Use of mechanical left ventricular unloading in acute decompensated systolic heart failure complicated by cardiogenic shock

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To assess the efficacy of early mechanical left ventricular unloading and standard of care (inotropes/vasopressors) versus inotropes/vasopressors alone (standard-of-care) in patients with ADHF and signs of cardiogenic shock.

Ethical review	Approved WMO
Status	Pending
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON53204

Source
ToetsingOnline

Brief title
UNLOAD HF-CS

Condition

- Heart failures

Synonym
heart failure, shock

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC

Source(s) of monetary or material Support: Abiomed

Intervention

Keyword: Acute Heart Failure, Cardiogenic shock, Mechanical support, Ventricular unloading

Outcome measures

Primary outcome

COMBINED CLINICAL ENDPOINT (90 days)

All-cause mortality

Renal replacement therapy

Rehospitalization/urgent hospital visit for HF

Secondary outcome

SECONDARY ENDPOINTS

In-hospital mortality (Time frame: index hospitalization)

In-hospital Worsening Heart Failure (Time frame: index hospitalization)

Urgent/rescue MCS implantation (Time Frame: index hospitalization)

Renal replacement therapy (Time frame: index hospitalization)

Mechanical ventilation (Time frame: index hospitalization)

ICU dependency (Time frame: index hospitalization)

SOFA scores (maximal) (Time frame: index hospitalization)

Vasoactive Inotropic Score (maximal) (Time Frame: index hospitalization)

Rehospitalization/urgent hospital visit HF (Time Frame: 90 days and 1 year)

Cardiac mortality (Time frame: 90 days and 1 year)

All-cause mortality (Time frame: 90 days and 1 year)

LVAD/Heart transplant (Time Frame: index hospitalization, 90 days, 1 year)

KCCQ-12 (Time frame: 90 days, 1 year)

SAFETY ENDPOINTS

Major bleeding (Time Frame: index hospitalization)

Stroke and TIA (Time Frame: index hospitalization)

Major vascular complications (Time Frame: index hospitalization)

Extremity ischemia (Time Frame: index hospitalization)

Hemolysis (Time Frame: index hospitalization)

Infection (proven) insertion site (Time Frame: 90 days)

Aortic valve injury (Time Frame: 90 days)

Study description

Background summary

Acute decompensated heart failure (ADHF) is a serious condition and leading cause of hospitalization. it carries a high morbidity and mortality. The average length of hospital stay is approximately 7 to 9 days, 30-day readmission rate around 20% and up to one in 10 patients dies in hospital, whereas one in three dies within the year following an hospitalization episode. Among hospitalized patients with AHF, approximately 15 to 20% have worsening of heart failure (WHF) with signs of cardiogenic shock during their hospitalization mandating escalation of therapy. Patients suffering from acuut heart failure and shock have worse outcomes than those with an uncomplicated admission for heart failure.
The natural history of HF is a progressive decline in ventricular function as compensatory remodeling ultimately fails and patients present with recurrent episodes of AHF and ultimately cardiogenic shock (CS) owing to advanced HF. The vast majority of AHF (especially acute-on-chronic) episodes are characterized by increasing symptoms and signs of congestion with volume overload. The goal of therapy in those patients is the early relief of congestion and to prevent end-organ damage through organ hypoperfusion. Inotropic support is considered first-line therapy, although the evidence is relatively scarce. Mechanical unloading by means of a temporally left ventricle assist device is clinically practised and forms an alternative approach. On the other hand, invasive treatment leads to complications. Equipoise exists. An RCT has not been conducted so far in ADHF patients complicated by cardiogenic shock that compares the addition of mechanical unloading to pharmacological therapy versus

pharmacological therapy alone.

Study objective

To assess the efficacy of early mechanical left ventricular unloading and standard of care (inotropes/vasopressors) versus inotropes/vasopressors alone (standard-of-care) in patients with ADHF and signs of cardiogenic shock.

Study design

Open label, randomized

Intervention

Mechanical left ventricular unloading with the Impella 5.5 and standard of care (inotropes/vasopressors) versus standard of care (inotropes/vasopressors)

Study burden and risks

All decompensated heart failure patients with evidence of cardiogenic shock who have consented and who are included in the trial will have a clinical indication for inotropic/vasopressor therapy. Initiation of inotropes/vasopressors in this specific condition, albeit recommended as first-line therapy, has been associated with no or only temporary improvement or even increased overall mortality. As such, this permits an approach in which a higher level of invasiveness, being mechanical cardiac support, is considered and can be encouraged. Since there are no randomized controlled trials which advocate the use of either inotropic/vasopressor therapy or mechanical support by the Impella 5.5 over one another in this setting, patients will not be exposed to extra known risk due to randomization in the trial.
Temporary mechanical circulatory support is a widely accepted and applied treatment modality in high-risk, complex PCI and in the setting of acute myocardial infarction related cardiogenic shock. In those circumstances the benefit (reversal of ischemia and cardiogenic shock) is hypothesized to outweigh the associated complications. The same arguments apply in the setting of decompensated heart failure with evidence of cardiogenic shock.
Complications, albeit with a reported wide occurrence rate, that are associated with the use of the Impella 5.5 are: arm ischemia (~0,5%), vascular injury that may or may not require intervention or surgery (~1,5%), stroke (~2%), infection of the insertion site (~1%), hemolysis (7-10%) and major bleeds (13% the latter greatly depending on the thrombolytic regimen applied).
We are aware of the potentially severe adverse events, however the deleterious clinical condition of decompensated heart failure with signs of cardiogenic shock, together with the meticulous attention and proper access site management (surgically) that is being attributed, justifies the application of temporary

mechanical support in our opinion. The benefits outweigh the associated risks.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Evidence of HFrEF according to ESC HF guidelines, (LVEF <= 35%)
2. Signs of (persistent) congestion (elevated CVP, edema, rales)
3. Evidence of CS with presence of at least 2 of the 3 following
a. hypotension (systolic blood pressure <90 mmHg or mean arterial pressure <60 mmHg)
b. oliguria (<= 0,5 ml/kg/h, <= 720 ml/24 h, lactate > 2 mmol/L,creatinine rise >= 0.3 mg/dl during first
24h (26,53 µmol/L, amino-L-transferase >200 U/L)
c. inotropes/vasoactive (use of)

4. Age 18-75 y

Exclusion criteria

1. Cardiovascular
a. Contraindications for Impella CP
b. Severe concomitant RV failure
c. Contraindications for inotropic usage
d. Dialysis for end-stage renal failure
e. Acute coronary syndrome during admission
2. Medical history
a. History of CVA or TIA within previous 90 days
b. History of acute myocardial infarction within previous 30 days
c. History of bleeding diathesis
3. Inflammatory
a. Active systemic infections, sepsis
4. General
a. Patient has other medical, social, or psychological problems
b. Patient belongs to a vulnerable population

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2023
Enrollment:	154

Type:	Anticipated

Medical products/devices used

Generic name:	Impella 5.5
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	14-07-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT05064202
CCMO	NL84199.018.23