Early Hemodynamic Phenotypes and Outcomes in Refractory Cardiogenic Shock Under Temporary Mechanical Circulatory Support: A Hemodynamic Registry from the **EURO**pean **C**ardiogenic **S**hock **W**orking **G**roup (**Euro-CS WG**)

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National and International Investigators:

To be precised

This is a prospective international registry from the European Cardiogenic Shock Working Group (EuroCS-WG) conducted from January 2026 to January 2030.

All investigators declare no conflicts of interest in relation to this protocol.

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OUTLINE

I. INTRODUCTION

Cardiogenic shock is a life-threatening condition characterized by critically reduced cardiac output resulting in systemic hypoperfusion and high mortality [1]. In its most severe and refractory forms, when pharmacological support fails to restore adequate tissue perfusion, temporary mechanical circulatory support (t-MCS) devices are required. Among these, veno-arterial extracorporeal membrane oxygenation (V-A ECMO) and Impella® have emerged as a cornerstone therapies owing to their rapid deployment and their ability to provide high circulatory support and respiratory suppliance in the case of V-A ECMO [1–4].

Recent efforts have refined the phenotypic classification and severity stratification of cardiogenic shock in order to better capture its clinical heterogeneity and improve prognostic assessment [5–7]. However, among the sickest patients requiring t-MCS substantial physiological diversity persists. Some patients exhibit predominant left ventricular failure, others present with biventricular dysfunction or isolated right ventricular failure. Vascular tone may vary widely, ranging from profound vasoplegia requiring high-dose vasopressors to preserved systemic vascular resistance with isolated inotropic dependence. Volume status and filling pressures also differ markedly: while some patients present with markedly elevated pulmonary capillary wedge pressure reflecting severe left-sided congestion, others display low or normal filling pressures despite profound circulatory collapse [8]. This marked hemodynamic heterogeneity likely reflects distinct underlying pathophysiological mechanisms and may influence both therapeutic response and outcomes.

To date, a few studies deriving from US registries have characterized the outcomes of patients supported with t-MCS for refractory cardiogenic shock [4,9–12]. However, these studies have

largely focused on global prognostic determinants and have not specifically examined how early hemodynamic profiles may influence clinical trajectories and outcomes under mechanical circulatory support.

The aim of the present multicenter registry is to create the first European cardiogenic shock working group (the Euro-CS WG) focusing on patients supported by t-MCS in order to better describe the distinct hemodynamic profiles of patients supported by t-MCS and their associated clinical trajectories and outcomes.

II. HYPOTHESIS AND OBJECTIVES OF THE EURO-CS WORKING GROUP

Hypothesis:

We hypothesize that early integrated hemodynamic profiling in refractory cardiogenic shock under t-MCS helps better identification of clinically meaningful subgroups of patients, reflecting distinct pathophysiological patterns carrying different clinical trajectories and outcomes.

Main Objective:

The main objective of this international registry, is to create a European cardiogenic shock working group focusing on hemodynamics of patients under t-MCS, allowing collection of unique granular hemodynamic data from a collaboration between European expert centers.

The Euro-CS Working Group will first focus on the description of the different hemodynamic patterns of patients under t-MCS for refractory cardiogenic shock —from device insertion until the seventh day of support or weaning (if the later occurs within this timeframe)— and their relation to short term outcomes.

Main Evaluation Criterion:

The primary evaluation criterion is all-cause mortality at 60 days following initiation of t-MCS. Death from any cause occurring within 60 days after t-MCS implantation will be considered an event. Patients alive at day 60 will be censored at that time point.

Secondary Objectives:

Key secondary objectives

The Euro-CS WG plans to explore different aspects of hemodynamic in cardiogenic shock.

- To evaluate the association between early hemodynamic phenotypes and transition to durable mechanical circulatory support or heart transplant.
- To develop a new classification of cardiogenic shock requiring t-MCS based on hemodynamic profiles of patients at implantation.
- To develop a mortality predicting score based on hemodynamic data of patients collected within the early phase of t-MCS support.
- To give granular description of the different hemodynamic profiles of cardiogenic shock among different t-MCS — namely VA-ECMO and Impella®— and their clinical trajectories and outcomes.
- To assess the association between early hemodynamic phenotypes and myocardial recovery allowing successful weaning from t-MCS. (successful t-MCS weaning is defined as the liberation of t-MCS without need for heart transplant, durable MCS or second t-MCS run within 30 days after t-MCS removal).
- To develop Machin learning-based algorithms to assess the readability of patients to be safely liberated from their MCS and to develop an online application allowing rapid decision making.

III. RESEARCH PROTOCOL

3.1 Type of Study

This is a prospective, multicenter, international observational registry conducted between January 2026 and January 2030 among European expert centers. The cohort is designed to characterize early hemodynamic phenotypes and their trajectories in adult patients with refractory cardiogenic shock supported by t-MCS and to assess their association with outcomes.

The study is non-interventional. All clinical decisions, including initiation and management of t-MCS, invasive monitoring, and therapeutic strategies, will be made according to local practice at each participating center.

3.2 Population

➢ Inclusion criteria

- Adult patients (≥18 years).

- Refractory cardiogenic shock requiring initiation of t-MCS (including VA-ECMO and Impella®)
- Availability of an early integrated hemodynamic assessment (invasive monitoring with Swan Ganz catheter and echocardiography) performed within the predefined early phase following t-MCS initiation.

➢ Exclusion criteria

- Absence of early invasive and/or echocardiographic hemodynamic data.
- Patients under 18 of age
- Patients under juridic protection
- Patients with durable MCS
- Patients treated with another t-MCS prior to inclusion

3.3 Data Collection

All data will be prospectively collected using a standardized electronic case report form across participating centers. The early hemodynamic assessment will be defined as the first comprehensive invasive and echocardiographic evaluation performed within 24 hours after initiation of t-MCS. The exact time from t-MCS initiation to hemodynamic assessment will be recorded for all patients.

➢ **Baseline data**

At the time of t-MCS initiation (Day 1), the following variables will be recorded: Severity scores (SOFA, SAPS II, SCAI), demographic characteristics, cardiovascular history and comorbidities, etiology of cardiogenic shock following the SHARC definition, relevant biological parameters at implantation, vasopressor and inotropic support, mechanical ventilation status.

A standardized integrated hemodynamic evaluation will be performed within the first 24 hours following t-MCS initiation. For each day, the t-MCS flow will be collected.

➢ **Invasive parameters**

- Arterial systemic pressures.
- Central venous pressure.
- Pulmonary artery pressures.

- Pulmonary capillary wedge pressure.
- Cardiac output and cardiac index.
- Mixed venous oxygen saturation (if available).

- **Echocardiographic parameters may include:**

- Left ventricular systolic function.
- Left ventricular outflow tract velocity-time integral.
- Right ventricular size and function.
- Estimation of filling pressures.
- Significant valvular abnormalities.

- **Daily monitoring from Day 1 to Day 7**

Invasive and echocardiographic pre-cited data will be collected daily from t-MCS initiation (Day 1) through Day 7 in order to characterize early hemodynamic trajectories.

- T-MCS Weaning Trial

During the t-MCS weaning trial, available hemodynamic data from echography and pulmonary arterial catheter will be collected.

- **Outcome data**

Vital status at Day 60 and all predefined secondary endpoints will be prospectively collected.

3.5 Data Management :

All relevant data, including demographic characteristics, medical history, clinical parameters, biological results, invasive hemodynamic measurements, and echocardiographic findings, will be prospectively recorded in the patients' electronic medical records at each participating center.

All clinical events occurring during the intensive care unit stay, including complications, need for organ support, duration of t-MCS, addition of unloading therapy in ECMO patients, and major therapeutic interventions, will be retrieved from the electronic medical records.

Vital status at day 60, as well as hospital discharge status, will be obtained from the electronic medical records and institutional databases.

Data will be extracted and entered into a standardized electronic case report form for analysis.

3.6 Statistical Analysis :

Continuous variables will be expressed as mean with standard deviation or median with interquartile range, as appropriate. Categorical variables will be presented as counts and percentages. Group comparisons will be performed using appropriate parametric or non-parametric tests according to data distribution.

Early hemodynamic phenotypes will be identified using an unsupervised clustering approach based on invasive and echocardiographic parameters collected within 24 hours after t-MCS. Variables will be standardized prior to clustering. The optimal number of clusters will be determined using internal validation criteria and clinical interpretability.

The association between identified phenotypes and 60-day all-cause mortality will be evaluated using survival analysis. Kaplan–Meier curves will be constructed and compared using the log-rank test. Multivariable Cox proportional hazards models will be used to estimate adjusted hazard ratios, accounting for clinically relevant confounders. Inter t-MCS devices comparisons will also be done.

Secondary endpoints will be analyzed using appropriate regression models depending on the nature of the outcome. Time-to-event outcomes will be analyzed using survival methods. Binary outcomes will be analyzed using logistic regression.

Hemodynamic trajectories from baseline to Day 7 using longitudinal modeling techniques.

All statistical tests will be two-sided, with a significance threshold set at $p < 0.05$.

3.7 Human and Material Ressources

Data collection will be conducted by the investigators at each participating center in accordance with the standardized study protocol. Statistical analyses will be performed by the principal investigators of the study. The study will rely on the existing clinical, monitoring, and imaging infrastructure of the participating intensive care units. Each center has access to invasive hemodynamic monitoring, echocardiography, and t-MCS management facilities required for the conduct of this study.

No additional material resources beyond standard clinical practice are required.

IV. ETHICAL CONSIDERATIONS

The study has received favorable approval in France from the SRLF Ethics Committee (reference CE-SRLF 25-084).

This is a prospective, observational, non-interventional registry that does not modify diagnostic strategies, therapeutic management, or clinical decision-making. All investigations, including invasive hemodynamic monitoring and echocardiography, are performed as part of routine clinical care in patients with refractory cardiogenic shock supported by t-MCS.
The study does not require any additional procedures, visits, or interventions beyond standard practice. Consequently, participation in the study does not expose patients to any additional risk. Patients and/or their legally authorized representatives will be informed of the study by the local investigator and provided with a written information notice. The study falls within the framework of research not involving interventional procedures and complies with the institutional commitment to the French reference methodology MR-004 in accordance with the Commission Nationale de l'Informatique et des Libertés.
Participating intensive care units provide all admitted patients and their relatives with an information booklet specifying that clinical, biological, and epidemiological data may be collected in computerized systems and reused in anonymized form for research purposes. In addition, an individual written information notice will be provided to ensure compliance with MR-004 requirements.
Patients will retain the right to oppose the reuse of their data at any time. For deceased patients, investigators will verify that no prior opposition to data reuse was expressed.
Data confidentiality and protection
Data will be pseudonymized at the time of collection using patient initials and a unique study inclusion number. Each participating center will collect and transmit data securely to the principal investigator.
The study database will be stored on a password-protected computer with restricted access. Access to the database will be limited to authorized investigators only. All data handling procedures will comply with applicable data protection regulations.
Given its strictly observational nature, this study does not expose participants to additional risks beyond standard clinical management. The expected benefit is collective rather than individual. The study aims to improve understanding of early hemodynamic profiles and trajectories in patients supported by veno-arterial extracorporeal membrane oxygenation. By identifying clinically meaningful phenotypes associated with prognosis, this research may contribute to improved risk stratification and more individualized management strategies in refractory cardiogenic shock.

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