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# ROLO The Renoprotective value of Leukodepletion in Heart Valve surgery

| Submission date | Recruitment status | [_] Prospectively registered |
|---|---|---|
| 18/02/2014 | No longer recruiting | [_] Protocol |
| **Registration date** | **Overall study status** | [_] Statistical analysis plan |
| 18/02/2014 | Completed | [X] Results |
| **Last Edited** | **Condition category** | [_] Individual participant data |
| 29/03/2021 | Circulatory System | |

## Plain English summary of protocol

Background and study aims
Having a heart operation can affect the functioning of other organs in the body and sometimes people suffer from damage to their kidneys as a result of their surgery. This is called acute kidney injury. The risk of acute kidney injury is greater in people having heart valve operations compared to other types of heart operation. Most people completely recover from heart surgery related acute kidney injury, but some people will experience long-term kidney disease, affecting their quality of life. Acute kidney injury can increase the length of time patients spend in hospital after their operation and therefore increase the cost of care. One of the reasons heart valve surgery patients suffer from acute kidney injury is because during the operation people are attached to a heart-lung bypass machine. This machine takes over the job of pumping blood around the body whilst the heart is being operated on. The white blood cells circulating in the blood then react to the materials in the heart-lung bypass machine, which activates them and causes inflammation throughout the body. This inflammation can damage the kidneys. This study is looking to see if removing the activated white blood cells from the blood (through a special filter in the heart-lung bypass machine) during surgery will reduce damage to the kidneys.

Who can participate?
Males and females, aged between 18-89 years, having planned heart valve surgery.

What does the study involve?
Participants are randomly allocated to one of two groups. In the standard group a standard filter will be used in the heart bypass machine. This will filter the blood in the normal way but it wont filter out the white blood cells. This is standard practice at the hospital where the study is being held. In the new group a new filter will be used in the heart bypass machine, which will filter the blood in the same way as the standard filter but will also filter out the white blood cells. Participants will be followed for 3 months to see if they develop acute kidney injury after surgery. We will also see how well participants recover in general.

What are the possible benefits and risks of participating?
Possible benefits for patients who have their surgery using the new filter may be reduced kidney damage after surgery. This may lead to reduced recovery times and improved health after surgery, although this cannot be guaranteed. Little is known in terms of risks or adverse effects

associated with the new filter. In theory there is a small risk of contamination when the new filter in inserted into the heart-lung bypass machine and also a small risk of the filter clotting, but these are both thought to be negligible. Patients who have their surgery using the standard filter as part of the study will have no benefits or risks above those patients who do not take part in the study , as the standard filter is used routinely during heart surgery outside of the study.

Where is the study run from?
The study is being run from Blackpool, Fylde and Wyre Hospitals NHS Foundation Trust with the University of Bristol providing management support.

When is the study starting and how long is it expected to run for?
September 2011 to April 2017

Who is funding the study?
National Institute for Health Research (NIHR), UK.

Who is the main contact?
Lucy Dreyer lucy.dreyer@bristol.ac.uk

# Contact information

### Type(s)
Scientific

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
15826

# Study information

## Scientific Title
The Renoprotective value of Leukodepletion in Heart Valve surgery: an external feasibility randomised controlled trial

## Study objectives
That leukodepletion during cardiopulmonary bypass will reduce the incidence and severity of cardiac surgery related acute kidney injury (CSA-AKI) and therefore improve clinical outcomes in patients undergoing heart valve surgery.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
North West - Preston REC, 04/11/2013, ref: 13.NW.0728

## Study design
Randomised; Interventional; Design type: Treatment

## Primary study design
Interventional

## Secondary study design
Randomised controlled trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

## Health condition(s) or problem(s) studied
Topic: Cardiovascular; Subtopic: Cardiovascular (all Subtopics); Disease: Cardiovascular

## Interventions
Current interventions as of 18/05/2017:
Eligible patients are randomised either to a LG6B leukocyte-depleting filter, or a standard 40µm filter into the arterial line of the extracorporeal circuit downstream from the CPB pump.

All patients are managed according to the local standard CPB protocol for valve surgery using mild hypothermic CPB and intermittent antegrade or combined antegrade and retrograde cold blood cardioplegic arrest. Surgical procedures, anaesthesia and post-intervention treatment are all managed according to local standard procedure.

The intervention lasts as long as the patient is attached to the CPB machine. After discharge from hospital, patients are followed up at 6-weeks and 3 months.

Previous interventions:
Control: Standard heart valve surgery will be carried out incorporating a Pall corporation standard 40 µm filter into the arterial line of the extracorporeal circuit downstream from the CPB pump.

Leukodepletion filter (LG6): Standard heart valve surgery will be carried out incorporating a Pall corporation LG6B leukocyte-depleting filter into the arterial line of the extracorporeal circuit downstream from the CPB pump.

Follow Up Length: 3 month(s)

## Intervention Type
Other

## Phase
Not Applicable

## Primary outcome measure
Current outcome measure as of 18/05/2017:
The development of AKI is measured using the Kidney Disease: Improving Global Outcomes" (KDIGO) definition of AKI, endorsed in the Renal Association Clinical Guidelines in the period from surgery until 6 weeks after the operation date.

Previous primary outcome measure:
Primary outcome; Timepoint(s): Development of AKI in the period from surgery until 6 weeks post-op using KDIGO criteria

## Secondary outcome measures
Current secondary outcome measures as of 18/05/2017:
1. Proportion of elective patients undergoing elective heart valve eligible for the trial
2. Proportion of eligible patients who agree to participate
3. Tubular kidney injury using the following biomarkers: urinary excretion ratio of Retinol Binding Protein (RBP) to Creatinine (RBP:Cr), urinary excretion ratio of Kidney Injury Molecule-1 to Creatinine (KIM-1:Cr) and urinary NGAL measured at the end of CPB, and at 4, 24, 48 and 72 hours after surgery. RBP:Cr has previously been validated in cardiac surgical patients (16, 17), but recently reviewed evidence suggests that KIM-1:Cr may be a superior biomarker (17, 18).
4. Glomerular kidney injury using the following biomarkers: urinary excretion ratio of Albumin to creatinine (A:Cr) and serum Cystatin C measured at the end of CPB, and at 4, 24, 48 and 72 hours after surgery. These markers, which have potentially better sensitivity compared to glomerular filtration rate(19), allow for early detection of renal injury before conventional clinical parameters, e.g. blood urea and serum creatinine become abnormal
5. Total diuretic dosage over first 5 postoperative days
6. Daily fluid balance (total input and output) over first 5 postoperative days
7. Adverse events including: in-hospital mortality, need for haemodialysis (continuous veno-venous hemofiltration, CVVH) and infection rates in the period from surgery to 12-weeks
8. Length of post-operative stay in hospital (intensive care and ward days) and other resource use in the period from surgery to 12-weeks
9. Health-related Quality of life (HRQoL) assessment: Minnesota Living with Heart Failure

Questionnaire (MLHFQ) and EQ-5D measured at baseline, 5 days, 6 and 12 weeks. The MLHFQ27 is recommended as the most responsive validated disease-specific measure for heart failure(20). It is also one of the few measures specifically validated for heart valve surgery, demonstrating superior sensitivity to the SF36(29) and good responsiveness with elderly patients(21). In order to evaluate the relative magnitude of changes in quality of life across health conditions, it is standard practice to include a generic HRQoL measure. The EQ-5D is a generic measure that enables the evaluation of both impact and cost in a single measure(22, 23), which has been widely used in a range of cardiac surgery studies(24-27). The recently revised version of the EQ-5D-5L(28), with 5 levels of impairment (the standard version has 3 levels), will be used.

Previous secondary outcome measures
1. Evaluation of tubular kidney injury using the following biomarkers: urinary excretion ratio of Retinol Binding Protein (RBP) to Creatinine (RBP:Cr) and urinary excretion ratio of Kidney Injury Molecule-1 to Creatinine (KIM-1:Cr)
2. Evaluation of glomerular kidney injury using the following biomarkers: urinary excretion ratio of Albumin to creatinine (A:Cr) and serum Cystatin C measurement
3. Total diuretic dosage over first 5 postoperative days
4. Daily fluid balance (total input and output)
5. Adverse events including: in-hospital mortality, need for haemodialysis (CVVH) and infection rates
6. Length of post-operative stay in hospital (intensive care and ward days) and other resource use required for the economic evaluation
7. Health-related Quality of life (HRQoL) assessment: Minnesota Living with Heart Failure Questionnaire (MLHFQ) and EQ-5D

### Overall study start date
01/09/2011

### Completion date
01/04/2017

# Eligibility

### Key inclusion criteria
1. Adults aged 18-89 years having single or multiple heart valve repair or replacement as a first time or redo operation as an elective or urgent procedure (i.e. non-emergency procedure), who are able to give informed consent
2. Patients with or without concomitant procedures. Concomitant procedures may include but are not restricted to: coronary artery bypass graft (CABG), ascending aortic and/or root replacement, and ablation for atrial fibrillation
3. Baseline urea and creatinine levels are within normal range, defined as follows: urea 2.5 to 7.8 mmol/L; creatinine 45 to 90 µmol/L for women and 60 to 110 µmol/L for men. Patients taking medications that may influence renal function, such as aspirin, statins, beta adrenergic antagonists, calcium channel antagonists, ACE inhibitors, diuretics and other cardiac medications, can be included provided that baseline urea and creatinine levels are within the normal ranges given above
Target Gender: Male & Female; Upper Age Limit 89 years ; Lower Age Limit 18 years

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
89 Years

### Sex
Both

### Target number of participants
Planned Sample Size: 108; UK Sample Size: 108; Description: Intervention (leukodepletion filter) = 54Control (standard filter) = 54

### Total final enrolment
64

### Key exclusion criteria
1. Baseline eGFR <30 ml/min/1.73m2
2. Patients on renal replacement therapy
3. Planned deep hypothermic circulatory arrest with cardiopulmonary bypass switched off
4. Patients participating in any other interventional research study (until the end of the follow-up period of the study). Participation in an observational study will not preclude participation in ROLO

### Date of first enrolment
01/02/2014

### Date of final enrolment
02/12/2015

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**Blackpool Teaching Hospitals NHS Foundation Trust**
Whinney Heys Road
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# Sponsor information

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Blackpool, Fylde and Wyre Hospitals NHS Trust (UK)

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### Sponsor type
Research council

### ROR
https://ror.org/03444yt49

# Funder(s)

### Funder type
Government

### Funder Name
NIHR (UK) - Research for Patient Benefit (RfPB); Grant Codes: PB-PG-0711-25090

# Results and Publications

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

### Intention to publish date
01/04/2018

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from bristol-cteu@bristol.ac.uk

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
| --- | --- | --- | --- | --- | --- |
| Results article | | 26/03/2021 | 29/03/2021 | Yes | No |