**SUPPLEMENTAL APPENDIX**

**Table S1 PRISMA checklist**

|  |  |  |  |
| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Reported on page #** |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | |  |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3 |
| **METHODS** | | |  |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | n.a. |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 4 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 5 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | 5 |

**Table S2 Cochrane Risk of Bias tool**

|  |  |  |
| --- | --- | --- |
| **Thiele et al.**[**1**](#_ENREF_1) | | |
|  | **Authors’ judgment** | **Support for judgment** |
| Random sequence generation (selection bias) | low risk | Quote: […] were randomized by drawing sealed envelopes […] |
| Allocation concealment (selection bias) | low risk | Quote: […] were randomized by drawing sealed envelopes […]  Principal investigator stated envelopes were opaque. |
| Blinding of participants and researchers (performance bias) | high risk | Blinding not possible due to the nature of the intervention |
| Blinding of outcome assessment (detection bias): clinical endpoints | high risk | It is unclear whether clinical endpoint assessors were blinded or not. However, a blinded clinical endpoint committee probably did not adjudicated clinical events. |
| Blinding of outcome assessment (detection bias): haemodynamic endpoints | low risk | Free of bias due to technical assessment. |
| Blinding of outcome assessment (detection bias): arterial lactate | low risk | Free of bias due to technical assessment. |
| Incomplete outcome data (attrition bias) | low risk | All analyses were performed according to the intention-to-treat principle. One patient did not receive the MCS due to rapid improvement after PCI. This is a reasonable attrition and not expected to affect results. No patient was lost to follow-up. |
| Selective reporting (reporting bias) | low risk | All prespecified outcomes were reported. |
| Other bias | unclear risk | No other bias seems to be present. |
| **Burkhoff et al.**[**2**](#_ENREF_2) | | |
|  | **Authors’ judgment** | **Support for judgment** |
| Random sequence generation (selection bias) | low risk | Original trial report did not state how random sequence was generated. However, principal investigator stated that random sequence was generated by drawing sealed opaque envelopes. |
| Allocation concealment (selection bias) | low risk | Original trial report did not state how allocation concealment was achieved. However, principal investigator stated that random sequence was generated by drawing sealed opaque envelopes. |
| Blinding of participants and researchers (performance bias) | high risk | Blinding not possible due to the nature of the intervention |
| Blinding of outcome assessment (detection bias): clinical endpoints | high risk | It is unclear whether clinical endpoint assessors were blinded or not. However, a blinded clinical endpoint committee probably did not adjudicated clinical events. |
| Blinding of outcome assessment (detection bias): haemodynamic endpoints | low risk | Free of bias due to technical assessment. |
| Blinding of outcome assessment (detection bias): lactate | not applicable | not applicable |
| Incomplete outcome data (attrition bias) | low risk | Trial report did not report that analyses were performed according to the intention-to-treat principle. However, no crossovers were reported and are very unlikely due to the nature of the intervention. No patient was lost to follow-up. |
| Selective reporting (reporting bias) | low risk | All prespecified outcomes were reported. |
| Other bias | unclear risk | Data Safety Monitoring Board recommended to stop the trial due to slow rate of patient accrual; therefore, only 33 (+9 patients in the roll-in group) of planned 45 patients were enrolled. |
| **ISAR-SHOCK**[**3**](#_ENREF_3) | | |
|  | **Authors’ judgment** | **Support for judgment** |
| Random sequence generation (selection bias) | low risk | Original trial report did not state how random sequence was generated. However, principal investigator stated that random sequence was generated by drawing sealed opaque envelopes. |
| Allocation concealment (selection bias) | low risk | Original trial report did not state how allocation concealment was achieved. However, principal investigator stated that random sequence was generated by drawing sealed opaque envelopes. |
| Blinding of participants and researchers (performance bias) | high risk | Blinding not possible due to the nature of the intervention |
| Blinding of outcome assessment (detection bias): clinical endpoints | high risk | It is unclear whether clinical endpoint assessors were blinded or not. However, a blinded clinical endpoint committee probably did not adjudicated clinical events. |
| Blinding of outcome assessment (detection bias): haemodynamic endpoints | low risk | Free of bias due to technical assessment. |
| Blinding of outcome assessment (detection bias): lactate | low risk | Free of bias due to technical assessment. |
| Incomplete outcome data (attrition bias) | low risk | Trial report did not report that analyses were performed according to the intention-to-treat principle. However, no crossovers were reported and are unlikely due to the nature of the intervention. No patient was lost to follow-up. |
| Selective reporting (reporting bias) | low risk | All prespecified outcomes were reported. |
| Other bias | unclear risk | No other bias seems to be present. |
| **IMPRESS in Severe Shock**[**4**](#_ENREF_4) | | |
|  | **Authors’ judgment** | **Support for judgment** |
| Random sequence generation (selection bias) | low risk | A computer generated sequence was used according to the principal investigator.  Quote: Randomization was performed in a 1:1 ratio using an internet-based application. |
| Allocation concealment (selection bias) | low risk | Quote: Randomization was performed in a 1:1ratio using an internet-based application. |
| Blinding of participants and researchers (performance bias) | high risk | Blinding not possible due to the nature of the intervention |
| Blinding of outcome assessment (detection bias): clinical endpoints | high risk | It is unclear whether clinical endpoint assessors were blinded or not. However, a blinded clinical endpoint committee probably did not adjudicate clinical events. |
| Blinding of outcome assessment (detection bias): haemodynamic endpoints | low risk | Free of bias due to technical assessment. |
| Blinding of outcome assessment (detection bias): lactate | low risk | Free of bias due to technical assessment. |
| Incomplete outcome data (attrition bias) | low risk | Only one patient was lost to follow-up and all analyses were conducted according to the intention-to-treat principle. Crossovers occurred in 3 patients in the IABP group and 2 patients in the MCS group did not get the MCS. |
| Selective reporting (reporting bias) | low risk | All prespecified outcomes were reported. |
| Other bias | unclear risk | No other bias seems to be present. |

IABP=intraaortic balloon pumping; MCS=mechanical circulatory support; PCI=percutaneous coronary intervention

**Table S3 In- and exclusion criteria of individual studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Thiele et al.** [**1**](#_ENREF_1) | **Burkhoff et al.** [**2**](#_ENREF_2) | **ISAR-SHOCK**[**3**](#_ENREF_3) | **IMPRESS in Severe Shock**[**4**](#_ENREF_4) |
| **Inclusion criteria** | Presence of CS complicating AMI and the intention to revascularize the infarcted artery by PCI as first line treatment option. | * Age ≥18 years, and * CS <24 h | * AMI <48 h, and * CS <24 h | * AMI with ST-segment elevation complicated by severe CS in the setting of immediate PCI * Mechanical ventilation |
| **Exclusion criteria** | * Age >75 years * Mechanical complications of AMI * Duration of CS >12 h * Right heart failure * Sepsis * Significant AR * Severe cerebral damage * Resuscitation >30 min * Severe peripheral vascular disease * Other diseases with reduced life expectancy | * Isolated right heart failure * Coagulopathy * Sepsis * Severe peripheral vascular disease * Stroke within 6 months * AR ≥II° * Ventricular septal rupture | * Age <18 years * Resuscitation >30 min * Hypertrophic obstructive cardiomyopathy * Definite thrombus in left ventricle * Treatment with intra-aortic balloon pump * Severe valvular disease or mechanical heart valve including AR >II° * CS due to mechanical complications of AMI * Predominant right ventricular failure or the need for a right ventricular assist device * Sepsis * Known cerebral disease * Bleeding with a need for surgical intervention * Pulmonary embolism * Allergy to heparin or any known coagulopathy * Pregnancy * Inclusion in another study or trial | * Severe aorto-iliac arterial disease impeding placement of mechanical support device * Known severe cardiac aortic valvular disease * Serious known concomitant disease with a life expectancy <1 year * Known participation in this study or any other trial within <30 days * Coronary artery bypass grafting <1 week |

AR=aortic regurgitation; AMI=acute myocardial infarction; CS=cardiogenic shock; PCI=percutaneous coronary intervention.

**Table S4 Definitions of individual studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Thiele et al.** [**1**](#_ENREF_1) | **Burkhoff et al.** [**2**](#_ENREF_2) | **ISAR-SHOCK**[**3**](#_ENREF_3) | **IMPRESS in Severe Shock**[**4**](#_ENREF_4) |
| **Cardiogenic shock** | * Persistent SBP <90 mmHg, or * Vasopressors required to maintain SBP >90 mmHg, and * Evidence of end-organ failure (e.g. urine output <30 mL/h, cold skin and extremities, and serum lactate >2 mmol/L), and * PCWP >15 mmHg, and * CI <2.1 L/min/m² | * CI ≤2.2 L/min/m², and * Mean arterial blood pressure ≤70 mm Hg, and * PCWP ≥15 mmHg, and * Evidence of end-organ hypoperfusion (e.g. decreased urine output, altered mental status), or * Need for administration of high-dose pressor and/or inotropic support to maintain the patient out of cardiogenic shock | Clinical criteria:   * SBP <90 mmHg, and * Heart rate >90 beats/min, or * Need for positive inotropic drugs to maintain a SBP >90 mmHg, and * End-organ hypoperfusion (cool extremities or a urine output of <30 ml/h), * Pulmonary oedema.   Haemodynamic criteria:   * CI ≤2.2 l L/min/m2, and * PCWP >15 mmHg, or * Angiographically measured left ventricular ejection fraction <30%, and * Left ventricular enddiastolic pressure >20 mmHg. | * SBP <90 mmHg for >30 minutes, or * Need for inotropes and vasopressors to maintain a SBP >90 mmHg |
| **Bleeding** | Major bleeding requiring  transfusion of blood components | Major bleeding defined according to TIMI major bleeding definitions:   * Drop of haemoglobin of ≥5 g/dL * Intracranial bleeding * Fatal bleeding | Major bleeding defined according to TIMI major bleeding definitions:   * Drop of haemoglobin of ≥5 g/dL * Intracranial bleeding * Fatal bleeding | * Bleeding with associated serum haemoglobin level decrease of ≥5 g/dL * Bleeding necessitating a ≥2 packed cells of blood product transfusion * Need for surgery to control the bleeding |
| **Leg ischaemia** | * Limb ischaemia with requirement for extraction of study device * Need for vascular surgery or intervention to correct limb ischaemia | * Need for vascular surgery or intervention to correct limb ischaemia | * Limb ischaemia with extraction of study device * Need for vascular surgery to correct limb ischaemia | * A thrombotic occlusion of the femoral artery * Limb ischaemia requiring extraction of either of the study devices |

CI=cardiac index; SBP=systolic blood pressure; PCWP=pulmonary capillary wedge pressure, TIMI=Thrombolysis In Myocardial Infarction.

**References Supplemental Material:**

1. Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J, Schuler G. Randomized comparison of intraaortic balloon support versus a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J 2005;**26**:1276-1283.

2. Burkhoff D, Cohen H, Brunckhorst C, O'Neill WW. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. Am Heart J 2006;**152**(3):469.e1-469.e8.

3. Seyfarth M, Sibbing D, Bauer I, Fröhlich G, Bott-Flügel L, Byrne R, Dirschinger J, Kastrati A, Schömig A. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol 2008;**52**(19):1584-1588.

4. Ouweneel DM, Eriksen E, Sjauw KD, van Dongen IM, Hirsch A, Packer EJ, Vis M, Wykrzykowska JJ, Koch KT, Baan J, de Winter RJ, Piek JJ, Lagrand WL, de Mol BA, Tijssen JG, Henriques JP. Impella CP versus intra-aortic balloon pump support in acute myocardial infarction complicated by cardiogenic shock. The IMPRESS in Severe Shock trial. J Am Coll Card 2017;**69**:278-287.