

Evaluating the accuracy of organ injury biomarkers to personalise protection interventions in adult cardiac surgery

Submission date 26/07/2021	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 03/09/2021	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 23/04/2025	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Organ injury and problems with the kidneys, heart and lungs are not uncommon after heart surgery and caring for patients who develop these issues takes a lot of resources. Progress towards preventing these problems is difficult because we don't fully understand the reasons why they happen. Cardiopulmonary bypass (CPB) during surgery is thought to be a cause, along with how generally healthy the patient is going into the surgery, but this is difficult to predict as there are lots of health problems that people can have. It is thought that these different kinds of health problems are what is behind the differences in how people are affected by organ injury as a result of their heart operation. These may also be the reason why treatments to prevent organ injury have a different effect in animal studies compared to humans. By learning more about these different health problems, patients may be grouped more accurately and we could develop ways to prevent organ injury in a more personal way. The aim of this study is to investigate how accurately organ injury can be predicted in patients having a heart operation using measurements within the body called biomarkers along with clinical research data about their health.

Who can participate?

Adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) enrolled in the COPTIC trial (ISRCTN20778544) in Bristol UK for whom there are available samples and data

What does the study involve?

Laboratory and computer analyses are carried out on stored samples from patients undergoing cardiac surgery with cardiopulmonary bypass.

What are the possible benefits and risks of participating?

Not applicable as the researchers are using stored samples and data.

Where is the study run from?

University of Leicester (UK)

When is the study starting and how long is it expected to run for?
October 2020 to April 2028

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
Hardeep Aujla
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
293173

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 48955, IRAS 293173

Study information

Scientific Title
Evaluating the diagnostic accuracy of novel organ injury biomarkers in adult cardiac surgery

Acronym

COPTIC-2

Study objectives

The overarching hypothesis is that existing clinical and biochemical definitions of post-cardiac surgery organ injury and dysfunction represent multiple molecular phenotypes. Identification of these different phenotypes will lead to new and effective prevention strategies and treatments.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 29/03/2021, South Central - Berkshire REC (Bristol REC Centre, Whitefriars Level 3 Block B, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8224, +44 (0)207 104 8270; berkshire.rec@hra.nhs.uk), REC ref: 21/SC/0118

Study design

Observational; Design type: Clinical Laboratory Study

Primary study design

Observational

Study type(s)

Diagnostic

Health condition(s) or problem(s) studied

Cardiac surgery with cardiopulmonary bypass

Interventions

The researchers will see how accurately they can use measurements in the body (biomarkers) to predict organ injury. These biomarkers have been identified before in an ethically approved study (COPTIC). They will carry this out in stored samples of 2463 patients from this previous study. They have information on them already, including their baseline status.

Only patients who consented for their samples and data to be used in future ethically approved studies will be used. The original study investigators in Bristol will undertake a consent audit to ensure this.

The researchers will check to see if there are enough samples, and if the data is complete enough before including them in this study.

They will then conduct laboratory and computer analyses to explore the study aims.

Intervention Type

Procedure/Surgery

Primary outcome(s)

Derived from data and samples collected pre- and post-surgery:

1. Novel biomarkers identified in existing studies including:
 - 1.1. Serum cytokines considered to be indicators of the severity of the inflammatory response to surgery, measured from serum on the Luminex MAGPIX Analyser (Oosterhout, NL)

- 1.2. Extracellular vesicles in plasma (EV) assessed by flow cytometry
- 1.3. Exosome and EV derived microRNA assessed by quantitative reverse transcription PCR (qRT-PCR) and next-generation sequencing
- 1.4. Targeted metabolomics for biomarkers of frailty, acute kidney injury acute lung injury, and coagulopathy, analysed using a targeted assay on a Thermo Qunativa interfaced with a Vanquish LC25
- 1.5. Other organ injury biomarkers; plasma proteins, coagulation assays, performed by next-generation sequencing and analysis of a panel of metabolites by mass spectrometry
2. Acute kidney injury (AKI) defined by clinical consensus criteria: RIFLE, AKIN, KDIGO, or by serial biomarker levels: serum creatinine, and soluble urokinase plasminogen activator receptor (uPAR)
3. Myocardial injury defined clinically as low cardiac output, which is new intra- or postoperative intra-aortic balloon pump insertion or a cardiac index of $<2.2 \text{ l min}^{-1} \text{ m}^{-2}$ refractory to appropriate intravascular volume expansion after correction or attempted correction of any dysrhythmias, or the administration of inotropes including dobutamine, enoximone, milrinone, levosimendan and adrenaline, or by serial biomarker levels: serum troponin
4. Acute lung injury (ALI) defined by clinical consensus criteria: ALI Score, Berlin ARDS Score, or by serial $\text{PaO}_2/\text{FiO}_2$ ratio
5. Coagulopathy defined using the COPTIC trial definition, or by point-of-care or laboratory tests of coagulopathy

Key secondary outcome(s)

Extracted from anonymised clinical trial data pre- and post-surgery:

1. Any red cell transfusion*
2. Red cell transfusion of ≥ 5 units*
3. Mortality
4. Myocardial infarction
5. Intra-aortic balloon pump
6. Stroke
7. Acute kidney injury (Yes/No)
8. Serum creatinine to estimate AKI grade 1, AKI grade 2, and AKI grade 3 on days 1-5 post surgery
9. Sepsis
10. Length of stay in ICU
11. Length of stay in hospital

*reoperation of red cell transfusion for surgical causes of bleeding are excluded

Completion date

01/04/2028

Eligibility

Key inclusion criteria

Adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) enrolled in the COPTIC trial (ISRCTN20778544) in Bristol UK for whom there are available samples and data

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Total final enrolment

2437

Key exclusion criteria

Participants of the COPTIC trial who did not provide consent for the use of samples and/or data for further ethically approved research (i.e., the present trial), and for whom there are insufficient samples and data

Date of first enrolment

01/09/2021

Date of final enrolment

01/09/2023

Locations**Countries of recruitment**

United Kingdom

England

Study participating centre**University of Leicester**

Cardiovascular Sciences

University of Leicester

Department of Cardiovascular Sciences

Clinical Sciences Wing

Glenfield Hospital

Leicester

United Kingdom

LE3 9QP

Sponsor information**Organisation**

University of Leicester

ROR

Funder(s)

Funder type

Charity

Funder Name

British Heart Foundation (BHF); Grant Codes: RG/17/9/32812

Alternative Name(s)

The British Heart Foundation, the_bhf, BHF

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Preprint results		17/10/2024	23/04/2025	No	No