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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

Registration date
03/09/2021

Overall study status
Ongoing

Last Edited
23/04/2025

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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
ha200@le.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Hardeep Aujla

ORCID ID
http://orcid.org/0000-0002-5823-848X

Contact details
Research Manager
Dept. Cardiovascular Sciences
University of Leicester
Leicester
United Kingdom
LE3 9QP
+44 (0)116 250 2427
ha200@le.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
293173

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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

Secondary study design
Clinical laboratory study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
No participant information sheet available

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 measure
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 l min-1 m-2 refractory to appropriate intravascular volume expansion after correction or attempted correction of any dysrhythmias, or the administration of ionotropes 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 PaO_2/FiO_2 ratio
5. Coagulopathy defined using the COPTIC trial definition, or by point-of-care or laboratory tests of coagulopathy

Secondary outcome measures
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

Overall study start date
01/10/2020

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

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 2463; UK Sample Size: 2463

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
England

United Kingdom

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

Sponsor details
c/o Cat Taylor
Research Governance Office
Academic Dept.
Leicester General Hospital
Leicester
England
United Kingdom
LE5 4PW
+44 (0)1162584867
rgosponsor@le.ac.uk

Sponsor type
University/education

Website
http://www.le.ac.uk/

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Charity

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

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. The researchers plan to publish the protocol
2. Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/04/2026

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