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# The Decision Study

**Submission date**
21/04/2015

**Recruitment status**
No longer recruiting

**Registration date**
22/04/2015

**Overall study status**
Completed

**Last Edited**
17/12/2020

**Condition category**
Haematological Disorders

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

## Plain English summary of protocol

Background and study aims
About 3000 children undergo major cardiac (heart) surgery each year in the UK and around 40% of these experience serious bleeding. This is usually caused by abnormalities in the blood clotting system which can develop quickly and change rapidly. Almost all children with serious bleeding receive blood transfusions or other blood components to correct clotting abnormalities. In addition, blood components are given to a further 40% of children because doctors think that there is a high risk of serious bleeding. Treatments for clotting abnormalities after cardiac surgery may be lifesaving, but may also cause complications or even death. After cardiac surgery in adults, a rapid blood test called thromboelastometry (TEM) is usually performed in the operating theatre to detect important clotting abnormalities. This helps doctors to select individualised treatments to treat or prevent serious bleeding and also to avoid treatments that are not needed. The TEM test is also feasible after cardiac surgery in children and we already know that TEM can detect some of the clotting abnormalities in children that cause serious bleeding. Unfortunately, we don't yet know all of the important clotting abnormalities or whether TEM is reliable enough to guide important treatment decisions. Our study will answer these questions by comparing the results of the rapid 'ROTEM' TEM (rotational thromboelastometry) test with 'gold standard' (but slower) laboratory tests for clotting abnormalities.

Who can participate?
Children aged under 16 undergoing major cardiac surgery.

What does the study involve?
For this study we will require two small extra blood samples and we will record routine information about each operation such as how much bleeding occurs and whether, and why, blood components are given. This information will be used to identify the most important clotting abnormalities in children after cardiac surgery and how well these are identified by the ROTEM test. We will use these results to create guidelines to help doctors in the future to select individualised treatments using ROTEM test results for all children after cardiac surgery. This research will be performed by an expert team that includes doctors who routinely care for children undergoing cardiac surgery in the NHS and specialists in blood transfusion and laboratory testing. Our design and analysis experts will ensure that the results are valid and can be applied to children having this surgery in the future.

What are the possible benefits and risks of participating?
Our research findings will help NHS doctors make better choices when selecting blood component treatments which will be of substantial benefit to this vulnerable patient group. The extra blood samples (just over 1 teaspoon each) will have a negligible impact on participating children and will not affect their NHS care.

Where is the study run from?
Bristol Royal Hospital for Children (BRHC) (UK).

When is the study starting and how long is it expected to run for?
From June 2012 to May 2015.

Who is funding the study?
NIHR Bristol Cardiovascular Biomedical Research Unit (UK).

Who is the main contact?
Dr Christine Rogers
Dr Andrew Mumford

# Contact information

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Public

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
N/A

# Study information

### Scientific Title
Detection of coagulopathy in paediatric heart surgery

### Study objectives
Blood clotting abnormalities in children after cardiac surgery are influenced by factors such as cardiac diagnoses and anaesthetic technique. Blood clotting abnormalities vary markedly between individuals and change within individuals over time. Low platelets and low fibrinogen were shown to be common after cardiac surgery in small single-centre or single-diagnosis groups of children and were associated with excessive bleeding. However, associations between these blood clotting abnormalities and excessive bleeding have not been tested in larger unselected cohorts. It is also unknown whether hyperfibrinolysis or platelet dysfunction, which cause bleeding in adults after cardiac surgery, also cause bleeding in children.

In common with adults after cardiac surgery, selecting individualised treatments for blood clotting abnormalities in children using TEM test results is an attractive and feasible strategy that promises significant patient and NHS benefits. Markedly abnormal TEM results are common in some children particularly at cessation of CPB before the highest risk period for excessive bleeding. Abnormalities in blood clotting have also been demonstrated at anaesthetic induction (particularly hypofibrinogenaemia) and were shown to be predictive of post-operative blood loss. Some abnormal TEM results also correlate with low platelets and low fibrinogen (determined using reference laboratory tests) and also predict excessive bleeding.

These data provide proof-of-concept of the diagnostic usefulness of TEM in children after cardiac surgery. However, it is unlikely that all of the blood clotting abnormalities that cause excessive bleeding have been identified. It is also unknown whether TEM has sufficient diagnostic accuracy for the important abnormalities, and predictive value for excessive bleeding, to guide individualised treatments correctly. Although TEM is now performed after cardiac surgery in about 25% of children in NHS hospitals, testing is not standardised and treatment decisions guided by TEM results are unvalidated. The best way of using TEM results to select treatments for blood clotting abnormalities cannot yet be defined and the potential benefit to children is unknown.

Testing for blood clotting abnormalities in children is much less developed than in adults and current clinical practice remains inadequate.

We hypothesise that testing for blood clotting abnormalities in children before or after cardiac surgery will confer benefit by helping to reduce excessive bleeding and transfusion of allogeneic blood components after cardiac surgery.

The potential benefits of testing for blood clotting abnormalities is two-fold:
1. Test results may enable us to improve selection of the best treatment products in children with blood clotting abnormalities.
2. Test results may enable us to prevent the use of unnecessary treatments in children who do not have blood clotting abnormalities.

The study objectives are as follows:
1. To describe the prevalence of the different types of blood clotting abnormality in children before and after cardiac surgery.
2. To estimate the association between (a) the laboratory test results and clinical concern about bleeding (CCB) after cardiac surgery, and (b) different types of blood clotting abnormality and clinical concern about bleeding after cardiac surgery.
3. To estimate the diagnostic accuracy of ROTEM tests vs. reference laboratory tests for the different types of blood clotting abnormality identified (a) before and (b) after cardiac surgery.
4. To investigate the agreement between the treatment recommended by the results of the reference tests and the treatment recommended by the ROTEM test results.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
NRES Committee London - City and East, Bristol Research Centre Committee, 24/04/2013

## Study design
Prospective single-centre observational study

## Primary study design
Observational

## Secondary study design

## Study setting(s)
Hospital

## Study type(s)
Diagnostic

## Participant information sheet

## Health condition(s) or problem(s) studied
Blood clotting abnormalities in children after cardiac surgery

## Interventions
Two 5.25 ml blood samples will be taken from existing intravascular lines at two time-points:
1. Following anaesthetic induction
2. After cessation of CPB, heparin reversal and all other routine pro-haemostatic interventions (e. g. cryoprecipitate administration and cell saver return). Sampling must occur before the start of the return of heparinised pump blood.

The volume of the blood required for this research may, in exceptional circumstances, be tolerated poorly by participants with small circulating volumes or critical cardiovascular function. In order to minimise the risk of harm to participants, clinicians will be instructed to consider the consequence of taking each blood sample on a case-per-case basis.

We observe until the patient is discharged and there is no follow up.

## Intervention Type
Other

## Primary outcome measure
The primary clinical outcome is clinical concern about bleeding. We will estimate the association between type of blood clotting abnormality (determined from sample 1 and 2 test results) and clinical concern about bleeding (objective 2) during three time intervals:

Interval A: The period between sample 1 and sample 2
Interval B: The period between sample 2 and chest drain on suction
Interval C: The first 12 hours after chest drain on suction

Clinical concern about bleeding is defined as either:
1. High blood loss. Chest drain volume of either >5ml/Kg /hr in any 1 hour interval or >3 ml/kg/hr for 3 consecutive hours (Hazinski guidelines) in interval C.
OR
2. Any non-routine pro-haemostatic treatment given in response to excessive bleeding. This is defined as any of: additional protamine after initial heparin reversal, fresh frozen plasma (FFP), cryoprecipitate, platelets, anti-fibrinolytic drug, recombinant factor 7 (rFVIIa) or fibrinogen concentrate that is given because clinicians consider that excessive bleeding has started to occur.

The composite endpoint is necessary because of two important constraints:
1. Blood loss is readily quantified after chest drain insertion by measuring drain volume; however, in intervals A and B (before chest drain on suction), measurement of blood loss is not feasible.
2. Non-routine pro-haemostatic therapies are usually given soon after the start of abnormal bleeding and, if effective, prevent further bleeding. Measuring only ‘high blood loss’ would result in the primary endpoint of excessive bleeding not being identified in these instances.

Routine vs non-routine pro-haemostatic therapy
There are two circumstances in which clinicians administer pro-haemostatic therapies:
1. As part of standard institutional protocols for all children in the study population. These are termed ‘routine’ pro-haemostatic therapies (e.g. cryoprecipitate infusion and protamine reversal of heparin at the end of interval A).
2. In response to a perceived risk of excessive bleeding but before excessive bleeding starts. These are termed ‘non-routine prophylactic’ pro-haemostatic therapies and are usually given during interval B.

Clinicians will be invited to classify all pro-haemostatic treatments in the study intervals A-C into one of the categories ‘routine’, ‘non-routine observed bleeding’; and ‘non-routine perceived bleeding’ on the study case report forms. The ‘routine’ and ‘non-routine perceived bleeding’ pro-haemostatic treatments will not be considered part of the primary outcome.

In some cases pump blood (which contains heparin) is returned to the patient during interval B and C and additional protamine is administered for reversal. This protamine dose is part of the

‘routine’ management of heparin after surgery irrespective of whether there is excessive bleeding. Pump blood return will be recorded but will not be considered to be part of a primary clinical outcome.

### Secondary outcome measures
1. Red cell transfusion expressed as any vs. none and total red cell transfusion volume
2. FFP, platelet and cryoprecipitate transfusion expressed as any vs. none and total volume of each blood component
3. Non-blood component pro-haemostatic treatments (extra protamine, rFVIIa, antifibrinolytic drugs or fibrinogen concentrate) expressed as total dose per Kg body weight of each agent
4. Post-operative complications (including death)

### Overall study start date
22/06/2012

### Completion date
31/05/2015

## Eligibility

### Key inclusion criteria
1. Undergoing cardiac surgery requiring CPB
2. Age ≤16 years old
3. Weight >2.5 Kg

### Participant type(s)
Patient

### Age group
Child

### Upper age limit
16 Years

### Sex
Both

### Target number of participants
200

### Key exclusion criteria
1. Emergency operation
2. Isolated Ostium secundum ASD (low bleeding risk)
3. Unable to give informed consent (16 year olds only)
4. In foster care and parents/guardians unavailable to consent

### Date of first enrolment
27/05/2013

### Date of final enrolment

01/05/2015

# Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**Bristol Royal Hospital for Children**
Bristol Heart Institute
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# Sponsor information

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### Sponsor type
Hospital/treatment centre

### ROR
https://ror.org/04nm1cv11

# Funder(s)

### Funder type
Government

**Funder Name**
NIHR Bristol Cardiovascular Biomedical Research Unit (UK)

# Results and Publications

## Publication and dissemination plan
We plan to publish the protocol and we will also be publishing the results when they have been analysed. This is to confirmed at a later date.

## Intention to publish date

## Individual participant data (IPD) sharing plan

## IPD sharing plan summary
Stored in repository

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | protocol | 19/08/2015 | | Yes | No |