OPTIMA-CC Statistical analysis plan
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Validated before unblinding
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Outcomes

Primary outcome

The change in cardiac index will be the primary outcome variable of this analysis. Cardiac index will be measured at baseline (H0) and at different time-points (H2, H4, H6, H12, H24, H48 and H72).

Secondary outcomes

The change in heart rate, cardiac power index, pro/anti-inflammatory cytokines, lactate clearance, SVO2, cardiac double product, catecholamine dosage used, organ failure (SOFA score), BNP, troponin, the occurrence of arrhythmia and the occurrence of refractory cardiogenic shock will be the secondary outcome variables.
Hemodynamic variables (heart rate, cardiac power index, SVO2, cardiac double product) will be recorded at H0, H2, H4, H6, H12, H24, H48 and H72.
Lactate clearance will be measured at H0, H2, H6, H12, H24 and H48.
Biological variables (BNP, troponin, pro/anti-inflammatory cytokines), catecholamine doses and organ failure will be collected at H0, H24, H48 and H72.

Statistical analysis plan

General considerations

All analyses will be performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA) and R software (the R foundation for Statistical Computing). The two-tailed significance level will be set at $p<0.05$.

Continuous variables

Continuous variables will be described by the number of non-missing values, mean, standard deviation, median, quartiles and extreme values. The normality of the distributions will be assessed. In case of violation of normality, the analysis will use non-parametric tests.

Categorical variables

Categorical variables will be summarized by the observed frequencies and the percentages relative to the total number of non-missing items.

Descriptive analysis

Continuous variables will be analyzed using unpaired t-test. The analysis of categorical variables will be performed using Fisher's exact test. The analysis will first compare baseline characteristics (demography, history of cardiogenic shock, clinical, medical history, biology, etc.) of patients according to treatment group. Variables significantly different across treatment groups will be considered as potential confounders in subsequent analyses.

Analysis of the primary outcome

The evolution of continuous variables following cardiogenic shock will be analyzed using ANOVA with the change from baseline at different time-points as repeated-measures, the baseline measurement as adjustment covariate, and treatment as fixed effect.
This classical approach could be questioned here, since the post-baseline values will be constrained by the clinical events observed during the follow-up (death or ECLS implantation). No data will be necessarily collected after a clinical event. To avoid introducing bias due to informative missing data after clinical events, the most appropriate solution is to attribute a rank for each patient and at each time-point, based on the change from baseline and the clinical events, from the lowest change to the highest change. Patients who died will be attributed the worst rank at each time-point following their death and patients who underwent ECLS will be attributed the second worst rank at each time-point following the implantation. The other patients without events will then be ranked according to the change from baseline values. Using this rank approach, the two treatment groups will be compared with ANOVA as described above. Ranks at all measured time-points will be considered here as repeated-measures outcome variable.
A similar analysis will be performed using measurements available at all time-points (except the H0 value) as repeated-measures instead of the change from baseline values.
A graphical representation of the evolution of each continuous variable will be produced in order to show, in a global manner, the differences between treatment groups.

Analysis of the secondary outcome
A similar analysis strategy to that used for the primary outcome will be used for the secondary continuous outcome
Secondary binary outcomes will be analyzed using logistic regression.

In both analyses of primary and secondary outcomes, additional multivariable analyses will be performed if significant differences according to treatment are identified in the descriptive analysis.