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Original paper

Long-term neurological outcomes after extracorporeal cardiopulmonary resuscitation for refractory cardiac arrest: a 14-year single-centre cohort study

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Abstract

Background: Extracorporeal Cardiopulmonary Resuscitation (ECPR) via Veno-Arterial Extracorporeal Membrane Oxygenation (ECMO) is a viable treatment for refractory cardiac arrest (r-CA). Data on long-term outcomes and predictors of favourable neurological prognosis remain limited, and definitive patient-selection recommendations are lacking.

Methods: We conducted a retrospective observational study of adult patients treated with ECPR for in-hospital (IHCA) and out-of-hospital (OHCA) r-CA at an Italian ECMO centre between 2011 and 2024. The primary outcome was long-term neurological performance, measured by the Cerebral Performance Category (CPC) scale six months after hospital discharge. Multivariable and latent class analyses assessed independent predictors and explored distinct pre-ECPR phenotypes.

Results: Among 295 consecutive patients (117 IHCA; 178 OHCA), 17.3% achieved CPC 1–2 at six months (28.2% IHCA vs 10.1% OHCA; $p < 0.0001$), and 4.4% survived with severe long-term neurological sequelae (CPC 3–4). Independent predictors of CPC 1–2 were younger age (OR 0.95 per year, 95% CI 0.92–0.98), an initial shockable rhythm (aOR 2.7; 95% CI 1.11–7.04), and shorter low-flow duration (OR 0.95 per minute increase, 95% CI 0.93–0.97). Stepwise selection based on these criteria progressively increased the proportion of favourable survivors but excluded a small proportion who might have recovered.

Conclusions: These results emphasise the importance of establishing pre-treatment selection criteria to optimise ECPR use and enhance long-term neurological outcomes. Age, initial rhythm, and low-flow time are key determinants, and exploratory phenotype-based analyses suggest multidimensional patient characterisation may complement traditional selection criteria.

Keywords: Cardiac arrest, CA, Refractory cardiac arrest, Extracorporeal cardiopulmonary resuscitation, ECPR, Veno-arterial extracorporeal membrane oxygenation, VA-ECMO, Long term outcome

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Background

Extracorporeal cardiopulmonary resuscitation (ECPR) is a rescue strategy for selected patients with refractory cardiac arrest when conventional advanced life support fails to achieve sustained return of spontaneous circulation (ROSC).[1–3] By rapidly establishing veno-arterial extracorporeal membrane oxygenation (VA-ECMO), ECPR provides immediate circulatory and respiratory support, stabilising systemic perfusion while potentially reversible causes are identified and treated.[1,2,4] Its use has expanded in both out-of-hospital (OHCA) and in-hospital cardiac arrest (IHCA), driven by technological advances, network organisation, and refined selection criteria.[5–7] Despite promising single-centre reports and early randomised trials, long-term favourable neurological outcome remains limited and variable (10–40%), depending on study design, setting, and inclusion criteria.[2,7–9] Recent randomised trials have indicated that stringent selection criteria and minimised low-flow times are crucial for achieving meaningful outcomes.[10–13] However, real-world data frequently reflect less stringent conditions, thereby underscoring the necessity for data from large observational cohorts treated within institutional protocols over extended periods.[2,8,9]

The proposed predictors of good neurological outcome after ECPR (younger age, initial shockable rhythm, shorter no-flow/low-flow times, lower pre-cannulation lactate, and cardiac aetiology), remain inconsistent across studies, due to differences in case mix, management, and modelling.[4,7,8,14–16]

Moreover, analyses frequently emphasise short-term endpoints, whereas long-term neurological recovery, central to post-discharge quality of life, is less frequently evaluated and available data remain fragmented.[6,9,17,18]

To address these gaps, we conducted a retrospective single-centre observational study of adult patients treated with ECPR for refractory OHCA or IHCA over 14 years. We aimed to describe long-term outcomes and identify independent predictors of favourable recovery. We leveraged real-world data across evolving local ECPR criteria and management strategies in order to refine prognostic assessment and support evidence-based decision-making in cases of refractory cardiac arrest.

Methods

Patient population and study design

This retrospective observational study was conducted between January 1, 2011 and December 31, 2024, at the Cardiac ICU of "IRCCS San Gerardo dei Tintori Foundation Hospital" (Monza, Italy), with follow-up through June 30, 2025. We included consecutive patients aged 18 years or older treated with ECPR for refractory IHCA or OHCA according to the institutional protocol. The primary outcome was long-term survival with good neurological outcome. The Institutional Ethics Committee approved the study (ID:5721_12.03.2025) and consent was waived.

Institutional ECPR protocol

OHCA

Given the long-time span, the ECPR protocol changed over the years (details in supplementary materials). Briefly, the pre-hospital emergency service referred patients eligible for ECPR when the following criteria were met (according to the last protocol update): age <70 years, witnessed OHCA with immediate bystander CPR, no-flow time <6 min, shockable presenting rhythm, and expected collapse-to-ECPR time <60 min. Criteria were refined according to emerging evidence, leading to stricter selection by excluding non-shockable rhythms and prolonged no-flow time. ECPR was provided by an intensivist-led ECMO team in the emergency department. The intensivist in charge could start treatment "out of protocol" in some patients with incomplete criteria, according to clinical judgment. Post-cannulation management remained unchanged over time (see supplementary materials).

IHCA

Patients aged <75 with witnessed, refractory IHCA were eligible at the intensivist's discretion. Refractory status was defined as the absence of ROSC after 10–15 min of conventional advanced CPR in the presence of a potentially reversible cause. Cannulation occurred at the arrest site, with subsequent management tailored according to patient conditions and cardiac arrest cause.

Inclusion and exclusion criteria

All consecutive patients aged >18 treated with ECPR during the study period were included. Incomplete medical records and inability to assess long-term outcomes were exclusion criteria.

Data collection

We collected data on patient demographics, pre-arrest comorbidities, and resuscitation variables in compliance with Utstein guidelines.[19,20] Comprehensive definitions of cardiac arrest variables, including criteria for witnessed arrest, no-flow and low-flow times, rhythm classification, transient ROSC, and signs of life, are provided in the Supplementary Materials.

Study outcomes

Neurological outcome was classified according to Cerebral Performance Category (CPC); CPC 1–2 was considered as good. The primary outcome, defined as survival with good neurological outcome, was collected six months after discharge from the intensive care unit (ICU) via interviews at the ICU follow-up clinic or telephone interviews for those unable to attend. Secondary outcomes included survival at ICU discharge and after six months, good neurological outcome at ICU discharge and organ donation after death.

Statistical analysis

Descriptive statistics reported data on patients characteristics and outcomes. Categorical data are presented as numbers and percentages, while continuous variables with median and interquartile range (IQR). Comparisons between patients with good and poor outcomes were performed using the Mann–Whitney *U* test for continuous variables and the χ^2 or Fisher's exact test for categorical variables, as appropriate. Univariable analyses were conducted in the overall cohort and stratified by cardiac arrest type (OHCA vs IHCA).

To investigate the effect of patient selection above outcome, patients were stratified by cardiac arrest type, initial rhythm (shockable vs. non-shockable), age (<70 years), and stepwise reductions in low-flow time. Subsequent to this, outcomes were subsequently evaluated within each subgroup.

Candidate predictors of good neurological outcome were selected based on clinical relevance and univariable screening. Variable selection was initially explored using penalised logistic

regression with a LASSO penalty, but no stable predictors emerged. A parsimonious, clinically driven multivariable model was therefore constructed including age, no-flow time, low-flow time, transient ROSC, and presenting rhythm. Further details on variable selection process are provided in supplementary material.

Adjusted odds ratios (ORs) with 95% confidence intervals (CI) were reported. Optimal cut-off values for continuous predictors were derived using receiver operating characteristic (ROC) curve analysis. The final model was used to predict the probability of a favourable neurological outcome, and these predictions were then graphically displayed against a range of continuous predictors, with stratification according to categorical predictors.

For post-hoc exploratory purposes, latent class analysis identified distinct phenotypes based on baseline characteristics. Six pre-ECPR categorical variables were included in the model: presenting rhythm (shockable vs non-shockable), transient ROSC, signs of life, cardiac aetiology, initial blood lactate (categorised using best value as a threshold), and low-flow duration (categorised using best value as a threshold). Models with two to four classes were compared using the Bayesian Information Criterion, and the optimal model was selected based on statistical fit and clinical interpretability. Patients were assigned to classes according to the highest posterior probability; individuals with low posterior probabilities were considered unclassified. Latent class results and outcome rates were reported descriptively, without formal inferential testing.

All tests were two-sided, and p values < 0.05 were considered statistically significant. Analysis was performed using JMP version 16 (SAS Institute Inc., Cary, NC, USA).

Results

We enrolled 295 patients, including 117 with IHCA and 178 with OHCA. Clinical data and long-term outcomes were available for all and no patients were excluded. Pre-arrest characteristics of included patients are summarised in Table 1 and Table S1 (Supplementary Material). Median age was 58 (50–65) years, 80% were male, median no-flow time was 0 (0–1) min and median low-flow time was 56 (30–70) min. 179 (60.7%) patients presented with shockable rhythm. IHCA and OHCA patients differed significantly in terms of age (p < 0.0001), sex (p < 0.0001), cardiac arrest aetiology (p < 0.0001) and duration (p < 0.0001), among others (Table 1 and Table S1). Subsequent clinical course of included patients is described in Table S2.

Primary outcome

Overall, 51 (17.3%) patients achieved favourable neurological outcome at 6 months. This was found to be significantly higher among patients who experienced IHCA compared with those with OHCA (33 [28.2%] vs 18 [10.1%], p < 0.0001) (Table 2 and Fig. S1). Within the overall population, 13 (4.4%) survived with severe long-term neurological sequelae (CPC 3–4) (Table S3, supplementary Material).

Secondary outcomes

Survival at ICU discharge and at six months, regardless of neurological status, occurred in 73 (24.7%) and 64 (21.7%) patients, respectively. Moreover, 48 (16.3%) patients had a good neurological outcome at ICU discharge. After stratification by IHCA and OHCA subgroups, survival and good neurological outcome were more frequent in IHCA patients (see Table 2 and Fig. S1). Furthermore, 9 patients died between successful ICU discharge and six months (6 from IHCA group and 3 from OHCA group). Moreover 45 (15.3%) patients underwent organ donation (Table 2 and Fig. S1).

Primary outcome according to clinical stratification

Patients were stratified by cardiac arrest type (IHCA vs OHCA), presenting rhythm, age <70 years, and progressively shorter low-flow time intervals.

In the IHCA group, stepwise selection increased the proportion of patients with favourable outcome from 28.2% in the overall cohort to 43% among those with an initial shockable rhythm, and further to 53.8% among patients aged <70 years, reaching 68% when low-flow time was <40 min, while reducing poor neurological outcomes (CPC 3–4) from 5.9% to 0% (Fig. 1, Table S4).

Applying the same criteria to patients with Pulseless electrical activity (PEA) or asystole resulted in more modest improvements (PEA: 22.7–30.3%; asystole: 14.2–20%), with a concomitant reduction in poor neurological outcomes.

In the OHCA group, favourable neurological outcomes increased from 10.1% to 33.3% among patients with a shockable rhythm, age <70 years, and low-flow time <40 min; however, poor neurological outcomes increased from 3.3% to 16.7%. Further stratification of patients with non-shockable rhythms was precluded by the low number of favourable outcomes (Fig. 1, Table S5).

Predictors of good neurological outcome

Results of univariate screening and penalised logistic regression with a LASSO penalty used for variable selection are reported in Tables S6 and S7 (Supplementary Material).

Younger age (OR 0.95 per year increase, 95% CI 0.92–0.98), shorter low-flow duration (OR 0.95 per minute increase, 95% CI 0.93–0.97), and a shockable presenting rhythm were independently associated with good neurological outcome. Specifically, the odds of good neurological outcome were higher for Ventricular Fibrillation (VF) and Ventricular Tachycardia (VT) compared with asystole (OR 9.43, 95% CI 2.16–69.64) and with PEA (OR 2.83, 95% CI 1.25–6.76) (Table 3). Predicted probabilities of good neurological outcome obtained from the final model were graphically displayed against age and low-flow time, with stratification according to presenting rhythm (Fig. 2).

Clinical phenotype of ECPR patients and relationship with outcome

Latent class analysis identified three distinct patient phenotypes (classes) based on six pre-ECPR variables (low-flow time <60 min, age <60 years, presenting rhythm, transient ROSC, blood lactate <8.3, IHCA vs OHCA). Thirty-seven patients (12.5% of the cohort) could not be reliably assigned to any class due to low posterior probabilities.

Class 1 (n = 132, 44.7%) had high probability of shockable rhythm (probability of VF/VT: 0.87), younger age (probability of age <60 years: 0.68), and an almost exclusive occurrence of out-of-hospital cardiac arrest (probability: 0.99). Despite a favourable rhythm profile, this cluster showed a low probability of transient ROSC (Probability: 0.15) and markedly elevated lactate levels.

Class 2 (n = 71, 24.1%) had a mixed rhythm profile (probability of VF/VT: 0.43; PEA: 0.49), the highest probability of transient ROSC (probability: 0.45), and predominantly lower lactate levels (probability of lactate <8.3 mmol/L: 0.73). This cluster was mainly composed of in-hospital cardiac arrest cases.

Table 1 – Clinical and demographic characteristics. Table resumes main pre-ECPR patients' characteristics, along with stratification according to Intra Hospital Cardiac Arrest or Out of Hospital Cardiac Arrest. P-value refers to the comparison between In-Hospital and Out-of-Hospital Cardiac Arrest groups.

	All (*n* = 295)	IHCA (*n* = 117)	OHCA (*n* = 178)	*p*-value
Age (years), median (IQR)	58 (50–65)	61 (54–70)	56 (48–63)	**<0.0001**
Sex (male), *n* (%)	236 (80%)	80 (68.4%)	156 (87.6%)	**<0.0001**
Body mass index (kg/m^2), median (IQR)	26 (24–29)	26 (23–29)	26 (24–28)	0.2387
Frailty index, median (IQR)	2 (2–3)	2 (2–3)	2 (2–2)	**<0.0001**
Cardiac arrest cause				**<0.0001**
Cardiac, n (%)	238 (80.7%)	79 (67.5%)	159 (89.3%)	
Hypoxic, n (%)	9 (3.1%)	4 (3.4%)	5 (2.8%)	
Drugs/toxics, n (%)	4 (1.4%)	1 (0.9%)	3 (1.7%)	
Pulmonary embolism, n (%)	13 (4.4%)	12 (10.3%)	1 (0.6%)	
Aortic dissection, n (%)	5 (1.7%)	5 (4.3%)	0 (0%)	
Haemorrhagic shock, n (%)	5 (1.7%)	5 (4.3%)	0 (0%)	
Other, n (%)	21 (7.1%)	11 (9.4%)	10 (5.6%)	
Location of cardiac arrest				**<0.0001**
Out of hospital, n (%)	178 (61.4%)	0 (0%)	178 (100%)	
Emergency Department, n (%)	30 (10.2%)	30 (25.6%)	0 (0%)	
Operating Room, n (%)	12 (4.1%)	12 (10.3%)	0 (0%)	
Cath lab, n (%)	20 (6.8%)	20 (17.1%)	0 (0%)	
ICU, n (%)	36 (12.2%)	36 (30.8%)	0 (0%)	
Other, n (%)	19 (6.5%)	19 (16.2%)	0 (0%)	
Witnessed cardiac arrest, *n* (%)	295 (100%)	117 (100%)	178 (100%)	
No flow, median (IQR)	0 (0–1)	0 (0–1)	0 (0–5)	**<0.0001**
Low flow, median (IQR)	56 (30–70)	22 (14–38)	65 (56–75)	**<0.0001**
Rhythm of presentation				**<0.0001**
Shockable Rhythm, n (%)	179 (60.7%)	37 (31.6%)	142 (79.8%)	
PEA, n (%)	80 (27.1%)	66 (56.4%)	14 (7.9%)	
Asystole, n (%)	36 (12.2%)	14 (12%)	22 (12.4%)	
Transient ROSC before ECPR, *n* (%)	76 (25.8%)	48 (41%)	28 (15.7%)	**<0.0001**
Sign of life during CPR, *n* (%)	5 (1.7%)	1 (0.9%)	4 (2.2%)	0.3810
Adrenaline administered, median (IQR)	5 (4–8)	4.5 (2–7)	5 (5–8)	**0.0188**
Blood lactate before ECPR, median (IQR)	11.5 (7.4–15.3)	7.6 (3.4–12.5)	12.9 (10.8–17)	**<0.0001**

PEA: Pulseless Electrical Activity; IHCA: Intra Hospital Cardiac Arrest; OHCA: Out of Hospital Cardiac Arrest. ROSC: Return of Spontaneous Circulation; ECPR: Extracorporeal Cardiopulmonary Resuscitation; ICU: Intensive Care Unit.

Table 2 – Primary and secondary outcomes. Table resumes Primary and Secondary Study Outcomes along with stratification according to Intra Hospital Cardiac Arrest or Out of Hospital Cardiac Arrest groups. P-value refers to the comparison between In-Hospital and Out-of-Hospital Cardiac Arrest groups.

	All (*n* = 295)	IHCA (*n* = 117)	OHCA (*n* = 178)	*p*-value
Primary outcome				
Good neurological outcome at six months, *n* (%)	51 (17.3%)	33 (28.2%)	18 (10.1%)	**0.0001**
Secondary outcomes				
Survival at ICU discharge, *n* (%)	73 (24.7%)	46 (39.3%)	27(15.1%)	**<0.0001**
Survival at 6 months, *n* (%)	64 (21.7%)	40 (34.2%)	24 (13.5%)	**<0.0001**
Good neurological outcome at ICU discharge, *n* (%)	48 (16.3%)	30 (25.6%)	18 (10.1%)	**0.0004**
Organ donation, *n* (%)	45 (15.3%)	6 (5.1%)	39 (21.9%)	**0.0018**

IHCA: Intra Hospital Cardiac Arrest; OHCA: Out of Hospital Cardiac Arrest; ICU: Intensive Care Unit.

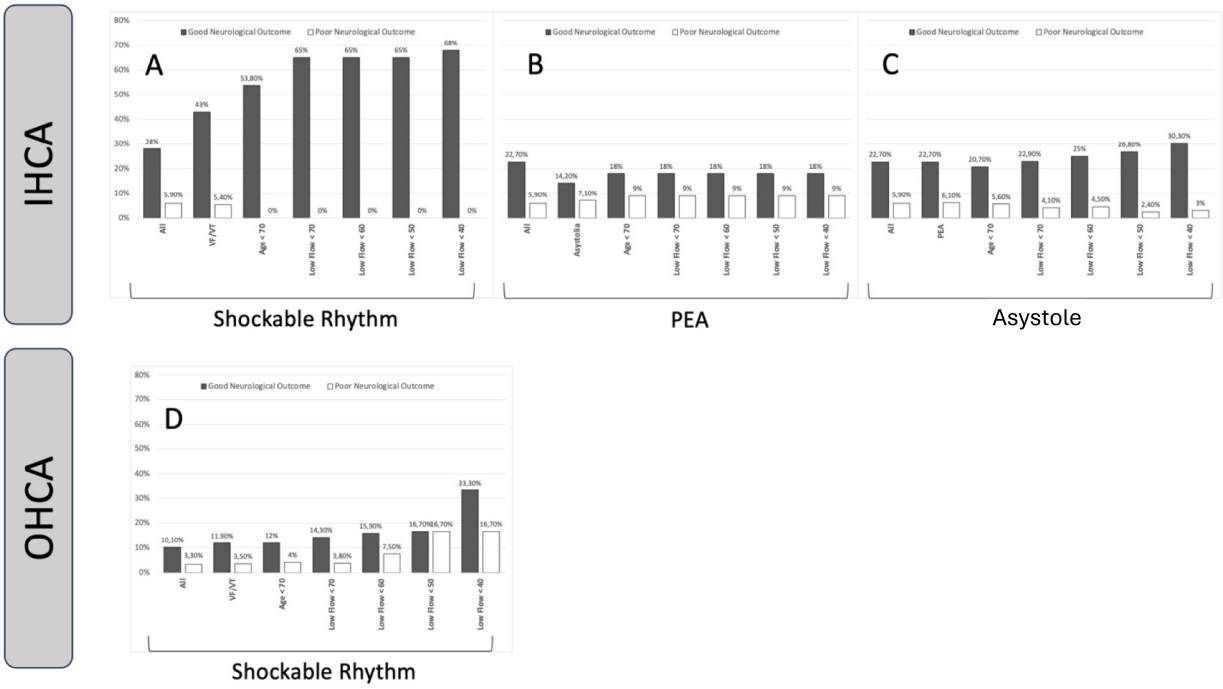

Fig. 1 – Stratification of whole IHCA and OHCA population according to rhythm of presentation, age and low flow time.
Whole population was stratified according to stepwise selection according to Rhythm of presentation, age and low flow duration. For IHCA group (first line), the criteria of rhythm of presentation (VT/VF in Panel A, PEA in Panel B and asystole in Panel C) was followed by stepwise selection according to age <70 years and decremental clusters of low flow duration (namely, <70, <60, <50 and <40 min). Grey columns show the percentage of patients achieving good neurological outcome in that subgroup, while white columns indicate the percentage of patients who survived with poor neurological outcome. In the second line the same selection is applied to OHCA group, for the sole criteria of shockable rhythm (Panel D).

Class 3 (*n* = 55, 18.7%) showed predominantly non-shockable rhythms, particularly PEA (probability 0.75), very low probability of VF/VT (0.01), and markedly elevated lactate levels; transient ROSC was infrequent, reflecting the most unfavourable pre-ECPR profile.

Conditional probabilities for each variable across classes are shown in Table S8 (Supplementary Material). A heatmap (Fig. S2, panel A, Supplementary Material) and a class profile plot (Fig. S2, panel B, Supplementary material) show variable distributions within each class.

Table 3 – Results of logistic regression model for good neurological outcome at six months (CPC 1–2).

Variable	OR	IC 95%	*p*-value	Best value
Age (1 year)	0.95	0.92–0.98	**0.0007**	**58**
No flow (1 min)	0.90	0.77–1.01	0.1226	2
Low flow (1 min)	0.95	0.93–0.97	**<0.0001**	**38**
Transitory ROSC (yes)	1.71	0.79–3.65	0.1642	–
Rhythm (VF/VT vs ASY)	9.43	2.16–69.64	**0.0014**	–
Rhythm (VF/VT vs PEA)	2.83	1.25–6.76	**0.0118**	–

OR: Odds Ratio; IC 95%: Confidence Interval 95%; ROSC: Return of Spontaneous Circulation; VF: Ventricular Fibrillation; VT: Ventricular Tachycardia; ASY: Asystole; PEA: Pulseless Electrical Activity.

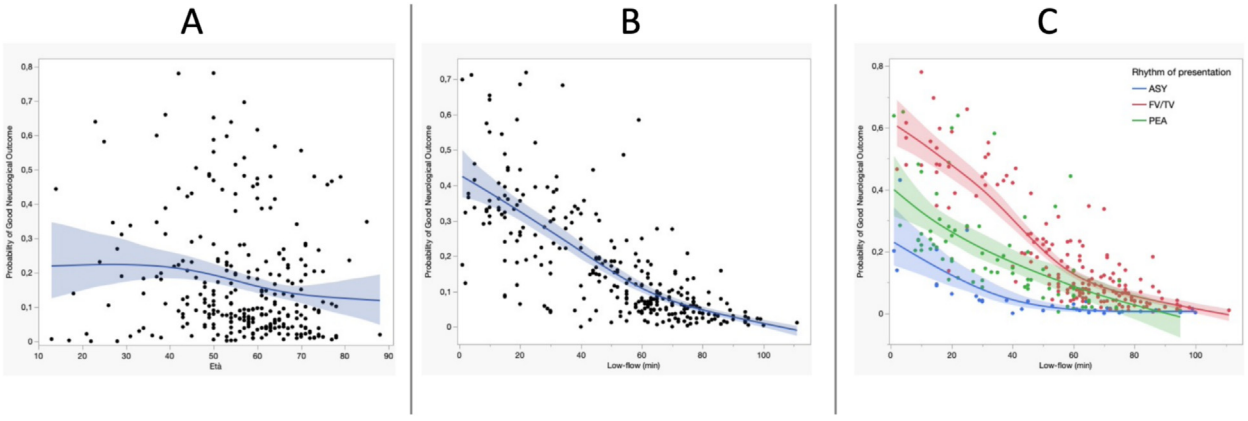

Fig. 2 – Adjusted probability of good neurological outcome.
Age (Panel A), Low Flow (Panel B) and Low Flow with stratification according to Rhythm of presentation (Panel C) were plotted against the predicted probability of having a good neurological outcome obtained from logistic regression model.

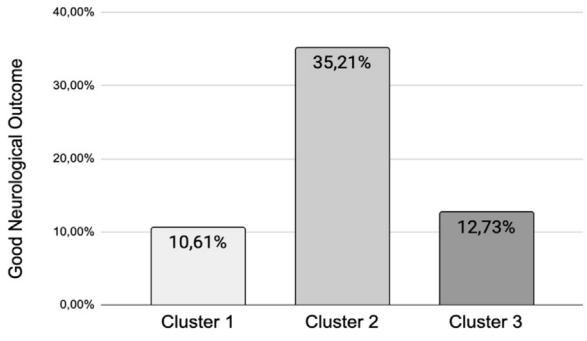

Fig. 3 – Observed rate of good neurological outcome at 6 months in different patient cluster identified by latent class analysis.

Outcome rates differed descriptively across classes: good neurological outcome was highest in Class 2 (35.2%), intermediate in Class 1 (12.7%), and lowest in Class 3 (10.6%) (Fig. 3). No formal inferential comparisons were performed, as class assignment was exploratory and descriptive.

Discussion

We retrospectively analysed patients undergoing ECPR in order to characterise long-term outcomes and identify independent predictors of long-term outcome. A favourable neurological outcome at six months was observed in 17.3% of the cohort, with significantly better results among patients with IHCA than among those with OHCA. Younger age, shockable rhythm, and shorter low-flow time emerged as independent predictors of long-term outcome. Furthermore, stepwise stratification based on these variables progressively increased the proportion of patients with favourable survival, particularly in the IHCA subgroup. Finally, latent class analysis identified distinct pre-ECPR phenotypes with possibly heterogeneous recovery potential.

Primary outcome

In recent years, ECPR in OHCA has been evaluated in three major randomised controlled trials (Table S9) that reported good neurological outcome ranging from 20% to 43%.[10–12] When selection criteria comparable to those used in randomised trials were retrospectively applied to our OHCA cohort, excluding non-shockable rhythm, prolonged low-flow time and older age, the proportion of patients

exhibiting favourable neurological outcomes increased and approached trial results. Importantly, our results are also consistent with those reported in previous large retrospective studies, confirming that our cohort is representative of the real-world ECPR population. These findings support the notion that differences in patient selection largely account for the discrepancy between outcomes observed in trials and those reported in unselected observational cohorts.

Consistent with previous observational studies, patients treated with ECPR for IHCA demonstrated better survival and neurological recovery than those with OHCA.[21,22] This difference likely reflects shorter no-flow and low-flow durations, immediate access to advanced life support, and earlier restoration of systemic perfusion in the hospital setting, as suggested by higher rates of transient ROSC and lower pre-ECMO lactate levels.

The stepwise stratification analysis illustrates the trade-off inherent in ECPR candidate selection. Restricting eligibility criteria progressively enriches the proportion of patients achieving favourable neurological outcomes, but this comes at the cost of excluding patients who might otherwise recover acceptable neurological function. Conversely, broader inclusion strategies increase the absolute number of survivors with good outcome, while also increasing the risk of survival with severe neurological impairment. These findings highlight the need for careful calibration of selection criteria to balance prognostic enrichment with inclusivity, taking into account clinical benefit, resource utilisation and ethical considerations. Accordingly, the overarching goal of an ECPR programme should be to maximise survival with good neurological outcome while minimising survival with severe neurological disability. Beyond the potential influence of post-ECPR management strategies, this balance underscores the importance of refining access criteria by integrating clinical evidence with ethical judgment.

The design of our study and the characteristics of the condition under investigation do not allow us to provide any information regarding the efficacy of ECPR compared with conventional CPR. Although this represents a research objective of primary importance, it must be acknowledged that, within the context of a clinical protocol aiming to treat all eligible patients, there are obviously no control patients available for comparison. The outcome for the vast majority of patients with refractory cardiac arrest who do not undergo ECPR is, in fact, death. Therefore, this type of comparison is only possible in the context of a randomised trial.[9–11]

Predictor of good neurological outcome

Lacking universal eligibility criteria for ECPR,[23] identifying reliable outcome predictors is critical to support clinical selection of appropriate candidates and to avoid futility and maximise recovery potential. Existing recommendations are largely based on low-quality evidence and typically consider factors such as age, witnessed cardiac arrest with early CPR, initial rhythm, cause of arrest, and time to ECPR initiation.[3] Many of these variables were confirmed as independent predictors of neurological outcome in our study, supporting their continued use in clinical decision-making. Compared with prior studies and guideline-based frameworks, our findings extend this evidence by demonstrating the prognostic relevance of key clinical variables such as age, presenting rhythm, and low-flow duration in a real-world, heterogeneous population treated outside strictly controlled trial settings.

Phenotype-based characterization

Latent class analysis has been widely applied in other areas of critical care research[24] to characterise clinical heterogeneity but remains relatively underexplored in cardiac arrest and ECPR. In our cohort, exploratory latent class analysis identified three clinically distinct phenotypes at the time of ECPR initiation: a predominantly out-of-hospital group with shockable rhythms and younger age but markedly elevated lactate levels (Class 1); an intermediate phenotype, mainly comprising IHCA patients, characterised by lower lactate concentrations and a higher incidence of transient ROSC (Class 2); and a severely compromised phenotype with non-shockable rhythms and high lactate levels (Class 3). Neurological outcomes followed a clear gradient across classes, with the intermediate phenotype showing the highest rate of favourable recovery.

Although descriptive in nature, these findings support the hypothesis that prognostic factors in ECPR do not act in isolation but cluster into recurrent combinations reflecting real-world patient profiles. Accordingly, approaches based solely on individual predictors may overlook how such variables coexist, or fail to coexist, in clinical practice. In this context, phenotype-based characterisation may offer a complementary framework to traditional single-variable selection strategies by capturing multidimensional patterns of risk and recovery potential.

Importantly, this analysis was exploratory and hypothesis-generating, and the identified phenotypes should not be interpreted as prescriptive or directly applicable to clinical decision-making. Future multicentre studies are needed to determine whether integrating phenotype-based approaches into ECPR activation algorithms can refine candidate selection and improve overall programme performance.

Study limitations

This study has several limitations. Its retrospective, single-centre design limits causal inference and generalizability to centres with different ECPR organisation, patient selection criteria, and post-resuscitation management strategies. Because the study spans a long period, ECPR protocols, team experience, and supportive care evolved, and temporal changes may have influenced outcomes and introduced heterogeneity not fully accounted for. Institutional protocols were not strictly mandatory, so some patients were treated outside predefined criteria, introducing selection bias but allowing evaluation in a broader, more heterogeneous population. Despite the relatively large cohort, few patients achieved good neurological outcome, limiting multivariable modelling complexity and granular subgroup analyses. Neurological outcome was assessed using the Cerebral Performance Category, which may not capture subtle cognitive or functional impairments. Finally, latent class analysis was exploratory and descriptive, and phenotypes should be considered hypothesis-generating and not for direct clinical application.

Conclusion

In this large single-centre cohort study, ECPR for refractory cardiac arrest was associated with good long-term neurological recovery in a small proportion of patients. Younger age, shockable presenting rhythm, and shorter low-flow duration were independently associated with favourable neurological outcome. While progressively restrictive

selection criteria enriched the proportion of favourable survivors, they also highlighted the trade-off between outcome optimisation and exclusion of patients who might otherwise recover, underscoring the importance of balancing prognostic enrichment with inclusivity. Exploratory phenotype-based analyses further suggest that multidimensional patient characterisation may complement traditional selection criteria. Future multicentre studies are needed to validate these observations and to further refine evidence-based, ethically sound frameworks for ECPR candidate selection.

CRediT authorship contribution statement

Matteo Pozzi: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Matteo Sola:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis. **Elena Maggioni:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Data curation. **Barbara Cortinovis:** Writing – review & editing, Investigation, Data curation. **Gianluigi Redaelli:** Writing – review & editing, Investigation. **Margherita Scanziani:** Writing – review & editing, Methodology, Investigation, Data curation. **Alice Annoni:** Writing – review & editing, Project administration, Investigation. **Elisa Del Frate:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation. **Cristina Costa:** Writing – review & editing, Investigation, Data curation. **Giovanni Marchetto:** Writing – review & editing, Methodology, Investigation, Conceptualization. **Fabio Sangalli:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Leonello Avalli:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Marco Giani:** Writing – review & editing, Supervision, Investigation, Formal analysis, Data curation, Conceptualization. **Giuseppe Foti:** Writing – review & editing, Supervision, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. POOLSE Study Group

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Appendix B. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.resuscitation.2026.111095.

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