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Troponin for predicting Weaning failure from temporary mechanical circulatory support in Infarction complicated by Cardiogenic Shock (TWICS)

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Abstract

Background: Although several risk-stratification models have been developed for patients with refractory cardiogenic shock requiring temporary mechanical circulatory support, most primarily predict short- and long-term mortality and do not reliably identify patients who can be successfully weaned from support. Cardiac troponin is routinely measured during the acute phase of myocardial infarction. Cumulative troponin exposure, quantified by the troponin area under the concentration–time curve (T-AUC), correlates with the extent of myocardial necrosis. The objective of this study was to evaluate whether T-AUC could improve prediction of temporary mechanical circulatory support weaning failure.

Methods: We conducted a single-centre retrospective cohort study including consecutive adults admitted to our cardiac intensive care unit between January 2014 and September 2025 with acute myocardial infarction-related cardiogenic shock requiring temporary mechanical circulatory support. From serial daily troponin I measurements, cumulative troponin exposure was reconstructed as T-AUC. The primary endpoint was temporary mechanical circulatory support weaning failure, defined as death, durable mechanical circulatory support, or heart transplantation during support or within 30 days after explantation.

Results: Among the 159 included patients, 97 (61.0%) reached the primary endpoint. In the adjusted time-dependent Cox model, higher cumulative troponin exposure was independently associated with temporary mechanical circulatory support weaning failure (hazard ratio [HR] 1.40 per 1,000,000 ng/L·day increase, 95% confidence interval [CI] 1.19–1.65; $p < 0.0001$). Restoration of TIMI 3 flow after revascularisation was associated with a significantly lower risk of failure (HR 0.50, 95% CI 0.31–0.80; $p = 0.004$). Addition of day-5 T-AUC to the clinical model provided the greatest improvement in discrimination (AUC 0.862, 95% CI 0.797–0.926), followed by peak troponin (AUC 0.848, 95% CI 0.779–0.918).

Conclusions: In patients with acute myocardial infarction-related cardiogenic shock requiring temporary mechanical circulatory support, cumulative troponin exposure, quantified by T-AUC, was independently associated with failure to wean from support and provided incremental predictive value beyond established clinical risk factors.

BACKGROUND

After initiation of temporary mechanical circulatory support (tMCS), early and accurate assessment of myocardial recovery potential becomes a key determinant of subsequent therapeutic decisions. Such stratification is essential to guide timely de-escalation of therapy and prevent complications that markedly worsen the functional prognosis or even preclude durable mechanical circulatory support or heart transplantation [1]. Several prognostic scores have been developed, including early mortality scores such as the SAVE score [2] and scores predicting long-term mortality and quality of life, such as the ENCOURAGE score [3]. Importantly, these scores primarily focus on mortality risk rather than the probability of successful weaning from tMCS. This lack of dedicated tools highlights a critical gap in current clinical decision-making and risk-stratification strategies. Although some echocardiographic parameters have been reported to predict veno-arterial extracorporeal membrane oxygenation (VA-ECMO) weaning success, these findings were derived from small sample sizes, heterogeneous populations, and practices that have substantially

evolved since those studies were conducted [4, 5]. Cardiac troponin is routinely measured during the acute phase of myocardial infarction (MI) and appears to provide prognostic value in cardiogenic shock [6]. This may be explained by the strong correlation between troponin levels and the extent of myocardial necrosis [7–9]. More than peak values or isolated measurements, cumulative troponin exposure, as assessed by the troponin area under the concentration–time curve (T-AUC), appears to represent the amount of troponin released more precisely and thus provides a more comprehensive quantification of myocardial injury [10, 11]. T-AUC has been identified as an independent predictor of mortality in patients with acute heart failure and in those undergoing coronary artery bypass graft surgery, and it may offer superior prognostic performance compared with peak troponin alone [12, 13]. In this context, cardiac troponin levels, or ideally T-AUC, could provide objective, reproducible, quantitative, and readily available information that complements clinical and imaging-based assessments for early risk stratification in patients supported with tMCS. Previous clinical studies have investigated the roles of cardiac troponin in predicting outcomes and VA-ECMO weaning success [14–16]. Overall, those studies share several important limitations, including reliance on isolated troponin values or limited kinetic assessments that do not capture the cumulative burden of myocardial injury over time, inclusion of heterogeneous populations with non-ischaemic cardiogenic shock, and small single-centre sample sizes limiting external validity. Together, these limitations restrict the ability to characterise fully the dynamic relationship between myocardial injury and the process of weaning from tMCS and highlight the need for longitudinal approaches integrating serial biomarker measurements within robust time-to-event frameworks.

Accordingly, we hypothesised that in patients with acute MI-related cardiogenic shock requiring tMCS, the addition of T-AUC to clinical parameters could improve the prediction of tMCS weaning failure.

METHODS

Study design

This single-centre, retrospective, observational cohort study included consecutive patients admitted to our tertiary referral university hospital between 1 January 2014 and 30 September 2025 for cardiogenic shock secondary to acute MI requiring tMCS. Data were collected retrospectively from the patients' electronic medical records. The patients were followed from the acute MI until death or the last recorded contact at our university hospital, defined as the most recent hospital admission, outpatient consultation, diagnostic examination, or laboratory assessment documented in the institutional electronic medical record system.

Participants

Eligible patients were aged ≥ 18 years and presented with cardiogenic shock related to acute MI requiring short-term mechanical circulatory support, including peripheral VA-ECMO, VA-ECMO combined with Impella (ECMELLA), and VA-ECMO combined with an intra-aortic balloon pump.

Patients with non-ischaemic cardiogenic shock or cardiogenic shock occurring in the setting of post-cardiotomy were excluded, including those presenting with mechanical complications of MI requiring

surgical repair under cardiopulmonary bypass before tMCS initiation. Patients supported with an intra-aortic balloon pump alone, those bridged directly to long-term mechanical circulatory support or heart transplantation without any attempt at weaning, those with insufficient troponin data to reconstruct early biomarker kinetics (defined as fewer than two measurements after the index infarction or the absence of any measurement within the first 48 hours), and those under judicial or administrative detention were also excluded.

Variables and outcomes

The primary outcome was tMCS weaning failure, defined as death while on mechanical support or within 30 days after device explantation, heart transplantation or durable ventricular assist device (VAD) implantation following a failed weaning attempt, or the requirement for tMCS within 30 days after initial explantation.

The secondary outcomes were 30-day mortality after explantation, death during the initial tMCS support, heart transplantation or durable VAD implantation following failed weaning or within 30 days after device removal, and re-implantation of tMCS within 30 days after initial explantation. In addition, the composite outcome of death, heart transplantation, or durable VAD implantation was assessed at 3 months, 6 months, and 1 year. For time-to-event analyses, the date of the first qualifying event was used as the event date for the composite endpoint.

Data sources and measurement

Clinical, laboratory, echocardiographic, therapeutic, and outcome data were retrospectively extracted from electronic medical records using the institutional system. Baseline data included demographic characteristics, cardiovascular risk factors, comorbidities, infarct characteristics, revascularisation strategy and delays, haemodynamic parameters, resuscitation status, and the type and duration of mechanical circulatory support. Laboratory variables included serial measurements of cardiac troponin I (cTnI), arterial lactate concentration, pH, creatinine, liver enzymes, and other routinely collected biomarkers. Echocardiographic data were also collected. Vital status and date of death were primarily obtained from hospital records. To minimise loss to follow-up, hospital data were cross-checked against national open-access mortality databases. These external sources were used solely to complement hospital follow-up information.

Troponin measurement and AUC calculation

High-sensitivity cTnI was measured by chemiluminescent immunoassay using an Architect ci8200 analyser (Abbott, Abbott Park, IL, USA). Before 2018, troponin I was measured using a chemiluminescent immunoassay on the DXI platform (Beckman Coulter, Brea, CA, USA). Consequently, values originally reported in ng/mL were converted to ng/L for harmonisation.

Method-comparison studies have demonstrated a strong correlation between conventional and high-sensitivity cardiac troponin I (hs-cTnI) assays for concentrations above the 99th-percentile upper reference limit, with reported correlation/regression coefficients consistently indicating close agreement across pathological concentration ranges, whereas differences in analytical sensitivity primarily affect low-range values near baseline [17–19].

Troponin measurements were obtained routinely once daily from the day of MI (day 0), resulting in approximately constant 24-hour sampling intervals. Patients transferred from another centre more than 48 hours after MI were excluded to ensure the availability of early troponin measurements and to limit missing data during the initial kinetic phase. Measurements were collected until troponin concentrations decreased below 100 ng/L, a pragmatic threshold chosen to capture the main phase of myocardial injury while limiting the influence of prolonged low-level residual elevations on cumulative exposure, or until occurrence of the primary endpoint. Peak troponin I concentration was defined as the highest measured value, whereas cumulative troponin exposure, quantified as the T-AUC, was estimated using the trapezoidal rule (**see Supplementary Methods**). Daily cumulative T-AUC values were constructed to obtain a time-updated estimate of cumulative exposure. Missing daily troponin values between two available measurements were estimated by linear interpolation, whereas the last available value was carried forward when no subsequent measurement was available.

Study size

The sample size calculation was based on comparison of two correlated receiver operating characteristic (ROC) curves using DeLong's method [20]. The baseline clinical model was expected to achieve an area under the ROC curve (AUC) of 0.65 according to recent literature [5, 21], and the addition of T-AUC was hypothesised to increase the AUC to 0.85. Assuming a two-sided type I error rate of 5%, 90% statistical power, and an expected incidence of VA-ECMO weaning failure of 65%, a minimum sample size of approximately 160 patients was considered necessary.

Statistical methods

Continuous variables are presented as the mean ± standard deviation when normally distributed or the median [interquartile range] otherwise and were compared using Student's t test or the Mann–Whitney U test, as appropriate. Categorical variables are presented as counts (percentages) and were compared using the chi-square test or Fisher's exact test, as appropriate.

T-AUC, expressed in ng/L·day, was analysed as a continuous time-updated variable in Cox proportional hazards models. Because T-AUC values were numerically large, the variable was rescaled per 1,000,000 ng/L·day. Peak troponin concentrations, defined as the highest troponin concentration recorded among all post-infarction measurements for each patient and expressed in ng/L, were analysed as continuous variables and rescaled per 100,000 ng/L.

Several strategies were implemented to minimise potential sources of bias. Because cumulative biomarker exposure inherently increases over time, analysing cumulative troponin exposure as a fixed variable could introduce immortal-time and time-dependent bias. The primary analysis evaluated the association between cumulative troponin exposure and the primary composite outcome using Cox proportional hazards regression. Troponin exposure was modelled as a time-updated cumulative troponin area under the concentration–time curve, denoted AUC(t), reconstructed daily from serial troponin measurements. Time-dependent Cox models were fitted using a start–stop counting-process formulation, allowing each patient to contribute risk time according to the cumulative biomarker exposure observed at each time point during follow-up. Follow-up was left-truncated at the first day with an available cumulative AUC(t) value, thereby avoiding attribution of person-time to periods during which the exposure could not yet be defined. Daily AUC(t) values were updated using a last-observation-carried-forward approach when intermediate daily measurements were missing.

Hazard ratios (HRs) are reported with 95% confidence intervals (CIs). Time-to-event analyses were administratively censored at day 100 after MI because the primary composite endpoint included events occurring up to 30 days after tMCS explantation, and the latest explantation observed in the cohort occurred at day 70.

Univariable time-dependent Cox models were first used to assess the association between cumulative troponin exposure and the primary and secondary outcomes. For multivariable modelling of the primary outcome, candidate covariates were identified *a priori* based on clinical relevance and the published literature and were retained after assessment of data availability, functional form, and collinearity. Because cumulative troponin exposure and peak troponin concentrations were strongly correlated (**Figure S1**), only cumulative troponin exposure was retained in the multivariable model. For cumulative troponin exposure, several parameterisations were explored, including raw, natural log-transformed, log10-transformed, and scaled forms. Because the scaled raw AUC(t) showed no evidence of major deviation from linearity and provided clinically interpretable estimates, the parameterisation AUC(t)/1,000,000 was retained in the final model. The linearity of continuous predictors was assessed using restricted cubic splines, with no evidence of relevant non-linearity.

The variables ultimately selected for the multivariable model included sex, age, Thrombolysis in Myocardial Infarction (TIMI) 3 flow after revascularisation, Simplified Acute Physiology Score II (SAPS II), arterial lactate concentration, left ventricular failure, extracorporeal cardiopulmonary resuscitation, and left ventricular unloading. The proportional hazards assumption was evaluated using Schoenfeld residual tests and visual inspection of Schoenfeld residual plots. Variables showing evidence of non-proportional hazards but considered clinically important were incorporated as stratification variables. Multicollinearity was assessed using variance inflation factors. The adjusted multivariable model was fitted using a complete-case approach without imputation. The number of covariates included in the adjusted model was restricted according to the number of observed events, with no more than one covariate per 10 observed events entered into the model to limit overfitting. Model discrimination was summarised using Harrell's C-index and overall fit using the Akaike information criterion.

In addition to the main time-dependent survival analysis, a landmark predictive analysis was performed at day 5 to assess discrimination for the occurrence of the primary endpoint between day 5 and day 100. Patients who had already experienced the primary endpoint before day 5 were excluded from the landmark analyses. For troponin-based predictors, cumulative exposure was truncated at day 5 and peak troponin corresponded to the highest value observed up to day 5. Day-5 T-AUC was categorised into quartiles, and Kaplan–Meier curves were generated for the landmark cohort, with groups compared using the log-rank test. Within this landmark cohort, univariable ROC analyses were first performed for individual biomarkers. A prespecified multivariable logistic regression model including the same covariates as the multivariable Cox model was constructed. Biomarker-augmented models were generated by adding each biomarker separately to this clinical model. Predicted probabilities from these logistic models were used to construct ROC curves. Discrimination was quantified using the area under the ROC curve (AUC) with 95% CIs, and ROC curves were compared using DeLong's test. Sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were calculated at the optimal threshold defined by the maximum Youden index.

Sensitivity analyses were performed to assess the robustness of the primary findings in the day-5 landmark population. These included a Cox model preserving cumulative troponin exposure as a time-updated covariate and a comparator model using peak troponin restricted to the day-5 landmark population. All tests were two-sided, and a p value of < 0.05 was considered statistically significant. Analyses were performed using R software version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Participants

Between January 2014 and September 2025, 810 consecutive patients were treated with tMCS and screened for eligibility. Among these, 569 patients were excluded: 407 because of non-ischaemic cardiogenic shock and 162 because they were < 18 years of age. In total, 241 adults with ischaemic cardiogenic shock related to acute MI who were treated with tMCS were assessed for eligibility. Of these, 82 patients were excluded for the following predefined reasons: intensive care unit (ICU) admission > 48 hours after MI (n = 26), direct bridge to durable VAD or heart transplantation without any attempt at tMCS weaning (n = 2), mechanical complications of MI requiring surgical repair under cardiopulmonary bypass before tMCS initiation (n = 47), and insufficient troponin data (< 2 measurements after the index MI) (n = 7). The final study cohort comprised 159 patients who met all eligibility criteria and were included in the primary analysis (Fig. 1).

Descriptive data

Among the 159 patients included in the study, 97 (61%) met the criteria for weaning failure. The baseline characteristics of the study population are presented in Table 1.

Table 1

Baseline characteristics according to temporary mechanical circulatory support weaning outcome

Variables	*N*	Overall (n = 159)	Successful weaning (n = 62)	Weaning failure (n = 97)	p-value
Baseline demographics and comorbidities					
Male sex	159	131 (82%)	50 (81%)	81 (84%)	0.64
Age (years)	159	59 ± 9	60 ± 9	58 ± 10	0.37
BMI (kg/m²)	155	26.1 ± 4.1	25.3 ± 4.1	26.6 ± 4.1	0.06
Hypertension	159	76 (48%)	34 (55%)	42 (43%)	0.16
Dyslipidaemia	159	59 (37%)	27 (44%)	32 (33%)	0.18
Smoking	159	113 (71%)	47 (76%)	66 (68%)	0.29
Diabetes	159	25 (16%)	10 (16%)	15 (16%)	0.91
Peripheral artery disease	159	21 (13%)	12 (19%)	9 (9%)	0.07
Heart failure	159	21 (13%)	11 (18%)	10 (10%)	0.18
Atrial fibrillation	159	4 (3%)	3 (5%)	1 (1%)	0.30
Baseline creatinine (µmol/L)	21	91 [70; 105]	88 [70; 104]	92 [82; 141]	0.54
Baseline eGFR (mL/min/1.73 m²)	20	72 [51; 76]	72.0 [58; 84]	75 [45; 84]	0.91
Cardiac arrest and resuscitation characteristics					
Prior cardiac arrest	159	74 (47%)	37 (60%)	37 (38%)	0.01
Glasgow Coma Scale score	138	3.0 [3.0; 15.0]	3.0 [3.0; 14.8]	6.0 [3.0; 15.0]	0.08
Adrenaline use	159	91 (57%)	38 (61%)	53 (55%)	0.41

Values are presented as the mean ± standard deviation, median [interquartile range], or n (%), as appropriate. Column *N* indicates the numbers of patients with available data for each variable. p values refer to between-group comparisons.

†The sum of VA-ECMO alone, VA-ECMO combined with IABP, ECMELLA, and Impella alone exceeds the total number of patients because some patients received more than one unloading strategy during their ICU stay.

Abbreviations: BMI, body mass index; BNP, B-type natriuretic peptide; ECMELLA, combined veno-arterial extracorporeal membrane oxygenation and Impella; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; KDIGO, Kidney Disease: Improving Global Outcomes; MI, myocardial infarction; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction; VA-ECMO, veno-arterial extracorporeal membrane oxygenation

Variables	*N*	Overall (n = 159)	Successful weaning (n = 62)	Weaning failure (n = 97)	p-value
Acute coronary syndrome presentation, coronary anatomy, and myocardial injury					
STEMI	159	152 (96%)	58 (94%)	94 (97%)	0.31
Fibrinolysis	159	8 (5%)	3 (5%)	5 (5%)	1.00
Time to revascularisation (h)	139	4.0 [2.0; 11.0]	4.0 [2.0; 13.0]	4.0 [3.0; 10.0]	0.69
Non-revascularised	159	15 (9%)	4 (7%)	11 (11%)	0.30
Culprit-only PCI	143	114 (80%)	46 (79%)	68 (80%)	0.92
Left main coronary artery culprit	159	33 (21%)	10 (16%)	23 (24%)	0.25
Electrical storm	159	32 (20%)	20 (32%)	12 (12%)	< 0.01
Mechanical complications of MI	159	16 (10%)	5 (8%)	11 (11%)	0.50
Shock severity and organ dysfunction					
SCAI shock stage D or E	159	146 (92%)	56 (90%)	90 (93%)	0.58
Right ventricular involvement	159	89 (55%)	40 (65%)	49 (51%)	0.08
pH	159	7.20 [7.08; 7.30]	7.22 [7.09; 7.31]	7.18 [7.07; 7.29]	0.29
Arterial lactate concentration (mmol/L)	159	6.7 [3.8; 12.6]	5.3 [3.4; 11.7]	7.8 [3.9; 13.3]	0.19
KDIGO stage	159				0.01
— 1		37 (23%)	19 (31%)	18 (19%)	
— 2		27 (17%)	8 (13%)	19 (20%)	

Values are presented as the mean ± standard deviation, median [interquartile range], or n (%), as appropriate. Column *N* indicates the numbers of patients with available data for each variable. p values refer to between-group comparisons.

†The sum of VA-ECMO alone, VA-ECMO combined with IABP, ECMELLA, and Impella alone exceeds the total number of patients because some patients received more than one unloading strategy during their ICU stay.

Abbreviations: BMI, body mass index; BNP, B-type natriuretic peptide; ECMELLA, combined veno-arterial extracorporeal membrane oxygenation and Impella; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; KDIGO, Kidney Disease: Improving Global Outcomes; MI, myocardial infarction; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction; VA-ECMO, veno-arterial extracorporeal membrane oxygenation

Variables	*N*	Overall (n = 159)	Successful weaning (n = 62)	Weaning failure (n = 97)	p-value
— 3		91 (57%)	31 (50%)	60 (62%)	
Temporary mechanical circulatory support configuration and left ventricular unloading strategy†					
VA-ECMO alone	159	61 (38%)	37 (60%)	24 (25%)	< 0.01
VA-ECMO + IABP	159	33 (21%)	13 (21%)	20 (21%)	0.96
ECMELLA	159	44 (28%)	5 (8%)	39 (40%)	< 0.01
Impella alone	159	23 (14%)	7 (11%)	16 (17%)	0.36
Baseline biochemical profile					
BNP (ng/L)	151	709 [374; 1188]	709 [375; 1198]	751 [369; 1180]	0.86
Creatinine (µmol/L)	159	142 [103; 189]	120 [89; 162]	156 [116; 202]	< 0.01
AST (U/L)	159	718 [307; 1500]	365 [174; 734]	965 [473; 1922]	< 0.01
ALT (U/L)	159	183 [84; 372]	123 [62; 258]	219 [99; 442]	0.02
Bilirubin (µmol/L)	159	21 [14; 33]	18 [13; 28]	23.0 [14; 37]	0.04

Values are presented as the mean ± standard deviation, median [interquartile range], or n (%), as appropriate. Column *N* indicates the numbers of patients with available data for each variable. p values refer to between-group comparisons.

†The sum of VA-ECMO alone, VA-ECMO combined with IABP, ECMELLA, and Impella alone exceeds the total number of patients because some patients received more than one unloading strategy during their ICU stay.

Abbreviations: BMI, body mass index; BNP, B-type natriuretic peptide; ECMELLA, combined veno-arterial extracorporeal membrane oxygenation and Impella; eGFR, estimated glomerular filtration rate; IABP, intra-aortic balloon pump; KDIGO, Kidney Disease: Improving Global Outcomes; MI, myocardial infarction; PCI, percutaneous coronary intervention; SCAI, Society for Cardiovascular Angiography and Interventions; STEMI, ST-segment elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction; VA-ECMO, veno-arterial extracorporeal membrane oxygenation

The cohort comprised 131 men (82%) and had a mean age of approximately 59 years. Sex and age were similar between the groups. Cardiovascular risk factors were common and similarly distributed between the groups. A history of coronary artery disease was more frequently observed among patients with successful weaning (37% vs. 18%, p = 0.01), as was underlying cardiomyopathy (34% vs. 19%, p = 0.03).

Prior cardiac arrest before tMCS implantation was documented in 74 patients (47%) and was more frequent in the successful group (60% vs. 38%, p = 0.01). By contrast, extracorporeal cardiopulmonary resuscitation

was performed in 37 patients (23%), with no significant difference between groups (23% vs. 24%, p = 0.87). Among the 91 patients with available rhythm documentation during cardiac arrest, a shockable rhythm was more frequent in the successful group (90% vs. 74%, p = 0.05). Low-flow duration was significantly shorter in the successful group (median 20 [8–40] min vs. 30 [13–77] min, p = 0.04), whereas no-flow duration was similar between the groups. Glasgow Coma Scale scores and adrenaline use at admission were also similar between groups.

ST-segment elevation MI was the initial presentation in 152 patients (96%), with no difference between groups. The median time to coronary revascularisation was 240 min in both groups (p = 0.69). TIMI 3 flow following percutaneous coronary intervention (PCI) was achieved more frequently in successfully weaned patients (87% vs. 70%, p < 0.01). An electrical storm occurred more often in the successful group (32% vs. 12%, p < 0.01). Mechanical complications of MI were uncommon and similarly distributed between the groups.

According to the Society for Cardiovascular Angiography and Interventions (SCAI) classification, 146 of 159 patients (92%) were classified as stages D or E. The median SAPS II was 63 [50–75] in the successful group and 71 [50–85] in the unsuccessful group (p = 0.05). The Kidney Disease: Improving Global Outcomes (KDIGO) stage distribution differed significantly between groups (p = 0.01), with stage 3 acute kidney injury observed in 50% of successfully weaned patients and 62% of unsuccessfully weaned patients. Laboratory variables at admission, including arterial pH, arterial lactate concentration, haemoglobin, and B-type natriuretic peptide (BNP), did not differ significantly between groups, whereas creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin levels were significantly higher in the unsuccessful weaning group.

Markers of myocardial injury differed markedly between groups. The peak troponin I concentration was significantly lower in the successful group than in the unsuccessful group (110,402 ng/L [31,235–245,931] vs. 442,315 ng/L [148,000–708,298], p < 0.01). Likewise, T-AUC was significantly lower in the successful group (282,962 ng/L·day [79,602–752,806] vs. 1,213,580 ng/L·day [395,824–2,078,183], p < 0.01). Serial troponin I trajectories from day 0 to day 21 according to tMCS weaning outcome are presented in Fig. 2, showing higher troponin concentrations in patients with weaning failure, particularly during the early phase after MI, with progressive attenuation of the between-group difference over time.

VA-ECMO alone or in combination with an intra-aortic balloon pump (IABP) or Impella was used in 138 patients (87%), with a similar distribution between groups. Active left ventricular unloading during VA-ECMO (IABP, Impella, or atrial septostomy) was more frequent in the unsuccessful group (59% vs. 29%, p = 0.01). Levosimendan was administered during tMCS support in 65 patients (41%), with similar use between successfully and unsuccessfully weaned patients (45% vs. 38%, p = 0.38).

No outcome data were missing at 30 days after device explantation. At the administrative censoring date, 76 patients (48%) were alive. Loss to follow-up at the prespecified time points was limited, with 2 patients (1%) lost at 3 months, 8 (5%) at 6 months, and 13 (8%) at 1 year.

Outcome data

In total, 97 of 159 patients (61%) reached the primary composite endpoint of tMCS weaning failure. Death while on tMCS occurred in 49 patients (31%), death within 30 days after explantation in 18 (11%), durable VAD implantation or heart transplantation following unsuccessful weaning or within 30 days after explantation in 29 (18%), and re-initiation of tMCS in 1 (0.6%). Overall, death while on tMCS or within 30 days after explantation occurred in 67 patients (41%). In addition, durable VAD implantation or heart transplantation following unsuccessful weaning or within 30 days after explantation occurred in 30 patients (19%).

After excluding patients classified as lost to follow-up at each time point, 102 of 157 patients (65%) had experienced the secondary composite outcome of death, heart transplantation, or durable VAD implantation by 3 months, 104 of 151 (69%) by 6 months, and 105 of 146 (72%) by 1 year. The cumulative numbers of patients undergoing durable VAD implantation or heart transplantation were 32 (20%), 34 (23%), and 40 (27%) at the corresponding time points.

Main results

Unadjusted time-dependent Cox proportional hazards models were used to evaluate the association between cumulative troponin exposure, modelled as AUC(t), and study outcomes in the 159 patients included in the cohort (Table 2). The primary composite outcome of tMCS weaning failure occurred in 97 patients and was associated with higher cumulative troponin exposure (HR 1.36, 95% CI 1.24–1.50; $p < 0.001$). Associations with the secondary outcomes are detailed in Table 2.

Table 2
Univariable time-dependent Cox models assessing the association between cumulative troponin exposure and study outcomes

Outcome	n	Events	HR	95% CI	p-value
Primary composite outcome					
Failure of tMCS weaning (primary composite)	159	97	1.36	1.23–1.50	< 0.01
Secondary outcomes					
Death during initial tMCS support or within 30 days after explantation	159	29	1.37	1.17–1.60	< 0.01
Bridge to heart transplantation or durable VAD, including implantation within 30 days after explantation	159	67	1.31	1.14–1.50	< 0.001
Re-initiation of tMCS within 30 days after initial explantation	159	1			
Secondary composite outcomes					
Death, heart transplantation, or durable VAD implantation (3 months)	157	102	1.20	1.09–1.32	< 0.01
Death, heart transplantation, or durable VAD implantation (6 months)	151	103	1.19	1.08–1.30	< 0.01
Death, heart transplantation, or durable VAD implantation (1 year)	146	105	1.18	1.0–1.30	< 0.01

Univariable time-dependent Cox proportional hazards models assessing the associations between cumulative troponin exposure and study outcomes in patients with MI-related cardiogenic shock requiring tMCS. Cumulative troponin exposure was modelled as the time-dependent variable AUC(t), representing the cumulative troponin area under the concentration–time curve, scaled per 1,000,000 ng/L·day and updated daily using a last-observation-carried-forward approach. The model was left-truncated at the first day with an available AUC(t) value. HRs with 95% CIs are reported.

Abbreviations: AUC(t), time-updated cumulative troponin area under the concentration–time curve; CI, confidence interval; HR, hazard ratio; tMCS, temporary mechanical circulatory support; VAD, ventricular assist device

The final multivariable time-dependent Cox proportional hazards model included AUC(t), representing cumulative troponin exposure quantified by T-AUC, as the main exposure and was adjusted for sex, age, TIMI 3 flow after coronary revascularisation, SAPS II, arterial lactate concentration, and left ventricular failure. The model was stratified by extracorporeal cardiopulmonary resuscitation (ECPR) and left ventricular unloading because these variables showed evidence of non-proportional hazards. The complete-case analysis included 154 patients with 93 primary composite events.

In the adjusted analysis, cumulative troponin exposure remained associated with the primary composite outcome. Each increase of 1,000,000 ng/L·day in AUC(t) was associated with a higher hazard of the primary composite outcome (HR 1.40, 95% CI 1.19–1.65; $p < 0.0001$). Restoration of TIMI 3 flow after coronary

revascularisation was associated with a lower risk of the primary composite outcome (HR 0.50, 95% CI 0.31–0.80; p = 0.004). Higher SAPS II was modestly associated with increased risk (HR 1.01 per point increase, 95% CI 1.00–1.03; p = 0.026), whereas sex, age, arterial lactate concentration, and left ventricular failure were not significantly associated with the outcome after adjustment (Table 3). Detailed linearity, collinearity, and proportional hazards diagnostics are reported in **Supplementary Figures S1 and S2** and **Supplementary Table S1**. No major violation of the proportional hazards assumption or problematic multicollinearity was observed in the final model, and model discrimination was moderate (C-index 0.709, standard error [SE] 0.031).

Table 3
Univariable and multivariable time-dependent Cox analyses of factors associated with the primary composite outcome

Variable	Univariable HR	Univariable 95% CI	Univariable p-value	Multivariable HR	Multivariable 95% CI	Multivariable p-value
AUC(t)	**1.36**	**1.23–1.50**	**< 0.001**	**1.40**	**1.19–1.65**	**< 0.001**
Male sex	1.20	0.70–2.04	0.514	1.26	0.72–2.23	0.42
Age (years)	0.99	0.97–1.01	0.526	1.02	0.996–1.045	0.10
TIMI 3 flow	0.47	0.31–0.73	**< 0.001**	0.50	0.31–0.80	**0.004**
SAPS II	1.02	1.01–1.03	**0.003**	1.01	1.002–1.027	**0.03**
Lactate (mmol/L)	1.04	1.002–1.072	**0.04**	1.01	0.966–1.061	0.61
LV failure	1.29	0.87–1.92	0.21	1.44	0.86–2.42	0.17
ECPR	1.24	0.77–1.98	0.37	Stratified		
LV unloading	1.90	1.26–2.85	**0.002**	Stratified		

Cumulative troponin exposure was modelled as the time-dependent variable AUC(t), representing the cumulative troponin area under the concentration–time curve, scaled per 1,000,000 ng/L·day and updated daily using a last-observation-carried-forward approach. The model was left-truncated at the first day with an available AUC(t) value. Covariates included sex, age, TIMI 3 flow after revascularisation, SAPS II, arterial lactate concentration, and left ventricular failure. The model was stratified by ECPR and left ventricular unloading because of their major clinical importance and evidence of non-proportional hazards in preliminary analyses; therefore, hazard ratios were not estimated for these variables. HRs with 95% CIs are reported.

Abbreviations: AUC(t), time-updated cumulative troponin area under the concentration–time curve; CI, confidence interval; ECPR, extracorporeal cardiopulmonary resuscitation; HR, hazard ratio; LV, left ventricular; SAPS II, Simplified Acute Physiology Score II; TIMI, Thrombolysis in Myocardial Infarction

To complement the time-dependent association analyses and provide clinically interpretable early risk stratification, a day-5 landmark analysis was performed among patients who were alive and free from the primary endpoint at that time. After application of the landmark definition, 133 patients remained eligible for

analysis, of whom 71 experienced the primary endpoint between day 5 and day 100. Primary outcome-free survival progressively decreased across increasing quartiles of cumulative troponin exposure at day 5. Patients in the highest T-AUC quartile had the poorest outcome profile, whereas those in the lowest quartile had the highest probability of remaining free from the primary composite outcome (log-rank $p < 0.0001$) (Fig. 3).

Predictive discrimination was then assessed in this landmark cohort. Because some biomarkers had missing data, all multivariable ROC analyses were performed on a common complete-case dataset including 124 patients and 66 events to ensure valid comparisons across models. Within this landmark cohort, multivariable logistic regression models were used to estimate the probability of the primary endpoint, from which ROC curves were constructed. The reference clinical model showed moderate discriminative performance, with an AUC of 0.750 (95% CI 0.662–0.838). Among the evaluated biomarkers, the addition of day-5 T-AUC provided the greatest improvement in discrimination (AUC 0.862, 95% CI 0.797–0.926), followed by peak troponin (AUC 0.848, 95% CI 0.779–0.918) and baseline troponin (AUC 0.800, 95% CI 0.719–0.881). DeLong comparisons showed that the addition of day-5 cumulative troponin exposure and peak troponin significantly improved discrimination compared with the clinical model alone, whereas baseline troponin did not. Detailed ROC curves and diagnostic performance metrics are presented in Fig. 4 **and Supplementary Figure S3**.

Other analyses

Sensitivity analyses are reported in the Supplementary Material (**Supplementary Table S2**). In the day-5 landmark sensitivity analysis, cumulative troponin exposure remained associated with the primary composite outcome in a Cox model restricted to patients still at risk at day 5. By contrast, peak troponin showed lower discriminative performance than cumulative troponin exposure.

DISCUSSION

In this single-centre cohort of patients with MI-related cardiogenic shock requiring tMCS, higher cumulative post-infarction troponin exposure, quantified by T-AUC, was independently associated with the risk of weaning failure. Its addition to clinical parameters could improve the prediction of tMCS weaning failure. By integrating both the magnitude and duration of myocardial injury, cumulative troponin exposure may provide a more comprehensive and clinically relevant assessment of the likelihood of tMCS weaning failure in patients with ischaemic cardiogenic shock supported with tMCS.

Overall, our findings suggest that in MI-related cardiogenic shock requiring tMCS, the prognostic value of troponin may depend not only on its concentration but also on how the myocardial injury is integrated over time. The concordance between the time-dependent and day-5 landmark analyses, together with consistent findings across sensitivity analyses, support the hypothesis that cumulative troponin exposure captures clinically relevant information about myocardial recovery potential, although this interpretation remains cautious given the observational design, the multiplicity of complementary analyses, and the absence of external validation. Importantly, the day-5 landmark analysis should be interpreted as a conditional

prediction analysis among patients who are alive and free from the primary endpoint at day 5, assessing the prognostic value of troponin information available at that clinically relevant time point. This interpretation is broadly consistent with previous studies showing that later or serial troponin measurements are more informative than isolated admission values for estimating subsequent ventricular damage after MI.

Some authors have reported that admission troponin I was not predictive, whereas post-PCI measurements obtained at between 6 and 72 hours predicted large infarct size and left ventricular dysfunction [22]. Arruda-Olson et al. likewise found that day 1 to day 3 and peak troponin T values, rather than the earliest measurements, were associated with infarct size [9], and Mayr et al. showed that serial troponin T release correlated with infarct size and left ventricular function assessed by cardiac magnetic resonance imaging [7]. In more critically ill populations, North et al. found that peak troponin I was associated with unsuccessful VA-ECMO weaning in infarction-related cardiogenic shock [14], whereas Li et al. reported persistently higher troponin T levels and a slower early decline in non-survivors receiving VA-ECMO support [23]. By contrast, Luyt et al. did not observe predictive value for early biomarker levels or short-term kinetics in refractory cardiogenic shock of mixed aetiologies [16]. Taken together, these findings suggest that troponin is most informative in a homogeneous ischaemic population when its trajectory is considered over time rather than reduced to a single measurement.

A plausible explanation is that cumulative troponin exposure more accurately reflects the overall burden of irreversible myocardial necrosis and residual myocardial viability than does baseline or peak troponin concentration alone. In infarction-related cardiogenic shock, recovery under tMCS depends not only on the severity of the initial ischaemic insult but also on the extent of viable myocardium remaining after reperfusion. Baseline troponin is highly dependent on the timing of sampling in relation to symptom onset and revascularisation, whereas peak troponin reflects the intensity of biomarker release without capturing its persistence over time. By integrating both magnitude and duration, cumulative troponin exposure may therefore provide a more faithful estimate of the burden of early myocardial injury and, consequently, of recovery potential under temporary support. This may also explain why other biomarkers or general severity scores provided less incremental predictive values and why previous studies conducted in more heterogeneous shock populations, or including non-ischaemic aetiologies, have reported less consistent findings.

Several limitations should be acknowledged. First, the retrospective observational design exposes the study to potential selection bias, information bias, and residual confounding despite multivariable adjustment. Although candidate variables were selected *a priori* based on clinical relevance and the published literature, levosimendan was not retained in the final multivariable model because its use was balanced between the weaning outcome groups and showed no significant association with successful weaning in the univariable analysis (data not shown). This is consistent with the LEVOECMO randomised trial [24], in which early levosimendan administration did not increase successful VA-ECMO weaning. Unmeasured or incompletely measured confounders may still have influenced the observed associations. In particular, treatment decisions such as left ventricular unloading, escalation of support, or the timing of weaning attempts may partly reflect confounding by indication. In addition, the study was conducted in a single tertiary referral centre with a high volume of patients and substantial expertise in tMCS; therefore, patient selection,

management strategies, and the timing of escalation or weaning may differ across institutions, which may limit external generalisability.

Methodological limitations related to biomarker measurement should also be considered. Troponin measurements were obtained using different assays during the study period. Although values were harmonised to a common unit and previous method-comparison studies suggest good correlation between conventional and high-sensitivity assays at clinically relevant concentrations, some degree of measurement heterogeneity cannot be excluded. Furthermore, cumulative troponin exposure was reconstructed from serial measurements obtained approximately once daily, and daily AUC(t) updating relied on a last-observation-carried-forward approach when intermediate values were missing, which may have introduced some approximation into the reconstructed biomarker trajectory.

Finally, the primary composite endpoint reflects overall failure of the tMCS strategy rather than isolated myocardial recovery. Although this definition is commonly used in studies evaluating tMCS weaning, deaths occurring during the clinical course may result from causes unrelated to persistent myocardial dysfunction, including neurological injury, sepsis, haemorrhagic shock, or multiorgan failure. Similarly, the transplantation component may have been influenced by changes in national allocation procedures over the study period, since the French national heart-allocation score was implemented in January 2018 but was not specifically accounted for in the analysis.

From a clinical perspective, these findings do not support the use of troponin as a standalone decision tool. However, they suggest that routinely collected serial troponin measurements may provide objective information that complements clinical, haemodynamic, and imaging assessments when estimating the risk of tMCS weaning failure in infarction-related cardiogenic shock. If externally validated, cumulative troponin exposure could help to refine risk stratification and inform discussions regarding weaning attempts or escalation to durable advanced therapies. Although the study focused on a particularly severe and selected subgroup of patients with cardiogenic shock, restricted to those with myocardial infarction requiring tMCS, troponin measurement is widely available and is routinely performed during the acute phase of myocardial infarction, supporting the potential applicability of this approach to early risk stratification in ischaemic cardiogenic shock.

CONCLUSION

In patients with acute MI complicated by cardiogenic shock requiring tMCS, cumulative troponin exposure, quantified by T-AUC, improved the prediction of tMCS weaning failure when incorporated into a clinical model and may therefore contribute to improved early risk stratification in this high-risk population.

Abbreviations

AIC
Akaike information criterion
AUC
area under the receiver operating characteristic curve

AUC(t)
time—updated cumulative troponin area under the concentration—time curve
ALT
alanine aminotransferase
AST
aspartate aminotransferase
BMI
body mass index
BNP
B—type natriuretic peptide
CI
confidence interval
COPD
chronic obstructive pulmonary disease
CPB
cardiopulmonary bypass
cTnI
cardiac troponin I
ECMELLA
veno—arterial extracorporeal membrane oxygenation combined with Impella support
ECPR
extracorporeal cardiopulmonary resuscitation
eGFR
estimated glomerular filtration rate
HR
hazard ratio
IABP
intra—aortic balloon pump
ICU
intensive care unit
KDIGO
Kidney Disease: Improving Global Outcomes
LVEF
left ventricular ejection fraction
LV
left ventricle / left ventricular
LVOT VTI
left ventricular outflow tract velocity—time integral
MI
myocardial infarction
NPV

negative predictive value
NSTEMI
non—ST—segment elevation myocardial infarction
PCI
percutaneous coronary intervention
PPV
positive predictive value
ROC
receiver operating characteristic
SAPS II
Simplified Acute Physiology Score II
SCAI
Society for Cardiovascular Angiography and Interventions
Se
sensitivity
SE
standard error
Sp
specificity
STEMI
ST—segment elevation myocardial infarction
T
AUC—troponin area under the concentration—time curve
TIMI
thrombolysis in myocardial infarction
tMCS
temporary mechanical circulatory support
VA
ECMO—veno—arterial extracorporeal membrane oxygenation
VAD
ventricular assist device
VIF
variance inflation factor

Declarations

ETHICs APPROVAL AND CONSENT TO PARTICIPATE: In accordance with the ethical standards of our hospital's institutional review board, the Committee for the Protection of Human Subjects, and French law, written informed consent was not required for the analysis of demographic, physiological, and hospital outcome data because this observational study did not modify existing diagnostic or therapeutic strategies.

The study protocol was reviewed and approved by the Health and Research Ethics Centre of Bordeaux (Centre Éthique et Recherche en Santé de Bordeaux) under reference CER-BDX 2026-10.

CONSENT FOR PUBLICATION: Written informed consent for publication was not required for this study. The research was conducted as a retrospective observational analysis using anonymised data extracted from routine clinical care records. No identifiable personal information is reported in the manuscript or Supplementary Material. In accordance with French regulations governing retrospective research using existing health data (MR-004 methodology), individual consent was waived because the study did not involve any intervention or modification of patient management and used data collected as part of routine clinical practice. The study protocol was reviewed and approved by the Health and Research Ethics Centre of Bordeaux (Centre Éthique et Recherche en Santé de Bordeaux) under reference CER-BDX 2026-10, and all procedures complied with applicable data protection regulations, including the General Data Protection Regulation (GDPR).

AVAILABILITY OF DATA AND MATERIALS: The datasets generated and analysed during the current study were extracted from patients' medical records and are not publicly available because of data protection and privacy regulations. However, they are available from the corresponding author upon reasonable request.

COMPETING INTERESTS: The authors declare that they have no competing interests.

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Author Contributions:

- QL, AB, FXH, HDC, JP, and AO contributed to the study design, data collection, statistical analysis, data interpretation, figure preparation, and manuscript drafting.
- All other authors contributed to critical evaluation of the manuscript.
- AO is the guarantor of this study.

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Figures

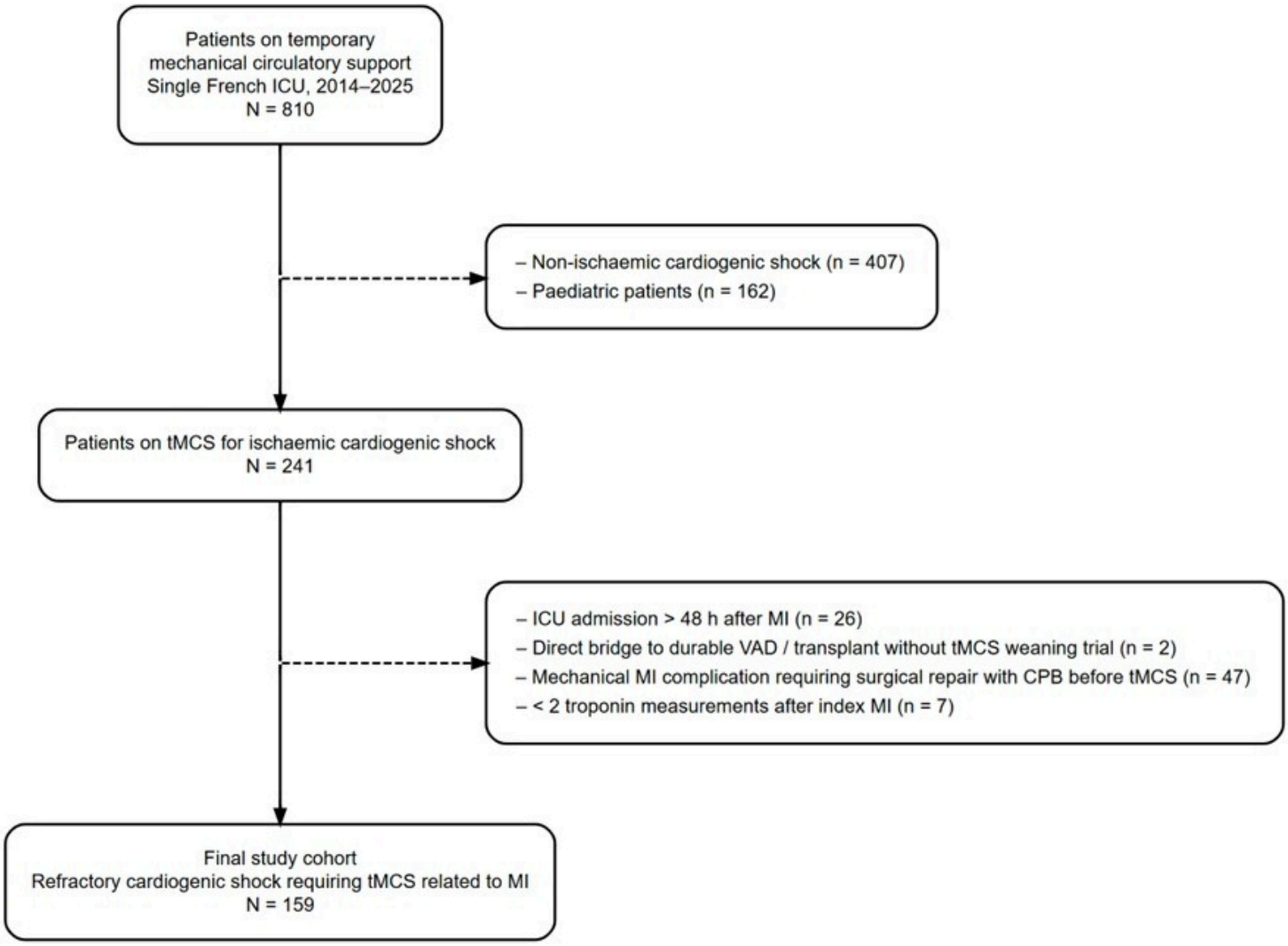


Figure 1

Flow diagram of patient selection

Among 810 patients treated with tMCS, 407 patients with non-ischaemic cardiogenic shock and 162 paediatric patients were excluded. Of the 241 patients receiving tMCS for acute MI-related cardiogenic shock, additional exclusion criteria were applied: ICU admission > 48 hours after MI (n = 26), direct bridge to durable VAD implantation or heart transplantation without a tMCS weaning attempt (n = 2), mechanical complications of MI requiring surgical repair under CPB before tMCS initiation (n = 47), and fewer than two troponin measurements after the index MI (n = 7). The final study cohort comprised 159 adult patients with MI-related cardiogenic shock requiring tMCS.

Abbreviations: CPB, cardiopulmonary bypass; ICU, intensive care unit; MI, myocardial infarction; tMCS, temporary mechanical circulatory support; VAD, ventricular assist device.

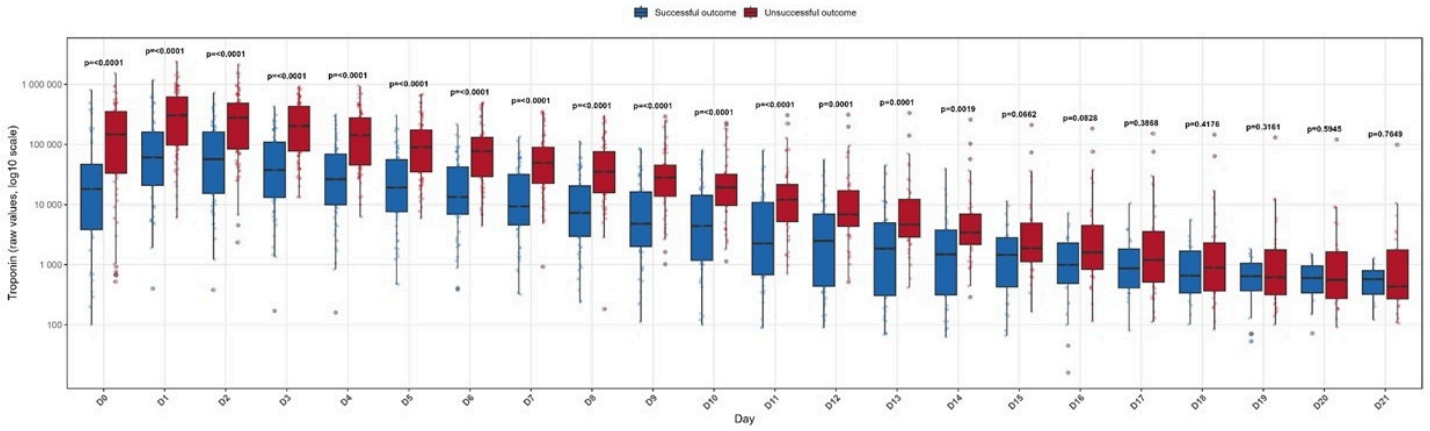


Figure 2

Serial troponin I concentrations from day 0 to day 21 according to tMCS weaning outcome

Boxplots show the median (horizontal line), interquartile range (box), and values within 1.5 × the interquartile range (whiskers). Individual observations are shown as jittered points. Troponin I concentrations are presented on a logarithmic (log10) scale while retaining the original values (ng/L). Patients were stratified according to the primary composite outcome of tMCS weaning failure. Blue indicates successful weaning, and red indicates weaning failure. Between-group comparisons at each time point were performed using the Mann–Whitney U test, and the reported p values are unadjusted. The sample size at each time point varies according to data availability and censoring over time.

Abbreviations: tMCS, temporary mechanical circulatory support

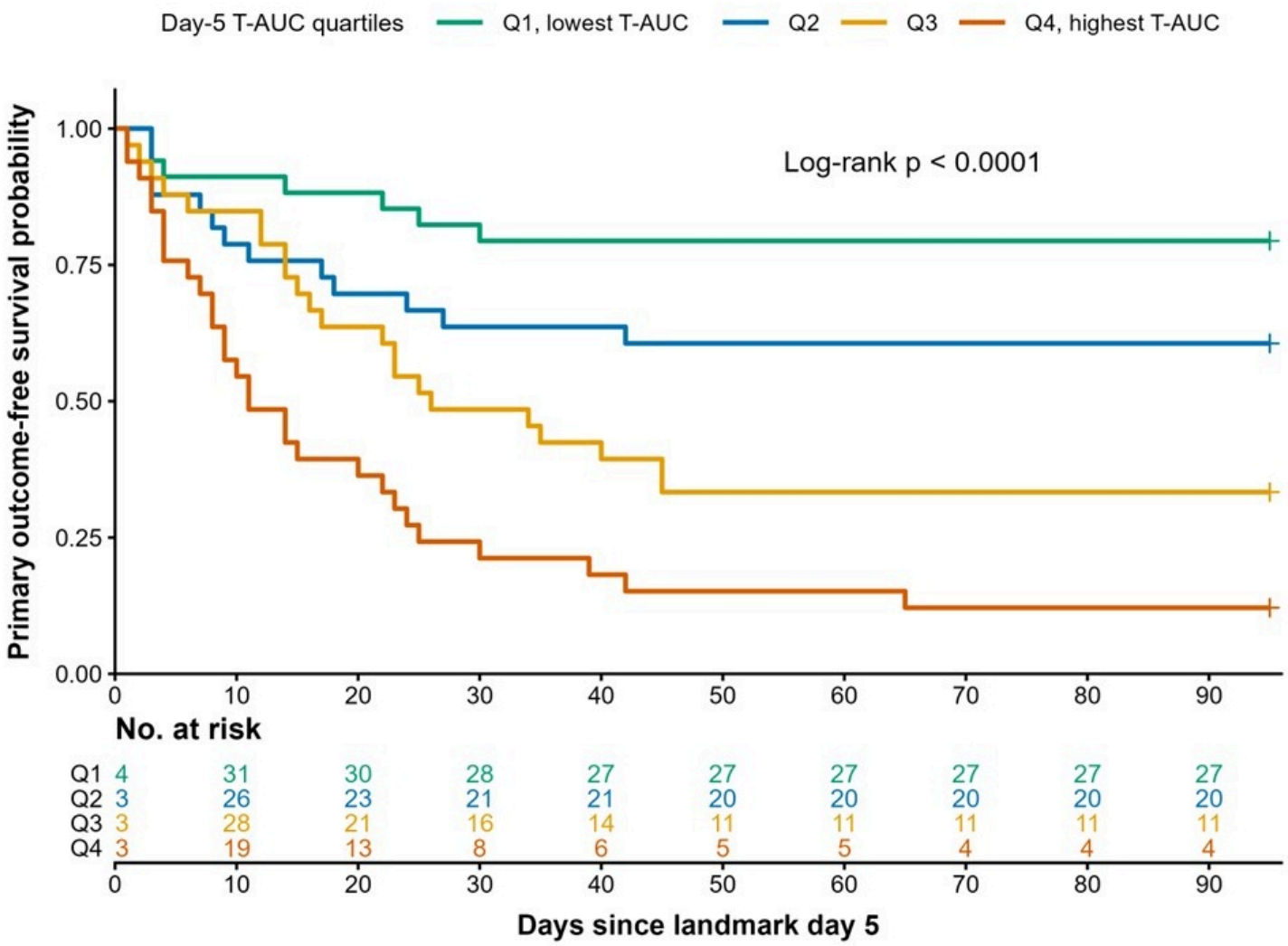


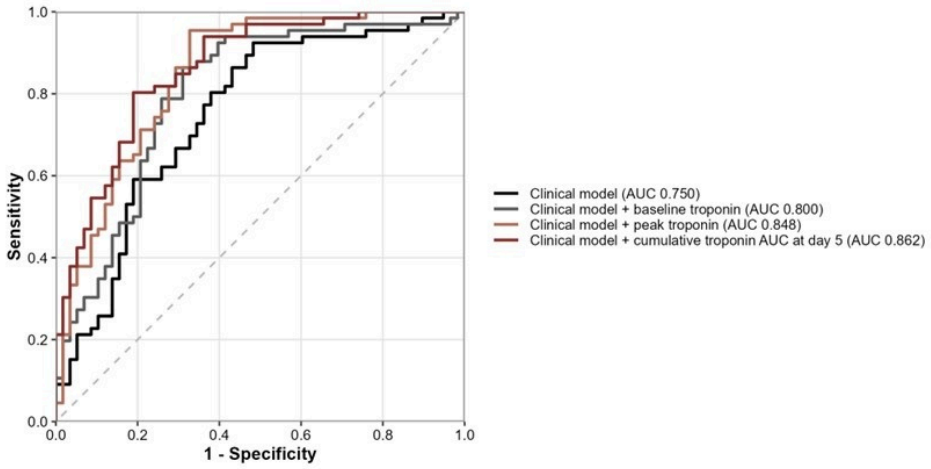
Figure 3

Primary outcome-free survival according to day-5 T-AUC quartiles in the landmark cohort

Kaplan–Meier curves show freedom from the primary composite outcome between days 5 and 100 after MI according to quartiles of day-5 T-AUC. Patients who experienced the primary composite outcome before or on day 5 were excluded from the landmark analysis. Follow-up was calculated from day 5 to day 100 after MI. Q1 represents the lowest day-5 T-AUC quartile and Q4 the highest. Tick marks indicate censored observations. The numbers at risk represent patients who remained under observation and free from the primary composite outcome at each time point. Groups were compared using the log-rank test.

Abbreviations: MI, myocardial infarction; Q, quartile; T-AUC, troponin area under the concentration–time curve

A



B

Model	N	Events	AUC	CI95	Sensitivity	Specificity	PPV	NPV	Youden
Clinical model	124	66	0.750	0.662 - 0.838	0.924	0.517	0.685	0.857	0.441
Clinical model + baseline troponin	124	66	0.800	0.719 - 0.881	0.864	0.690	0.760	0.816	0.553
Clinical model + peak troponin	124	66	0.848	0.779 - 0.918	0.955	0.672	0.768	0.929	0.627
Clinical model + cumulative troponin AUC at day 5	124	66	0.862	0.797 - 0.926	0.803	0.810	0.828	0.783	0.613

Figure 4

Predictive performance of the clinical model and biomarker-augmented models for tMCS weaning failure

ROC analysis evaluating the predictive performance of the clinical model and biomarker-augmented models for the primary endpoint. A landmark analysis was performed at day 5 that included patients alive and free from the primary endpoint at that time. The prediction horizon was set at day 100 to ensure complete follow-up of all weaning attempts, as the latest device explantation in the cohort was at day 70. Logistic regression models were fitted using complete-case data from the landmark population. The clinical model included sex, age, TIMI 3 flow, SAPS II, arterial lactate concentration, left ventricular failure, extracorporeal cardiopulmonary resuscitation, and left ventricular unloading. Separate biomarker-augmented models were constructed by adding baseline troponin, peak troponin, or day-5 T-AUC to the clinical model. All biomarker predictors were defined using data available on or before day 5. Panel A shows the ROC curves for the clinical model and the biomarker-augmented models. Discrimination was quantified using the AUC. Panel B reports the corresponding model performance metrics, including AUCs with 95% confidence intervals, sensitivity, specificity, PPV, NPV, and the Youden index. The optimal classification threshold for each model was determined by maximising the Youden index.

Abbreviations: AUC, area under the receiver operating characteristic curve; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic; SAPS II, Simplified Acute Physiology Score II; T-AUC, troponin area under the concentration–time curve; TIMI, Thrombolysis in Myocardial Infarction

Supplementary Files

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