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Testing whether a commonly used drug to treat Diabetes can reduce injury to the lung following heart surgery and in critical illness.

Submission date
14/10/2025

Recruitment status
Recruiting

Registration date
24/12/2025

Overall study status
Ongoing

Last Edited
24/12/2025

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute respiratory distress syndrome (ARDS) is a common condition in critically ill patients, in which the lung lining becomes damaged by white blood cells and the lungs fill with fluid, causing difficulty breathing and a need for breathing support on a ventilator. There is no cure for ARDS despite decades of research.
Metformin is a drug that is commonly used to treat diabetes. Researchers have found that metformin reduces inflammation by several different mechanisms. Excitingly, many of these mechanisms are implicated in how inflammation causes damage to the lung in ARDS. This raises the possibility that metformin might be useful in treating ARDS, and indeed in several animal models it appears to be effective. We now want to test metformin in human models of ARDS. If it is effective in these then we could progress rapidly to a clinical trial in patients who have ARDS or who are at risk of developing it. Patients undergoing coronary artery bypass grafting (CABG) experience mild lung inflammation during their surgery. We can find evidence in their blood of mild damage to the lung lining and mild inflammation, mimicking the types of changes we see in ARDS, but the inflammation in patients undergoing bypass is mild and transient.
The information from this study will help us really understand the therapeutic potential of metformin and ensure we designed the best possible clinical trials to test it in patients with ARDS.

Who can participate?
Adult patients ≥18 years of age undergoing elective coronary artery bypass graft surgery using cardiopulmonary bypass.

What does the study involve?
We will treat patients undergoing CABG with metformin and measure whether these markers of inflammation and lung injury are reduced in the group given metformin compared to a group who are undergoing standard care for their CABG procedure.

What are the possible benefits and risks of participating?
Benefits:

Not provided at time of registration
Risks:
Potential Risk:
Metformin is a marketed for use in type II diabetes at the same doses as used for this study. The summary of product characteristics (SPC) lists all known side effects of the medication.
The SPC states common side effects to be decreased appetite, abdominal pain, diarrhoea, gastrointestinal disorder, nausea, vomiting and altered taste. Gastrointestinal side effects are listed as the most frequent side effects and usually resolve spontaneously. Metformin cannot be used in patients with impaired kidneys due to risk of lactic acidosis (a significant a potentially dangerous change in the blood)

Mitigation Strategy:
Metfomin will be introduced gradually and using a regime similar to those seen to work in other trials. A modified released preparation will be used which is better tolerated.
Those with lactic acidosis or B12 deficiency will be excluded as well as those with pre-existing kidney impairment.
All trial patients will be advised of the possibility of all potential side effects and how to report them.

Potential Risk:
It had been suggested in the past that metformin increased the risk of lactic acidosis.
Large studies have demonstrated that the risk of lactic acidosis is no higher in those taking metformin as compared to those not taking metformin.

Mitigation strategy:
A baseline lactate will be taken and those with a history of lactic acidosis will be excluded. Furthermore, those with pre-existing kidney impairment will be excluded. In addition, the serum lactate will be followed closely as a safety outcome

Potential Risk:
A listed side effect of metformin within the SPC is B12 deficiency.

Mitigation Strategy:
Those with vitamin B12 deficiency will be excluded.

Potential Risk:

The majority of the clinical procedures will be undertaken as per normal clinical care. Most blood tests will be taken at the same time with routine blood tests procedure to reduce need for further blood sampling.
Blood sampling carries a very low risk of introducing infection and repeated blood draws can, in theory, contribute to anaemia. Blood sampling can also be painful.

A biopsy of pectoral muscle will be taken from the patient on entry to the chest.

Mitigation Strategy:
Taking blood for research alongside routine clinical blood tests will reduce the risk of the need for further blood draws. Where this is not possible for timed blood draws post-operatively, the blood will be taken from the existing lines which is a commonly undertaken procedure post cardiac surgery.

The muscle biopsy will be taken from pectoralis major through the sternotomy incision and it would be standard practice to encounter these muscles during this surgery. A surgical biopsy will not affect function or add risk to the procedure.

Potential Risk:
Consent not being recorded properly prior to study entry.
Site staff taking consent are not adequately trained or delegated this task.

Mitigation Strategy:
No patient will be recruited unless informed consent has been achieved. The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. The Chief Investigator (CI) is responsible for ensuring that informed consent for trial participation is given by each patient or a legal representative.

The person taking informed consent must be trained, suitably qualified and experienced. Appropriate signatures and dates must be obtained on the informed consent documentation prior to collection of trial data and randomisation. If no consent is given a patient cannot be randomised into the trial.

Potential Risk:
Data breaches of sensitive information can cause significant harm to patients.

Mitgation Strategy:
Patient confidentiality will be maintained at every stage in compliance with the General Data Protection Regulations (GDPR) & the UK Data Protection Act 2018. Patient identification will be through their unique study number allocated at the time of recruitment to the trial.

Potential Risk:
Failure to act on a participant's request to withdraw from the study.
Patient does not feel able withdraw from the study as procedures to do so are not made clear.

Mitigation Strategy:
Patients can withdraw their consent to the trial at any time without giving a reason. This will be made clear in the participant information. Should a patient elect to withdraw from the study the researcher will discuss what information remains on the database and what is removed.

Potential Risk:
Staff or participants coming into contact with violent patients.

Mitigation Strategy:
Patients can develop delirium (confusion) after surgery and can behave out of character. This is commonly dealt with in the post-operative patient. They will be treated per standard clinical practice and therefore harm should be no higher than in standard care.

Where is the study run from?
Belfast Health and Social Care Trust (UK)

When is the study starting and how long is it expected to run for?
October 2025 to August 2029

Who is funding the study?
HSC Research and Development (UK)

Who is the main contact?
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Contact information

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Additional identifiers

Integrated Research Application System (IRAS)
1011434

Protocol serial number
24030KOS-UC

Study information

Scientific Title
Metformin to reduce pulmonary INjury and systemic Inflammation after Coronary Artery Bypass surgery? (MINICAB)

Acronym

MINICAB

Study objectives
Primary objective:
Can metformin, a commonly used medication in the treatment of diabetes, reduce blood markers of lung injury in patients undergoing coronary artery bypass grafting operations?

Secondary objectives:
1. Can metformin, a commonly used medication in the treatment of diabetes, reduce blood markers of inflammation in the patients undergoing coronary artery bypass grafting surgery?
2. Can metformin, a commonly used medication in the treatment of diabetes, improve clinical outcomes following coronary artery bypass grafting surgery?
3. To evaluate how metformin works and how it might reduce lung injury and inflammation if it does have this effect.

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Acute Respiratory Distress Syndrome, post-operative coronary artery bypass graft patients

Interventions
Patients will be randomised 1:1 to either a standard care arm or treatment (metformin arm) using the sealed envelope platform.
In the treatment arm of the trial, patients will receive a total of 14 days of modified release metformin with the final dose on the morning of surgery. For the first 7 days of this course patients will receive 500mg Modified Release Metformin twice daily. The subsequent 7 days of therapy will consist of 1g Modified Release Metformin twice daily.
In the standard care arm the patient will receive their no change to the standard surgical workup undertaken at the trial site.
Participants and clinicians involved in the patient care will be unblinded to the arm allocation. Laboratory staff undertaking the analysis will be blinded to allocation. Patients will be followed up for 30 days to for clinical outcomes.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome(s)
Plasma RAGE measured using ELISA from baseline to immediately post cardiopulmonary bypass (RAGEimmediately post bypass – RAGEimmediately pre bypass)

Key secondary outcome(s)
At baseline and post-operative timepoints unless noted:

1. Inflammation
1.1. Total and differential white blood cell count and plasma NETs (neutrophil extracellular traps) measured using automated hematology analyser
1.2. Plasma markers of inflammation - CRP, TNFα, sTNFR, IL-6, IL-8, IL-18, IL-1Ra measured using immunoassay
2. Markers of organ or cell injury
2.1. Type I alveolar epithelial cell dysfunction – In addition to the timepoints for the primary outcome, plasma RAGE will be taken using ELISA at 24, 48 and 72 hours.
2.2. Type II alveolar epithelial cell dysfunction – measured by plasma SP-D measured using ELISA
2.3. Endothelial dysfunction – plasma vWF, Ang2 measured using ELISA
2.4. Urinary markers of injury – NGAL, Albumin: Creatinine ratio measured using ELISA

Additional outcomes:
3. Mechanistic effects of metformin
3.1. Anti-inflammatory:
a. PBMC AMPK phosphorylation from PBMCs +/- LPS ex vivo stimulation
b. PBMC NFkB in PBMCs +/- LPS ex vivo stimulation
c. PBMC inflammasome activation in PBMC +/- LPS ex vivo stimulation; including ASC speck formation, flow cytometry, IL-1beta/IL-18/LDH, caspase 1, gasdermin and other inflammasome markers.
d. GDF 15
3.2. Mitochondrial modulation
a. Blood mtDNA
b. PBMC Mitophagy markers (PNIK1, PARKIN, MFN2, NIX, LC3-II, LAMP2) on lysates from PBMC +/- ex vivo LPS stimulation
3.3. Blood transcriptome
3.4. Blood epigenome
3.5. Muscle transcriptome and muscle/plasma metabolome
4. Clinical outcomes:
4.1. Clinical outcomes will be recorded although it is recognised the study will not be powered for these. Outcomes include rate of post-operative pneumonia, rate of acute kidney injury; post-operative neurological dysfunction; rate of wound infection; prolonged ventilation (>24 hours after procedure); rate of re-operation on the same hospital admission; length of hospital stay; length of hospital stay; inpatient and 30 day mortality.
5. Muscle mass and strength:
5.1. Mid-thigh circumference and grip strength manometry will be measured at timepoints of pre-surgery, Day 1, Day 3 and, where possible, Day 7.

Completion date
01/08/2029

Eligibility

Key inclusion criteria
Adult patients ≥18 years of age undergoing elective coronary artery bypass graft surgery using cardiopulmonary bypass.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
110 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Age < 18 years
2. Patients with surgery planned within 14 days who would therefore be unable to take full course of metformin
3. Pre-existing diabetes mellitus (DM) requiring therapy
4. Participation in a clinical trial of an IMP within 30 days
5. Untreated vitamin B12 deficiency
6. eGFR<60ml/min or history of chronic kidney disease
7. Chronic hepatic disease - defined by ALT or AST >3x upper limit of normal
8. Patients with known mitochondrial disorders
9. Inability to take oral medication pre-operatively
10. Known hypersensitivity or intolerance to the study medication
11. Lack of capacity to consent to trial

Date of first enrolment
09/02/2026

Date of final enrolment
01/08/2029

Locations

Countries of recruitment

United Kingdom

Study participating centre
-
-
NO COUNTRY SPECIFIED, assuming England
England
-

Sponsor information

Organisation
Belfast Health and Social Care Trust

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Government

Funder Name
HSC Research and Development

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date