

## Supplementary material

*Josiassen J, Frydland M, Hassager C, et al. Randomised clinical trials of patients with acute myocardial infarction-related cardiogenic shock: a systematic review of used cardiogenic shock definitions and outcomes. Kardiol Pol. 2021.*

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**Table S1.** Ongoing and future trials

| Study name             | Sample Size | Intervention                                   | Length of follow-up | Primary endpoint                                                                                           | Main secondary endpoints                                                    |
|------------------------|-------------|------------------------------------------------|---------------------|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| <b>DANGER-shock</b>    | 360         | Impella CP<br>vs<br>no Impella CP              | 180 days            | 180-day mortality                                                                                          | Composite of cardiovascular events (need for additional mechanical support) |
| <b>ECLS-SHOCK</b>      | 420         | ECLS<br>vs<br>No ECLS                          | 12 months           | 30-day mortality                                                                                           | Time to death within 6- and 12-months follow-up                             |
| <b>Dafsah A. Juzar</b> | 92          | IABP<br>vs<br>No IABP                          | 30 days             | 30-day mortality                                                                                           | –                                                                           |
| <b>COCCA</b>           | 380         | Hydrocortisone +<br>Flucortac<br>vs<br>Placebo | 90 days             | Patients not treated with corticosteroids at day 7                                                         | Mortality at 28 and 90 days after randomisation. Change in cardiac index    |
| <b>REVERSE</b>         | 96          | VA-ECMO + Impella CP<br>vs<br>VA-ECMO          | 60 days             | 30-day survival, free from mechanical circulatory support, heart transplantation or inotropic support      | Survival to discharge                                                       |
| <b>ECMO-CS</b>         | 120         | VA-ECMO<br>vs<br>No VA-ECMO                    | 12 months           | 30-day composite of death from any cause, resuscitated circulatory arrest, and implantation of another MCS | 30-day, 6 months and 12 months all-cause mortality                          |

|                       |     |                                           |           |                                                                                                              |                                               |
|-----------------------|-----|-------------------------------------------|-----------|--------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| <b>DAPT-SHOCK-AMI</b> | 304 | CANGRELOR<br>vs<br>TICAGRELOR             | 12 months | 30-day combined endpoint of death/MI/stroke                                                                  | Individual components of the primary endpoint |
| <b>ANCHOR</b>         | 400 | VA-ECMO + IABP<br>vs<br>No VA-ECMO + IABP | 12 months | 30-day treatment failure. 30-mortality death in the ECMO group and death OR rescue ECMO in the control group | 30-day all-cause mortality MACE               |

Abbreviations: ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MACE, major adverse cardiovascular events; MCS, mechanical circulatory support; MI, myocardial infarction; OR, odds ratio; VA-ECMO, veno-arterial ECMO

**Table S2.** Ongoing and future trials

| Study name          | Inclusion criteria                                                                                                                                                                                                                                                                 | Exclusion criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Including comatose out-hospital cardiac arrest patients? |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|
| <b>DANGER-shock</b> | <p><b>Blood pressure:</b><br/>— Systolic blood pressure &lt;100 mm Hg for &gt;30 minutes or catecholamines required</p> <p><b>Cardiac function:</b><br/>— LVEF &lt;45%</p> <p><b>End-organ perfusion:</b><br/>— Arterial lactate &gt;2.5 mmol/l</p> <p><b>Other:</b><br/>STEMI</p> | <ul style="list-style-type: none"> <li>— CS duration &gt;24 hours</li> <li>— Mechanical cause of CS</li> <li>— Severe valvular disease</li> <li>— Severe peripheral artery disease precluding Impella insertion</li> <li>— VA-ECMO</li> <li>— Mechanical aortic valve prosthesis</li> <li>— Infective endocarditis</li> <li>— Predominantly RV failure</li> <li>— Left ventricular thrombus</li> <li>— Life expectancy &lt;12 months prior to admission</li> <li>— Out-hospital cardiac arrest with GCS &lt;8 after return of spontaneous circulation</li> </ul> | No                                                       |
| <b>ECLS-SHOCK</b>   | <p><b>Blood pressure:</b><br/>— Systolic blood pressure &lt;90 mm Hg for &gt; 30 minutes or catecholamines required</p>                                                                                                                                                            | <ul style="list-style-type: none"> <li>— CS duration &gt;12 hours</li> <li>— Resuscitation &gt;45 min</li> <li>— Mechanical cause of cardiogenic shock</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                | Yes                                                      |

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|                        | <p><b>Cardiac function:</b></p> <p>—</p> <p><b>End-organ perfusion:</b></p> <p>— Arterial lactate &gt;3 mmol/l</p> <p>At least 1 of the following:</p> <p>— Altered mental status</p> <p>— Cold, clammy skin and limbs</p> <p>— Urine output &lt;30 ml/h</p> <p><b>Other:</b></p> <p>—</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <p>— Severe peripheral artery disease precluding ECLS insertion</p> <p>— Age &gt; 75 years</p> <p>— Life expectancy &lt;6 months prior to admission</p> <p>— Shock of other cause than AMI</p> <p>— Pregnancy</p>                                                                                                                                                          |     |
| <b>Dafsah A. Juzar</b> | None mentioned                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <p>— CS duration &gt;12 hours</p> <p>— Resuscitation &gt;30 min</p> <p>— Mechanical cause of cardiogenic shock</p> <p>— Severe valvular disease</p> <p>— Severe peripheral artery disease precluding IABP insertion</p>                                                                                                                                                    | Yes |
| <b>COCCA</b>           | <p><b>Blood pressure:</b></p> <p>— Systolic blood pressure &lt;90 mm Hg or map &lt;65mm Hg for &gt;30 minutes or catecholamines required</p> <p><b>Cardiac function:</b></p> <p>At least 1 of the following:</p> <p>— cardiac index <math>\leq 2.2</math> l/min/m<sup>2</sup></p> <p>— LVEF <math>\leq 40\%</math></p> <p>— full time velocity (ITV) under aortic <math>\leq 18</math> cm</p> <p><b>End-organ perfusion:</b></p> <p>At least 1 of the following:</p> <p>— Altered mental status</p> <p>— Marbling</p> <p>— Urine output &lt;25 ml/h</p> <p>— Arterial lactate &gt;2 mmol/l</p> <p><b>Other:</b></p> <p>At least 1 of the following:</p> <p>— Clinical signs of right or pulmonary congestion</p> <p>— E/A &gt;2 if FEVG <math>\leq 40\%</math> or E/Ea &gt;13 if LVEF &gt;40%</p> <p>— PAPS &gt;35 mm Hg</p> <p>— PCWP &gt;15 mm Hg</p> <p>— PAPm &gt;25 mm Hg</p> | <p>— CS duration &gt;24 hour</p> <p>— Septic shock</p> <p>— Myocarditis</p> <p>— ECMO prior to randomisation</p> <p>— Pregnancy</p> <p>— Cardiac arrest recovered within the last 7 days</p> <p>— Prior treatment corticosteroid therapy &gt;30 mg</p> <p>— Treatment with one of: ketoconazole, rifampicin, phenytoin, phenobarbital, cyclosporine and clarithromycin</p> | Yes |

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| <b>REVERSE</b>        | <p><b>Blood pressure:</b><br/>— Systolic blood pressure &lt;90 mm Hg for &gt;30 minutes or catecholamines required</p> <p><b>Cardiac function:</b><br/>— Cardiac index &lt;1.8 l/min/m<sup>2</sup> or &lt; 2.0 l/min/m<sup>2</sup> on moderate to high doses of inotropes and vasopressor for &gt;30 minutes</p> <p><b>End-organ perfusion:</b><br/>— “signs of tissue hypoxia”</p> <p><b>Other:</b><br/>—</p>                                                                                                                                                                                                                                                                                                                | <p>— Non-AMI cause of CS</p> <p>— Sepsis</p> <p>— Resuscitation &gt;20–30 min</p> <p>— TTM treatment</p> <p>— Mechanical aortic valve prosthesis</p> <p>— Recent significant pulmonary embolus</p> <p>— Awaiting transplant or on permanent MCS</p> <p>— Left ventricular thrombus</p> <p>— Severe liver failure</p> <p>— Active malignancy</p> | Yes |
| <b>ECMO-CS</b>        | <p><b>Blood pressure and cardiac function:</b><br/>At least 1 of the following:<br/>— Cardiac index &lt; 2.2 l/min/m<sup>2</sup> + norepinephrine dose &gt;0.1 µg/kg/min + dobutamine dose &gt;5 µg/kg/min<br/>— Systolic blood pressure &lt;100 mm Hg on norepinephrine dose &gt;0.2 µg/kg/min + dobutamine dose &gt;5 µg/kg/min and LVEF &lt;35%<br/>— LVEF 35%–55% in case of severe mitral regurgitation or aortic stenosis</p> <p><b>End-organ perfusion:</b><br/>At least 1 of the following:<br/>— Arterial lactate &gt;3 mmol/l (2 consecutive samples)<br/>— SvO<sub>2</sub> &lt;50% (2 consecutive samples)</p> <p><b>Other:</b><br/>At least 1 of the following:<br/>— CVP &gt;7 mm Hg<br/>— PCWP &gt;12 mm Hg</p> | <p>— Mechanical cause of shock</p> <p>— Life expectancy &lt;12 months prior to admission</p> <p>— Severe peripheral artery disease precluding ECMO insertion</p> <p>— Hypertrophic obstructive cardiomyopathy</p> <p>— Severe aortic disease</p> <p>— Major bleeding</p> <p>— Aortic dissection</p> <p>— Known encephalopathy</p>               | No  |
| <b>DAPT-SHOCK-AMI</b> | <p><b>Blood pressure:</b><br/>— Systolic blood pressure &lt;90 mm Hg for &gt;30 minutes or catecholamines required</p> <p><b>Cardiac function:</b><br/>—</p> <p><b>End-organ perfusion:</b><br/>At least 1 of the following:<br/>— Altered mental status<br/>— Cyanosis</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                   | <p>— Contraindications of antiplatelet therapy with ticagrelor/cangrelor</p> <p>— Administration of P2Y<sub>12</sub> inhibitor prior to admission</p> <p>— Need of concomitant anticoagulation therapy due to indications such as atrial fibrillation, artificial valve, thromboembolic disease etc.</p>                                        | Yes |

| <b>Other:</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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| —             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>ANCHOR</b> | <p><b>Blood pressure:</b></p> <ul style="list-style-type: none"> <li>- Systolic blood pressure &lt;90 mm Hg for &gt;30 minutes or catecholamines required</li> </ul> <p><b>Cardiac function:</b></p> <p>—</p> <p><b>End-organ perfusion:</b></p> <p>At least 1 of the following:</p> <ul style="list-style-type: none"> <li>— Altered mental status</li> <li>— Cold, clammy skin and limbs</li> <li>— Urine output &lt;30 ml/h</li> <li>— Arterial lactate &gt;2 mmol/l</li> </ul> <p><b>Other:</b></p> <ul style="list-style-type: none"> <li>— Signs of pulmonary congestion</li> </ul>        |
|               | <ul style="list-style-type: none"> <li>— Resuscitation &gt;30 min</li> <li>— No intrinsic heart action</li> <li>— Expected severe deficit in cerebral function</li> <li>— Mechanical cause of cardiogenic shock</li> <li>— CS duration &gt;24 hours</li> <li>— Patient moribund on the day of randomization or SAPS II &gt;90</li> <li>— Severe peripheral artery disease precluding ECMO or IABP insertion</li> <li>— Massive pulmonary embolism</li> <li>— Life expectancy &lt;12 months prior to admission</li> <li>— Proven heparin-induced thrombocytopenia</li> <li>— Pregnancy</li> </ul> |
|               | Yes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

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Abbreviations: AMI, acute myocardial infarction; CS, cardiogenic shock; CVP, central venous pressure; ECLS, extracorporeal life support; GCS, Glasgow Coma Scale; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; PAPm, pulmonary arterial mean pressure; PAPS, systolic pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; RV, right ventricle; SAPS, simplified acute physiology scores; STEMI, ST-segment elevation myocardial infarction; TTM, targeted temperature management; VA-ECMO, veno-arterial extracorporeal membrane oxygenation

### Search strategy

Pubmed: (((((((("Clinical Studies as Topic"[Mesh]) OR "Clinical Trial"[Publication Type])) OR (((((((("Observational Studies as Topic"[Mesh]) OR "Observational Study"[Publication Type])) OR observational) OR registry)) OR ((randomized controlled trials) OR randomized controlled trial)))) AND (((("Myocardial Infarction"[Mesh]) OR "Myocardial Infarction"[Title/Abstract])) AND ((cardiogenic shock[Title/Abstract]) OR "Shock, Cardiogenic"[Mesh])). Filter: "Randomized Controlled Trial"

Embase: (Cardiogenic shock or cardiogenic shock.ab.ti.) and (exp heart infarction or myocardial infarction.ab.ti.) and (clinical study/or exp clinical trial/or exp intervention study/or exp longitudinal study/ or exp major clinical study/or exp prospective study/or exp retrospective study) only (full text and human and English language).

Types of study to be included

Studies included will be randomized controlled trials, clinical trials, comparative studies, cohort studies and pragmatic clinical trials, validation studies and observational studies. Case reports, review papers and case series will not be included. Animal studies will not be included. Only studies from 1999 until 2019 will be included. Articles not published in English will be excluded.