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Propofol in cardiac surgery: ProMPT-2

Submission date 11/03/2019	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 26/03/2019	**Overall study status** Completed	[X] Statistical analysis plan [_] Results
Last Edited 27/03/2025	**Condition category** Circulatory System	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Almost 2.3 million people in the UK are living heart disease and > 36,000 cardiac surgery operations are carried out each year. During surgery the heart is isolated from the rest of the circulation and a heart-lung machine is used to supply oxygen to the blood and pump it around the body. The heart is stopped and provided with nutrients by a cardioplegic solution that is injected directly into the heart arteries. This allows the surgeon to operate on the heart while it is still and not filled with blood, but looking after the heart in this way during surgery is not ideal. The heart muscle can become short of oxygen, and when the heart is restarted, and blood starts to flow again the muscle can be harmed.
The damage is believed to be caused mainly by the formation of highly reactive molecules known as ‘free radicals’ in the heart muscle during the time it is short of oxygen. Propofol is a general anaesthetic widely used in cardiac surgery and research suggests that propofol could protect the heart muscle against damage from free radicals. We want to investigate whether adding propofol to the cardioplegic solution in patients having isolated coronary artery bypass grafting (CABG) surgery using the heart-lung machine is beneficial and if the benefit is greater the more propofol that is used.

Who can participate?
Anyone having elective or urgent isolated CABG with cardiopulmonary bypass (CPB)

What does the study involve?
During heart surgery, it is important that the heart be kept still while the surgical team are working on it. This is done by injecting a solution called cardioplegia. We believe that adding propofol to this solution will protect the heart muscle during its period of inactivity, and this in turn may lead to fewer complications after the operation.
The purpose of this study is to compare the results from three different approaches: adding a low dose of propofol to the cardioplegia solution, adding a higher dose, and not adding any at all. Propofol is widely used as an anaesthetic, and you will receive this anyway as part of usual general anaesthesia.

What are the possible benefits and risks of participating?
Whilst we cannot promise taking part in this study will help you, the information gained will help us make decisions which could potentially improve the treatment of heart surgery patients in the future.

Patients in all groups are at risk of operative and postoperative complications, your doctor will discuss this with you prior to your operation and inform you of the possible side effects of propofol as part of routine care. However, no extra complications are expected due to adding the propofol to the cardioplegia solution with propofol, but if you would like further information, please ask a member of the research team.

Where is the study run from?
The University of Bristol is the sponsor for this study and has overall responsibility for the study. The study is managed by the Bristol Trials Centre (CTEU).

When is the study starting and how long is it expected to run for?
August 2018 to March 2024

Who is funding the study?
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Who is the main contact?
Beth Fitzgerald, Prompt2-trial@bristol.ac.uk

Contact information

Type(s)
Public

Contact name
Ms Beth Fitzgerald

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Additional identifiers

Clinical Trials Information System (CTIS)
2018-000169-35

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 37464

Study information

Scientific Title
Efficacy of propofol-supplemented cardioplegia on biomarkers of organ injury in patients having cardiac surgery using cardiopulmonary bypass: Propofol cardioplegia for myocardial protection randomised controlled trial: the PROMPT2 Study

Acronym
ProMPT 2

Study objectives
Adding propofol to the cardioplegic solution used during cardiac surgery reduces organ damage

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/10/2018, South Central - Berkshire B Research Ethics Committee (Whitefriars, Level 3, Block B Lewins Mead, Bristol BS1 2NT; nrescommittee.southcentral-berkshire@nhs.net; +44 (0)207 104 8059), ref: 18/SC/0472

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Reperfusion injury of the heart following coronary artery bypass grafting (CABG) surgery

Interventions
Study patients will be randomly allocated in a 1:1:1 ratio to one of the following:
Placebo: Blood cardioplegia with sham supplementation (normal saline 0.9% weight/volume sodium chloride, NaCl),
Propofol - LD: Blood cardioplegia with low dose (6mcg/ml) propofol supplementation
Propofol - HD: Blood cardioplegia with high dose (12mcg/ml) propofol supplementation
The total duration of treatment is for as long as the cardiac surgery takes.
The follow-up period is at 3 and 12 months, by QoL questionnaires.

Randomisation will be carried out as close to the planned operation as possible, after eligibility has been confirmed and written informed consent given. Randomisation will be performed by a member of the research team not involved in data collection using a secure internet-based randomisation system ensuring allocation concealment. Randomisation will take place as soon as it is confirmed the surgery will go ahead, which is typically 30 minutes before the patient is taken to theatre. Patients will be allocated in a 1:1:1 ratio to either i) high dose propofol supplementation or ii) low dose propofol supplementation or iii) sham supplementation. The allocation will be computer-generated and stratified by centre. Baseline quality of life (QoL) will be collected from the patients prior to randomisation.

Intervention Type

Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Propofol

Primary outcome(s)
Myocardial injury, assessed by serial measurements of cTnT in serum from blood samples collected pre-operatively and during the first 48-hours post chest closure.

Key secondary outcome(s))
Current secondary outcome measures as of 06/06/2023:

1. Systemic metabolic stress as measured by blood lactate at pre-op, 10 mins post cross clamp, 1, 6, 12, 24, 48 hours post chest closure
2. Renal function, as measured by creatinine in serum at pre-op, 1, 6, 12, 24, 48 hours post chest closure
3. Markers of Inflammation and oxidative stress as measured by tumour necrosis factor (TNF)-alpha, interleukin (IL)-10, IL-8, IL-6 and myeloperoxidase (MPO) in serum (Bristol cohort only) at pre-op, 1, 6, 12, 24, 48 hours post chest closure
4. Blood pH at pre-op, 1, 6, 12, 24, 48 hours post chest closure
5. Length of intensive care unit (ICU) stay
6. Length of postoperative hospital stay
7. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g. MI, permanent stroke, acute kidney injury) and death from any cause
8. QoL measured using the Coronary Revascularisation Outcome Questionnaire (CROQ) and the EQ-5D-5L questionnaire at baseline, 3 months and 12 months

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Previous secondary outcome measures as of 27/05/2022:

1. Systemic metabolic stress as measured by blood lactate at pre-op, 10 mins post cross clamp, 1, 6, 12, 24, 48 hours post chest closure
2. Renal function, as measured by creatinine in serum at pre-op, 1, 6, 12, 24, 48 hours post chest closure
3. Markers of Inflammation and oxidative stress as measured by tumour necrosis factor (TNF)-alpha, interleukin (IL)-10, IL-8, IL-6 and myeloperoxidase (MPO) in serum (Bristol cohort only) at pre-op, 1, 6, 12, 24, 48 hours post chest closure
4. Blood pH at pre-op, 1, 6, 12, 24, 48 hours post chest closure
5. Investigate the association between cTnT and circulating level of cardiac-released microRNA-1 and exosomal microRNA-1 content at pre-op, 1, 6, 12, 24, 48 hours post chest closure (Bristol cohort only)
6. Examine whether the association between cTnT and microRNA and exosomal microRNA-1 content differs between groups (i.e. differs with the propofol supplementation received) at pre-op, 1, 6, 12, 24, 48 hours post chest closure (Bristol cohort only)
7. Length of intensive care unit (ICU) stay
8. Length of postoperative hospital stay
9. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g.

MI, permanent stroke, acute kidney injury) and death from any cause
10. QoL measured using the Coronary Revascularisation Outcome Questionnaire (CROQ) and the EQ-5D-5L questionnaire at baseline, 3 months and 12 months

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4. Blood pH at pre-op, 1, 6, 12, 24, 48 hours post chest closure
5. Investigate the association between cTnT and circulating level of cardiac -released microRNA-1 and exosomal microRNA-1 content at pre-op, 1, 6, 12, 24, 48 hours post chest closure.
6. Examine whether the association between cTnT and microRNA and exosomal microRNA-1 content differs between groups (i.e. differs with the propofol supplementation received) at pre-op, 1, 6, 12, 24, 48 hours post chest closure.
7. Length of intensive care unit (ICU) stay
8. Length of postoperative hospital stay
9. Clinical outcomes and serious adverse events, i.e. serious post-operative complications (e.g. MI, permanent stroke, acute kidney injury) and death from any cause.
10. QoL measured using the Coronary Revascularisation Outcome Questionnaire (CROQ) and the EQ-5D-5L questionnaire at baseline, 3-months and 12-months.

Completion date
31/03/2024

Eligibility

Key inclusion criteria
1. Aged >= 18 years
2. Having elective or urgent isolated CABG with CPB
3. Ability to give informed consent
Women only:
4. Negative pregnancy test, or be surgically or post-menopausal for >12 months

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
240

Key exclusion criteria
Current participant exclusion criteria as of 20/05/2020:
1. Previous cardiac surgery
2. Planned concomitant procedure
3. Emergency or salvage operation
4. Long-term steroid therapy (taking tablets on a daily basis for at least 1 month prior to surgery)
5. Pre-operative estimated glomerular filtration rate ≤ 30 ml/min/1.73m2
6. Current congestive heart failure
7. Left ventricular (LV) ejection fraction <30% (i.e. poor LV function)
8. Allergy to peanuts, eggs, egg products, soybeans or soy products
9. Already participating in another interventional clinical study
10. Prisoners
11. Patients taking immunosuppressants (e.g. methotrexate or azathioprine)
12. Patients known to have cTnT level >500 ng/l (or cTnI level >600 ng/l) in the last 4 days (prior to eligibility check)
Women only:
13. Breast feeding

Previous participant exclusion criteria:
1. Previous cardiac surgery
2. Planned concomitant procedure
3. Emergency or salvage operation
4. Long-term steroid therapy
5. Pre-operative estimated glomerular filtration rate < = 60 mls/min/1.73m2
6. Current congestive heart failure
7. Left ventricular (LV) ejection fraction < 30% (i.e. poor LV function)
8. Allergy to peanuts, eggs, egg products, soybeans or soy products
9. Already participating in another interventional clinical study
10. Prisoners

Women only:
11. Breastfeeding

Date of first enrolment
31/08/2018

Date of final enrolment
07/11/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Bristol Heart Institute
Marlborough Street
Bristol
United Kingdom
BS2 8HW

Study participating centre
National Heart and Lung Institute
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
Glenfield Hospital
Groby Road
Leicester
United Kingdom
LE3 9QP

Study participating centre
Harefield Hopsital
Hill End Road
Harefield
United Kingdom
UB9 6JH

Study participating centre
Wythenshawe Hospital
Southmoor Rd
Roundthorn Industrial Estate
Wythenshawe
United Kingdom
M23 9LT

Study participating centre
Royal United Hospitals Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Musgrove Park Hospital (taunton)
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

Sponsor information

Organisation
University of Bristol

ROR
https://ror.org/0524sp257

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: 15/180/55

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
Anonymised individual patient data (baseline, intervention, outcome data and adverse events) will be made available for secondary research, conditional on assurance from the secondary researcher that the proposed use of the data is compliant with the with the UK Policy Framework for Health and Social Care Research and MRC Policy on Data Preservation and Sharing regarding scientific quality, ethical requirements and value for money. Please contact

Prof. Chris Rogers (prompt2-trial@bristol.ac.uk) to discuss any data requests. Data will be made available after the study has been closed and the primary publication is out. It will be made available indefinitely. Only data from patients who have consented for their data to be shared with other researchers will be provided.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		16/02/2023	17/02/2023	Yes	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan		29/02/2024	01/03/2024	Yes	No