ISRCTN82431978 https://doi.org/10.1186/ISRCTN82431978

Evaluation of unloading the heart in patients with cardiogenic shock treated with mechanical circulatory support devices

Submission date	**Recruitment status**	[X] Prospectively registered
17/01/2022	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/01/2022	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
15/06/2026	Circulatory System	[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Cardiogenic shock occurs when the heart suddenly fails and is unable to meet the body's demands, often leading to death. Cardiogenic shock is becoming more common particularly in patients suffering heart attacks and therefore research into potential treatments to improve the high death rate is urgently needed. Current treatment options are limited and can be associated with an increased death rate.

A promising new treatment is veno-arterial extracorporeal membrane oxygenation (VA-ECMO). This mechanical support system works like a heart bypass to support the body whilst the heart recovers. However, while beneficial to most other organs, VA-ECMO can put additional pressure on the heart by pumping blood backwards into the aorta (the main artery that carries blood away from the heart), preventing it from recovering. If the heart is unable to overcome this increased pressure (or afterload) a number of dangerous events can occur such as the formation of blood clots in the heart or the build-up of fluid in the lungs which can be potentially fatal. This problem can be solved by using additional devices in the circulation to “unload” the heart. Two devices are commonly used for this task - the intra-aortic balloon pump (IABP) and Impella - but it is not known which one works better as they have never been directly compared. Additionally, each device has a distinct mechanism of action, the effect of which has never been studied in patients treated with VA-ECMO. Currently therefore hospitals are treating such patients differently due to the lack of available evidence as to the best treatment strategy. This study aims to directly compare the effects of the IABP and Impella on parameters of supply and demand of oxygen to the heart which are the key determinants of heart recovery.

Who can participate?

Patients aged 18 years and over who are being treated in an intensive care unit for cardiogenic shock and are either treated with VA-ECMO or are being considered for treatment with VA-ECMO by their doctors are eligible to participate.

What does the study involve?

Participants are randomly allocated to be treated with either an IABP or Impella. They will have specialised measurements of blood flow in their coronary (heart) arteries and pressures within

the ventricle (the main pumping chamber of the heart) taken in the cardiac catheterisation laboratory. These will be repeated after the unloading device is inserted. The remainder of the participants care will be as they would normally receive if not participating in the research study.

What are the possible benefits and risks of participating?
Because it is not known which device works better, there are no direct benefits from taking part in this study. The researchers will obtain information which it is hoped will improve the treatment of patients with the same condition in the future.
Participating in the study will not increase risk substantially compared to standard treatment with VA-ECMO. Taking the additional measurements will involve placing a small sensor in the coronary arteries and the heart itself under X-ray guidance: the risk of causing damage to either the heart or the arteries is likely to be around 1 in 300. A small additional dose of ionising radiation will be required to acquire the study measurements. Ionising radiation may cause cancer many years or decades after the exposure. We are all at risk of developing cancer during our lifetime. 50% of the population is likely to develop one of the many forms of cancer at some stage during our lifetime. Taking part in this study will add only a very small chance of this happening (<0.1% added risk).

Where is the study run from?
King's College London (UK)

When is the study starting and how long is it expected to run for?
February 2020 to November 2026

Who is funding the study?
1. British Heart Foundation (UK)
2. RBH-KHP Partnership Transformation Funding (UK)

Who is the main contact?
Dr Saad Ezad
saad.ezad@kcl.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Saad Ezad

ORCID ID
https://orcid.org/0000-0002-3008-5290

Contact details
Cardiovascular Division
Rayne Institute
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

+44 (0)207 188 3026
saad.ezad@kcl.ac.uk

Type(s)
Principal investigator

Contact name
Prof Divaka Perera

ORCID ID
https://orcid.org/0000-0001-6362-1291

Contact details
Cardiovascular Division
Rayne Institute
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH
+44 (0)207 188 3026
divaka.perera@kcl.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
300145

Central Portfolio Management System (CPMS)
51137

Study information

Scientific Title
HEmodynamic effects of Reducing left ventricular Afterload with impella or intra-aortic balloon CounterpuLsation during veno-arterial Extracorporeal membrane oxygenation in cardiogenic Shock (HERACLES)

Acronym
HERACLES

Study objectives
It is hypothesised that ventricular unloading of patients supported with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) with an Impella will result in a greater increase in the coronary device flow reserve as compared to unloading with an intra-aortic balloon pump.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/01/2022, London - Queen Square Research Ethics Committee (HRA NRES Centre Bristol, 3rd Floor, Block B, Whitefriars Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)2071048225; queensquare.rec@hra.nhs.uk), REC ref: 21/LO/0853

Primary study design
Interventional

Study design
Randomized; Interventional; Design type: Treatment, Device

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cardiogenic shock

Interventions
HERACLES is a randomised control trial designed to compare the physiological effects on myocardial oxygen supply and demand of ventricular unloading with either an IABP or Impella in patients supported with VA-ECMO. Patients who are either supported with VA-ECMO or being considered for VA-ECMO support will be eligible for inclusion in the trial. At the time of cardiac catheterisation participants will be randomised in a 1:1 fashion to unloading with either an IABP or Impella. Randomisation will be performed via a computer using a web-based bespoke KCTU randomisation system. Coronary flow and ventricular pressure volume measurements will be recorded prior to insertion of the randomised unloading device and then repeated following device insertion. The randomised unloading device will remain in situ for as long as clinically indicated at the discretion of the treating physician. No further study related procedures are performed after completion of the study protocol in the cardiac catheterisation laboratory. Patients will be followed up 6 months post randomisation. Results will be compared between the two groups to identify if one device has a greater beneficial impact on the ratio of myocardial oxygen supply and demand.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
IABP, Impella

Primary outcome(s)
Coronary device flow reserve measured using a coronary guidewire post left ventricular (LV) unloading

Key secondary outcome(s)
1. Early effect of LV unloading measured using an LV catheter post LV unloading
2. Minimal microvascular resistance calculated from pressure and flow measurements post LV unloading
3. Time to VA-ECMO decannulation (days) measured using patients' medical records

4. Days alive and off ICU (at 30 days post randomisation) measured using patients' medical records

Completion date
28/11/2026

Eligibility

Key inclusion criteria
1. Patients aged ≥18 years with cardiogenic shock of any aetiology
2. On veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support or starting VA-ECMO post PCI
3. Undergoing clinically indicated cardiac catheterisation

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. Post-cardiotomy cardiogenic shock
2. Confirmed left ventricular thrombus on imaging
3. Age <18 years
4. Pregnancy or peripartum cardiomyopathy
5. Contraindication to either intra-aortic balloon pump (IABP) or percutaneous left ventricular assist device (pLVAD) insertion i.e. ≥moderate aortic regurgitation (AR), severe peripheral vascular disease (PVD) prohibiting insertion of either device
6. Mechanical aortic valve replacement (AVR)

Date of first enrolment
09/03/2022

Date of final enrolment
01/08/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
St Thomas' Hospital
Westminster Bridge Road
London
England
SE1 7EH

Study participating centre
King's College Hospital
Denmark Hill
London
England
SE5 9RS

Study participating centre
Harefield Hospital
Hill End Road
Harefield
Uxbridge
England
UB9 6JH

Study participating centre
Royal Brompton Hospital
Sydney Street
London
England
SW3 6NP

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation; Grant Codes: FS/CRTF/21/24118

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

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Funder Name
RBH-KHP Partnership Transformation Funding

Results and Publications

Individual participant data (IPD) sharing plan

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