Next Generation SedLine monitor

Key secondary outcome(s))
1. Total doses of vasopressors, anaesthetics and muscle relaxants measured using data from the medical files after the end of the surgical procedure
2. Prevalence of awareness during anaesthesia measured using the modified Brice questionnaire at the ICU after the patient's extubation on the second or third postoperative day (depending on the patient's condition to respond)

Completion date
31/01/2026

Eligibility

Key inclusion criteria
1. Patients with chronic thromboembolic pulmonary hypertension (CTEPH) undergoing elective pulmonary endarterectomy (PEA)
2. Aged 18 years old and over.
3. No history of chronic renal or hepatic failure
4. No history of opioid withdrawal
5. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Refusal to sign the informed consent
2. History of renal or hepatic failure
3. Age off the limit

Date of first enrolment
16/01/2024

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
Czech Republic

Study participating centre
Department of Anaesthesia, Resuscitation and Intensice Care, General University Hospital in Prague
Department of Anaesthesia, Resuscitation and Intensive Care
U Nemocnice 2
Praha 2
Czech Republic
12808

Sponsor information

Organisation
General University Hospital in Prague

ROR
https://ror.org/04yg23125

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Všeobecná Fakultní Nemocnice v Praze (General University Hospital in Prague)

Alternative Name(s)
General University Hospital in Prague, VFN

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location
Czech Republic

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available upon request from Jan Kunstyr (jan.kunstyr@vfn.cz). The type of data that will be shared on request includes all perioperatively recorded patient data (hemodynamic data, depth of anaesthesia, etc.) in the form of an Excel sheet. All samples for lab analysis will be collected and stored in a fridge until the last patient goes through the study. Only after that, will these data be analysed and available on request. The data may be available the next working day after a request. Consent from all participants was required and obtained. All data and samples collected in the study will be processed in pseudonymised form only. This means that codes will be assigned to the data and samples. Thus, the patient's personally identifiable information will not leave the doctor's office. Authorised persons can associate this code with the patient's name on a list that will be stored securely in the study centre for as long as necessary to fulfil the purpose of the study. There are no ethical or legal restrictions.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			10/01/2024	No	Yes
Participant information sheet			10/01/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file			10/01/2024	No	No