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Understanding how critical illness and liver disease affect blood clotting

Submission date
07/05/2024

Recruitment status
Recruiting

Registration date
22/05/2024

Overall study status
Ongoing

Last Edited
25/04/2025

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
The blood that circulates within our bodies consists of many different cells, each with unique functions. One type of blood cell is the platelet; these cells become activated and attach to sites of injury to help form a blood clot and reduce or prevent further bleeding. In some unwell individuals, the number and/or function of these platelets can become altered. In many critically ill patients, the number of platelets can be reduced below a safe level, a condition known as thrombocytopenia. Thrombocytopenia is problematic, as in many cases, it is linked to worse patient outcomes. Within critically unwell patients, one group at risk of both thrombocytopenia and other bleeding disorders (e.g. overactivation of clotting) are patients with liver disease. Patients with liver disease in the Intensive Care Unit (ICU) at the Royal Berkshire Hospital (RBH) include those with established diseases such as alcohol-related cirrhosis, as well as those with liver dysfunction as part of their critical illness, for example, patients with sepsis. In this study, RBH and the University of Reading will collaborate to analyse the platelets using a range of complex, state-of-the-art techniques to study blood samples taken from patients with liver disease and critically unwell patients in the ICU at RBH. The goal is to analyse their platelet function in the laboratory and monitor how the function changes throughout their time in the ICU. This information will allow us to relate patient experiences, such as bleeding, clotting, and organ dysfunction, back to the laboratory results. While participation in this study will not have immediate benefits for the patients, upon the completion of this study, its results will be used to support future studies in making improvements to treatment strategies for this patient category.

Who can participate?
Patients with pre-existing liver disease or acute liver dysfunction as part of their critical illness in the ICU

What does this study involve
While the patient is in the ICU they will have blood taken from their indwelling vascular access devices which will allow for sampling of blood without any additional procedures being performed. At each sample, a maximum of 50 ml of blood will be taken each time up to a maximum of five separate occasions. Patients who are subsequently discharged onto a ward will then have a maximum of one other 50 ml sample taken as part of this study.

What are the possible benefits of participating?
This study will not be of immediate benefit to those who participate, but it may help us to improve the standard of care for patients in the future who are admitted to ICU. It is hoped that the information collected will help better understand the effect of critical illness on platelets, eventually improve patient care in the future, and ultimately save lives.

What are the potential risks of participating?
This study is simply designed to study the function of patients' blood cells rather than alter the care received by the patient in any way. It is highly unlikely that a patient would suffer any harm by taking part.

Where is the study run from?
1. The Royal Berkshire Hospital
2. The University of Reading (UK)

When is the study starting and how long is it expected to run for?
February 2024 to September 2026

Who is funding the study?
University of Reading Healthcare Innovation Partnership

Who is the main contact?
Dr Matthew Frise, Consultant in Acute Medicine and Intensive Care, matthew.frise@royalberkshire.nhs.uk

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil Known

IRAS number
IRAS 335135

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 335135

Study information

Scientific Title
PLAtelet function in Critical Illness and liver Disease (PLACID)

Acronym
PLACID

Study objectives

It is hypothesized that platelet function will be impacted by the co-existence of liver disease in critically ill patients and platelet functionality will also change over time in these individuals.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/04/2024, South Central - Oxford C (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8271; oxfordc.rec@hra.nhs.uk), ref: 24/SC/0053

Study design
Single-center observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital, Laboratory

Study type(s)
Screening

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Liver disease, critical illness, platelet function

Interventions
This is an observational study, there are no interventions. The following is a brief summary of our methodologies.

A total of 30 patients will be recruited for this study from the ICU at the Royal Berkshire Hospital.

Up to 5, 50 ml blood samples will be taken from venous and/or arterial access during their stay in the ICU. An additional sample (not exceeding 50 ml) may also be requested when the patient is recovering on a ward.

Molecular analysis will also be performed on the samples of recalled patients to identify molecular differences in platelet function between the groups.

Several tests will be performed to understand which stage/ stages during platelet activation are affected in patients with liver disease as part of their critical illness. The tests performed will be carried out in an order which will make the best use of the blood samples taken from each individual participant.

Intervention Type

Other

Primary outcome measure
Platelet reactivity measured using Platelet Phenomics Analysis (Flow Cytometry and Thrombus formation under flow) combined with mathematical analysis, correlated according to liver disease type, burden, and stage, in blood collected during the study

Secondary outcome measures
The following secondary outcome measures will be assessed in blood collected during the study:
1. Thrombus size generated measured using an in vitro thrombus formation assay
2. Clotting parameters measured using thromboelastography and related haemostatic assays
3. Platelet receptor levels measured using flow cytometry
4. Signalling protein absolute levels and phosphorylation state measured using proteomic analysis
5. Signalling-pathway-specific experiments including modelling changes in cell lines

Overall study start date
01/02/2024

Completion date
01/09/2026

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 24/05/2024:
1. Admitted to ICU at the Royal Berkshire Hospital
2. Aged 18 years old and above
3. Evidence of established liver disease, or acute liver dysfunction related to underlying illness, as determined by the clinicians caring for the patient at the time of eligibility assessment.

Previous participant inclusion criteria:
1. Known liver disease or
2. Acute liver dysfunction

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
30

Key exclusion criteria
1. Patients on P2Y12 inhibitors (including clopidogrel, ticagrelor and prasugrel)
2. Patients on treatment-dose anticoagulation, including warfarin or novel anticoagulant drugs
3. Patients under 18 years of age
4. Active or recent malignancy (< 1 year) or on active treatment

Date of first enrolment
15/05/2024

Date of final enrolment
01/04/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Reading
School of Biological Sciences
Reading
United Kingdom
RG6 6UR

Study participating centre
Royal Berkshire Hospital
Royal Berkshire Hospital
London Road
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Sponsor information

Organisation
Royal Berkshire NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Website
https://www.royalberkshire.nhs.uk/

ROR
https://ror.org/034nvrd87

Funder(s)

Funder type
University/education

Funder Name
University of Reading Healthcare Innovation Partnership

Alternative Name(s)
UoR

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/09/2027

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available on reasonable request from the corresponding author, Dr Matthew Frise, Consultant in Acute Medicine and Intensive Care, matthew.frise@royalberkshire.nhs.uk.

Raw data will be shared, stored and backed up in a repository. Fully analysed data will be shared on request in the form of flow cytometry files and microscopy image files along with the associated analysis e.g. excel, image J and R files. Data can be made available upon request upon completion of the study and after publication in peer-reviewed journal(s). Fully linked anonymised data can be made available upon request. Data is linked anonymised, no data that links the patients to the study will leave the RBFT or be used in any analysis.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1	28/03/2024	20/05/2024	No	Yes
Protocol file	version 1.1	28/03/2024	20/05/2024	No	No