Randomized Embedded Multifactorial Adaptive Platform in ExtraCorporeal Membrane Oxygenation (REMAP ECMO)

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To study the effects of left ventricular unloading by means of IABP or Impella as an adjunct to ECMO versus ECMO alone on ECMO weaning success, mortality, quality of life and cost-effectiveness, and intermediating physiological parameters....

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

Summary

ID

NL-OMON56072

Source
ToetsingOnline

Brief title
REMAP ECMO

Condition

- Heart failures

Synonym
Cardiogenic shock, Heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: de Hartstichting

Intervention

Keyword: ECMO, Intra-aortic balloon pump, Left ventricular unloading, Weaning success

Outcome measures

Primary outcome

Successful ECMO weaning at 30 days, defined by; a) being alive, b) without ECMO, IABP or Impella support, and c) not having received a heart transplantation or left ventricular assist device (LVAD).

For the physiological substudy:

The difference in left ventricular end diastolic volume (as estimated by transesophageal echocardiography) measured at the first time point (after hemodynamic stabilization (defined by stable hemodynamic parameters such as blood pressure and heart rate, and adequate ECMO flow) and within 24h after ECMO initiation) in the cohort of patients supported by V-A ECMO with- versus without- IABP at baseline (mechanical ventilation set at clinical PEEP).

Secondary outcome

1.. Treatment failure defined by: insertion of an IABP (only in the ECMO alone arm), Impella (IABP unloading arm) or left atrial/ventricular vent (in all arms).

2. 30 day, 90 day, and 1 year mortality,

3. ECMO support duration,

4. ICU- and hospital- admission duration,

5. The occurrence of major bleeding events (fatal, in a critical area (intracranial, intraspinal, or intraocular), requiring intervention (coiling or

surgery)

and/or transfusion of >=3 packed cells) during or until 24 hours after

ECMO- or IABP-support, whichever comes last. (22)

6. Unplanned surgical or catheter based intervention of the leg(s) in which

ECMO and/or IABP was inserted during, or until 24 hours after ECMO- or

IABP-support, whichever comes last.

7. Time to lactate normalization (<2 mmol/L).

8. Time to first negative net fluid balance (counted per 24 hours).

9. The occurrence of continuous venovenous hemofiltration (dialysis) (CVVH(D))

initiation during ECMO support.

10. Course in PF ratio during ECMO support.

11. Duration of mechanical ventilation. Patients on mechanical ventilation via

tracheostomy need to be 24 hours free of mechanical ventilation.

12. Left ventricular ejection fraction 30 days after ECMO initiation.

13. Time course in vasoactive inotropic score (VIS) during ECMO support

14. Quality of life (QoL on basis of EQ5D questionnaires) after 1 year.

15. Total health care costs based on validated questionnaires (iMCQ and iPCQ)

at 6 months and 12 months follow up.

For the physiological substudy:

1. Heart rate

2. Pulmonary artery catheter: pulmonary capillary wedge pressure, cardiac

output, central venous pressure

3. Echocardiography: Left ventricular ejection fraction, TAPSE, VTI LVOT

4. Microcirculation measurements: Perfused vessel density (PVD [mm/mm2], Total

vessel density (TVD [mm/mm2],

5. Respiratory: FiO2, PEEP, Respiratory System Compliance (CRS) as the ratio

between Vt/Dp.

6. Laboratory: delta NT-pro BNP

Study description

Background summary

Extracorporeal membrane oxygenation (ECMO) can be of lifesaving effect in patients with severe and refractory circulatory and/or respiratory failure. Nevertheless, even today, 30-70 percent of patients cannot be weaned from ECMO support and up to 50 percent of all patients die within one year. These high weaning failure- and mortality- rates seem in part attributable to the occurrence of major complications.
One of the inherent problems related to the application of venoarterial (VA) ECMO in the context of a failing heart pertains to the occurrence of left ventricular (LV) overload. Higher afterload can contribute to an increased myocardial oxygen demand and higher LV end-diastolic pressure causing LV dilatation, pulmonary oedema and thrombi in the heart and aortic root. Eventually, this could lead to failure to wean from ECMO and an increased mortality risk.
Several strategies could reduce or mitigate the effects of LV overload, so called *unloading*. Unloading of the LV can be achieved by placing an intra-aortic balloon pump (IABP) or an Impella in conjunction with VA ECMO. Several observational studies have suggested that addition of an IABP or Impella on top of ECMO may significantly reduce ECMO support duration and improve survival, especially when used in a prophylactic fashion and as soon as possible. Findings from these studies must however be interpreted with great caution because of the effects of confounding by indication and selection bias. Also, LV unloading through mechanical devices is associated with higher rates of complications including bleeding, ischemia of the leg, haemolysis and infection.
This randomized clinical trial will serve to randomize the existing variation in treatment practice regarding the placement of an IABP or Impella as an adjunct to VA ECMO, and thereby infer a conclusion on the best strategy.

Physiological effects of IABP in patients receiving V-A ECMO
In patients with refractory cardiac arrest and profound cardiogenic shock

undergoing V-A ECMO, a complex pathophysiological interaction is set between the mechanically assisted heart and other organ systems, such as the mechanically ventilated lungs and the circulatory system (macro- and micro-circulation). This pathophysiological framework becomes even more complex with the addition of an extra mechanical unloading device, such as the IABP. The effects of IABP as adjunct to V-A ECMO on physiological variables have never been studied in a randomized way. The framework of this platform and the currently undergoing RCT enable us to add a physiological substudy to the this trial that assesses the physiological impact of IABP in the context of V-A ECMO on respiratory and hemodynamic.

Study objective

To study the effects of left ventricular unloading by means of IABP or Impella as an adjunct to ECMO versus ECMO alone on ECMO weaning success, mortality, quality of life and cost-effectiveness, and intermediating physiological parameters.

Physiological substudy
To assess the effects of left ventricular unloading through IABP, in the setting of VA ECMO support, on cardiovascular and respiratory physiology by integrating a physiological substudy (by additionally recording physiological parameters which are already collected in light of clinical routine).

Study design

An open-label, multicentre, response-adaptive, randomized clinical trial studying the effects of left ventricular unloading by means of IABP or Impella as an adjunct to ECMO versus ECMO alone on ECMO weaning success. This trial will implement a contemporary Bayesian approach.

Physiological substudy:
A nested physiological observational substudy within the ongoing REMAP ECMO RCT, using the trial arms where patients are randomized between receiving V-A ECMO with or without IABP in two of the participating centres (Erasmus MC and Haga hospital)

Intervention

The LV unloading trial domain will study the effects of ECMO + IABP vs ECMO + Impella vs ECMO alone on weaning success and will encompass three arms:
1. *ECMO alone arm*: VA ECMO without mechanical unloading
2. *IABP unloading arm*: the combination of VA ECMO with an IABP.
3. * *Impella unloading arm*: the combination of VA ECMO with an Impella.
*During the trial, an *Impella unloading arm* will be added. Specifics of the

integration of this arm will be provided in an amendment during the study.

Study burden and risks

potential risks are considered moderate at maximum as a majority of patients already receive an IABP or Impella in all centres. Patient burden is also considered small for the same reason and the fact that no additional transports are required. In addition, patients suffer from a severely reduced state of consciousness due to the effects of sedation and severity of their illness.

Performing transesohageal echocardiography and a decremental PEEP trial are all done in light of standard of V-A ECMO care. Patients will therefore not be exposed to additional risks.
Sublingual measurements of the microcirculation are currently already applied in the ICU setting but is not routinely used in all patients. These measurements therefore represent the only extra measurements collected outside of standard clinical practice. Sublingual measurements are non-invasive and there are no risks associated with this monitoring device. Patients won*t notice it because they suffer from a severely reduced state of consciousness, due to deep sedation and the severity of their illness. There is no additional burden related to microcirculation measurements.

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

- Having received ECMO support for severe circulatory and/or respiratory insufficiency.
- Age >= 18 years
- Cardiogenic shock
- Initiation of intra-aortic balloon pump (IABP) possible <= 8 hours after ECMO initiation

Exclusion criteria

- Raised objection during the deferred consent procedure
- ECMO usage confined to the period during surgery or another intervention (the ECMO was
removed at the end of the intervention).
- Isolated right ventricular failure (e.g. due to pulmonary embolism).
- Left ventricular assist device (LVAD), Impella or IABP in situ.
- Ventricular septal defect or papillary muscle rupture as the cause of shock.
- Thoracic or abdominal aortic dissection.
- Moderate or severe aortic regurgitation
- Mechanical prosthesis in mitral valve position
- Pregnancy

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-06-2023
Enrollment:	430
Type:	Actual

Medical products/devices used

Generic name:	Intra-aortic balloon pump and Impella
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	03-05-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-12-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NCT05913622
CCMO	NL82979.078.23