Critical Care and Resuscitation 26 (2024) 279–285

Contents lists available at ScienceDirect

Critical Care and Resuscitation

journal homepage: www.elsevier.com/locate/ccrj

Original Article

Long-term outcomes of patients who received extracorporeal cardiopulmonary resuscitation (ECPR) following in-hospital cardiac arrest: Analysis of EXCEL registry data

G. Pound, BSc(Hons) Physio [a], D. Jones, BSc(Hons) MBBS FRACP FCICM MD PhD [a, b, c], G.M. Eastwood, RN BN BN(Hons) GDipNurs(CriCare) PhD [a, b], E. Paul, BSc, MSc, PhD [a], A. Serpa Neto, MD MSc PhD FCICM [a, b, c, d], C.L. Hodgson, PhD FACP BAppSc(PT) MPhil PGDip(Cardio) [a, c, e, *], for the EXCEL Study Investigators on behalf of the International ECMO Network and the Australian and New Zealand Intensive Care Society Clinical Trials Group[1]

[a] *Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia;* [b] *Intensive Care Department, The Austin Hospital, Melbourne, Australia;* [c] *Department of Critical Care, Melbourne Medical School, University of Melbourne, Austin Hospital, Melbourne, Australia;* [d] *Department of Critical Care Medicine, Hospital Israelita Albert Einstein, São Paulo, Brazil;* [e] *Intensive Care Unit, Alfred Hospital, Melbourne, Australia*

ARTICLE INFORMATION

Article history:
Received 31 July 2024
Received in revised form
21 August 2024
Accepted 21 August 2024

Keywords:
Emergency medicine
Extracorporeal life support
Resuscitation
Intensive care

ABSTRACT

Objective: To describe the six-month functional outcomes of patients who received extracorporeal cardiopulmonary resuscitation (ECPR) following in-hospital cardiac arrest (IHCA) in Australia.
Design: Secondary analysis of EXCEL registry data.
Setting: EXCEL is a high-quality, prospective, binational registry including adult patients who receive extracorporeal membrane oxygenation (ECMO) in Australia and New Zealand.
Participants: Patients reported to the EXCEL registry who received ECPR following IHCA and had the six-month outcome data available were included.
Main outcome measures: The primary outcome was functional outcome at six months measured using the modified Rankin scale (mRS). The secondary outcomes included mortality, disability, health status, and complications.
Results: Between 15th February 2019 and 31st August 2022, 113/1251 (9.0%) patients in the registry received ECPR following IHCA (mean age 50.7 ± 13.7 years; 79/113 (69.9%) male; 74/113 (65.5%) non-shockable rhythm). At 6 months, 37/113 (32.7%) patients were alive, most (27/34 [79.4%]) with a good functional outcome (mRS 0–3). Patients had increased disability [WHODAS % Score 25.58 ± 23.39% vs 6.45 ± 12.32%; mean difference (MD) [95% (confidence interval) CI] −19.13 (−28.49 to −9.77); $p < 0.001$] and worse health status [EuroQol five-dimension, five-level (EQ-5D-5L) index value 0.73 ± 0.23 vs. 0.89 ± 0.14; MD (95% CI) 0.17 (0.07 to 0.26); $p = 0.003$] at six months compared with the baseline. The patients reported a median of 4.5 (2–6) complications at six-month follow-up.
Conclusion: One in three patients who received ECPR following IHCA were alive at six months and most had a good functional outcome. However, survivors reported higher levels of disability and a worse health status at six months compared with the baseline and ongoing complications were common.

1. Introduction

In-hospital cardiac arrest (IHCA) is a sudden, life-threatening event that affects approximately 3000 Australians annually.[1] Although survival rates appear to be improving,[2,3] the prognosis

* Corresponding author at: ANZICS-RC, School of Public Health and Preventive Medicine, Monash University, 553 St Kilda Road, Melbourne, VIC 3004, Australia.
E-mail addresses: gemma.pound@monash.edu (G. Pound), carol.hodgson@monash.edu (C.L. Hodgson).
[1] EXCEL Study Investigators are listed in the online supplement (Appendix A and B).

https://doi.org/10.1016/j.ccrj.2024.08.008

for patients who experience an IHCA remains poor.[4–6] The most common cause of death is failure of return of spontaneous circulation (ROSC), with sustained ROSC occurring in only 40–50% of patients.[7,8] Of those that achieve ROSC, approximately half survive to hospital discharge, with death most frequently attributed to neurological injury, multiorgan failure, and persistent cardiogenic shock.[9] For those that survive, most appear to have a good neurological outcome. However, recovery is variable and some patients are left with significant, long-term disability.[10] Strategies to improve the frequency of ROSC and to augment cardiac function following ROSC are needed.

In recent years, extracorporeal cardiopulmonary resuscitation (ECPR) has emerged as a promising intervention to improve the outcomes of patients who experience IHCA.[11] ECPR involves the use of extracorporeal life support during cardiac arrest when conventional cardiopulmonary resuscitation (CPR) efforts are unsuccessful. ECPR aims to stabilise the patient by supporting circulation and oxygenation, providing time to identify and reverse the cause of the cardiac arrest.[12] However, ECPR is a complex, invasive, resource intensive, and costly intervention that requires a team of highly trained healthcare professionals posing significant challenges outside of specialised, high-volume centres.[13,14]

The use of longer-term functional assessments and health-related quality-of-life (HRQoL) tools are recommended as core outcomes for cardiac arrest and ECMO trials.[15,16] Despite such recommendations, there are relatively fewer studies that report outcomes beyond hospital discharge,[17–19] and the long-term functional outcome of survivors of ECPR following IHCA is not well understood. The primary aim of the study was to describe the six-month functional outcomes of patients who received ECPR following IHCA in Australia.

2. Methods

2.1. Study design and setting

This was a secondary analysis of prospectively collected EXCEL registry data (NCT03793257) between 15th February, 2019, and 31st August, 2022. EXCEL is a high-quality, prospective, binational registry including adult patients (≥18 years) admitted to intensive care who receive extracorporeal membrane oxygenation (ECMO) for any indication in Australia and New Zealand.[20] The study was overseen by a writing and management committee, along with dedicated site investigators (Appendix A and B). Human Research and Ethics Committee approval for the EXCEL registry was obtained at Monash University (MUHREC 18376), the lead site (Alfred Health – 43134; Local Reference: Project 534/18), and all participating hospital sites; including a waiver of consent for the collection of hospital data and opt-out consent for six-month follow-up interviews. Approval for the present study was granted through an amendment to the original ethics application by the Human Research and Ethics Committee at Monash University (MUHREC 18376).

2.2. Study population

Patients reported to the EXCEL registry who were ≥18 years old, received ECPR following IHCA, were admitted to ICU and had six-month outcome data available were included in this study. Patients who received ECMO for indications other than IHCA (e.g., respiratory failure, out-of-hospital cardiac arrest, cardiac arrythmias, heart failure, postoperative) and those supported with ventricular assist devices were excluded. The criteria for commencing ECPR in Australia are outlined in the appendix (Appendix C).

2.3. Data collection and management

Details regarding the collection, monitoring, and management of the EXCEL registry data have been published elsewhere.[20] For this study, data for patients who met inclusion criteria were extracted from the registry by EXCEL management personnel and transferred to the study coordinator via a secure file transfer. Extracted data included patient demographics, cardiac arrest characteristics, ECMO, intensive care and hospital outcome data, and baseline and six-month functional outcomes. Information regarding baseline function was obtained retrospectively during the six-month follow-up interview.

2.4. Outcome measures

The primary outcome for this study was functional outcome at six months, assessed using the modified Rankin scale (mRS). The mRS is a clinician-reported measure of global disability with a score ranging from 0 (no symptoms or clinically significant disability) to 6 (death). Scores were dichotomised into good functional outcome (mRS score 0–3) and poor functional outcome (mRS score 4–6) (eTable 1).[21] The mRS has been identified as part of the core outcome set for cardiac arrest,[15] and has recently been added to the core outcome set for ECMO.[16]

The secondary outcomes included global health and disability, severity of disability, new disability, level of financial distress and work status measured using the WHO Disability Assessment Schedule 2.0, 12-level questionnaire (WHODAS); health status and new health status problems measured using the EuroQol five-dimension, five-level questionnaire (EQ-5D-5L); independence with activities of daily living measured using the Barthel Index and Lawton Instrumental Activities of Daily Living scale, all at six months (eTable 1). Clinical outcomes included duration of ECMO and mechanical ventilation, ICU and hospital length of stay, survival to hospital discharge and to six months, and reported ECMO complications at six months.

2.5. Statistical analysis

Continuous data were reported as mean ± standard deviation (SD) or median and interquartile range (IQR) depending on the underlying distribution, which was assessed using the Shapiro–Wilk test of normality. Categorical data were expressed as counts and percentages. Comparisons between total cohort and patients with six-month follow-up were performed using Student's *t*-test or Mann–Whitney 'U' test as appropriate for continuous variables and chi-square or Fisher's exact test for categorical data. Within group comparisons between baseline and six-month outcomes were made using paired sample *t*-test and Wilcoxon signed rank test for continuous variables and McNemar's test for categorical data. Changes in outcomes were assessed and reported with 95% confidence intervals (95% CI). All calculated *p* values were two-tailed and $p < 0.05$ was considered statistically significant. There was no imputation for missing data. Analyses was conducted using SPSS version 25 (IBM SPSS Inc, Armonk, NY) or SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Demographics, cardiac arrest characteristics, and hospital outcomes

Between 15th February, 2019, and 31st August, 2022, 113 (9.0%) of 1251 patients enrolled in the EXCEL registry received ECPR following an IHCA (Fig. 1) across 22 Australian centres [median 4

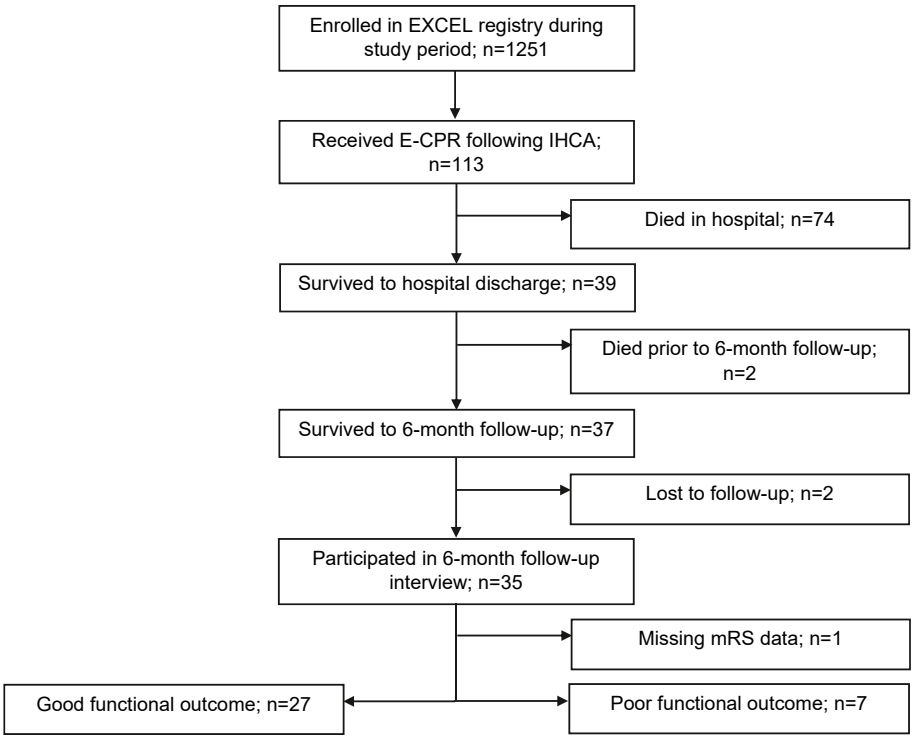

Fig. 1. Flow of patients through the study.

patients per centre; range 1–18 (eTable 2)]. No patients received ECPR following IHCA at the single New Zealand centre reporting to the registry during the study period. The mean age of patients was 50.7 ± 13.7 years, 79/113 (69.9%) were male and the majority of patients had a non-shockable arrest rhythm (74/113 [65.5%]). Approximately half [62/113 (54.9%)] of IHCA occurred on the first day of hospital admission, almost all were witnessed [110/113 (97.3%)] with immediate commencement of CPR [median no flow time 0 (0–0) minutes, range 0–15 min]. The median duration of CPR prior to commencement of ECPR (low flow time) was 40.5 (29.0–57.3) minutes (range 5–128 min). Demographics and cardiac arrest characteristics are shown in Table 1 with the specific diagnosis associated with IHCA reported in eTable 3. Of note, the three leading causes of IHCA were acute myocardial infarction (41.6%), pulmonary embolism (13.3%), and acute decompensated heart failure (8.8%).

The median ECPR duration was 3 (1.0–6.2) days. Patients were in ICU for a median of 8.7 (2.1–17.7) days, and in hospital for a median of 11.5 (3.5–34.9) days, with 39/113 (34.5%) of patients surviving to hospital discharge. ECMO, intensive care treatment, and hospital outcomes are shown in Table 2.

3.2. Six-month outcomes

Thirty-seven of the 113 patients (32.7%) were alive at six months, of whom 35 (94.6%) completed the follow-up interviews.

Table 1
Demographics and cardiac arrest characteristics of patients receiving ECPR following IHCA and those that completed the six-month follow-up interview.

	Total cohort; n = 113	Six-month follow-up; n = 35	*p*-value
Demographics			
Age (years), mean ± SD	50.7 ± 13.7	49.8 ± 13.5	*ns*
Gender (male), n/N (%)	79/113 (69.9)	27/35 (77.1)	*ns*
Charlson comorbidity index (CCI) score at hospital admission, median (IQR)	2 (1–3)	2 (1–3)	*ns*
Clinical frailty scale (CFS) score at hospital admission, median (IQR)	3 (2–4)	3 (2–3)	*ns*
Cardiac arrest characteristics			
Initial arrest rhythm; n/N (%)			
Asystole	9/113 (8.0)	0/35 (0)	*ns*
PEA	65/113 (57.5)	18/35 (51.4)	
VT/VF	39/113 (34.5)	17/35 (48.6)	
Non-shockable arrest rhythm; n/N (%)	74/113 (65.5)	18/35 (51.4)	*ns*
Witnessed cardiac arrest, n/N (%)	110/113 (97.3)	34/35 (97.1)	*ns*
No flow time (minutes), median (IQR)	0 (0–0)	0 (0–0)	*ns*
Low flow time (minutes), median (IQR)	40.5 (29.0–57.3)	37.0 (29.0–55.5)	*ns*
ROSC prior to ECMO cannulation; n/N (%)	21/111 (18.9)	7/35 (20.0)	*ns*

Data are n/N (%), median (IQR), or mean ± SD. All available data were reported; some categories have denominators that are not the full sample size owing to missing data (eTable 4).
Abbreviations: ECPR: extracorporeal cardiopulmonary resuscitation; IHCA: in-hospital cardiac arrest; PEA: pulseless electrical activity; VT: ventricular tachycardia; VF: ventricular fibrillation; ROSC: return of spontaneous circulation; ECMO: extracorporeal membrane oxygenation; *ns*: nonsignificant.

Table 2
ECMO, intensive care, and hospital outcomes of patients receiving ECPR following IHCA and those that completed six-month follow-up interview.

ECMO, intensive care, and hospital outcomes	Total cohort; n = 113	Six-month follow-up; n = 35	*p*-value
Chest compressions performed during ECMO cannulation; n/N (%)	101/112 (90.2)	33/35 (94.3)	*ns*
ECMO commencement location; n/N (%)			*ns*
Bedside	75/111 (67.6)	23/35 (65.7)	
Operating theatre	7/111 (6.3)	2/35 (5.7)	
Catheter laboratory	29/111 (26.1)	10/35 (28.6)	
Days between hospital admission and ECMO commencement (days); median (IQR)	0.6 (0.1–3.3)	0.3 (0.1–3.8)	*ns*
ECMO commencement outside usual working hours (0800–1800); n/N (%)	42/113 (37.2)	12/35 (34.3)	*ns*
APACHE IV score (within 6 h of ECMO commencement); mean ± SD	108.6 ± 36.2	98.1 ± 32.1	*ns*
ECMO duration (days), median (IQR)	3.0 (1.0–6.2)	5.3 (2.7–7.7)	0.02
Mechanical ventilation duration (days); median (IQR)	6.9 (1.2–12.9)	12.8 (7.9–29.6)	<0.001
ICU length of stay (days), median (IQR)	8.7 (2.1–17.7)	17.5 (13.9–32.0)	<0.001
Hospital length of stay (days), median (IQR)	11.5 (3.5–34.9)	37.9 (29.8–55.6)	<0.001
Survival to hospital discharge; n/N (%)	39/113 (34.5)	35/35 (100)	–

Data are n/N (%), median (IQR), or mean ± SD. All available data were reported; some categories have denominators that are not the full sample size owing to missing data (eTable 4).
Abbreviations: ECMO: extracorporeal membrane oxygenation; ECPR: extracorporeal cardiopulmonary resuscitation; IHCA: in-hospital cardiac arrest; APACHE: acute physiology and chronic health evaluation; ICU: intensive care unit; *ns*: nonsignificant.

The remaining two patients could not be contacted and were deemed nonresponders. Patients who completed six-month follow-up interviews had a longer duration of ECMO, mechanical ventilation, intensive care unit, and hospital admission compared with the total cohort (Table 2). This is not unexpected, given the follow-up group consists of survivors, while the total cohort includes patients who died and thus had a shorter duration of support. The six-month functional outcomes are summarised in Table 3. The number of patients with available data varied across individual outcome measures as some patients did not wish to answer all of the interview questions. The amount of missing data is reported in the appendix (eTables 4 and 5).

Data for the primary outcome of modified Rankin scale score at six months were available in 108/113 (95.6%) of the total cohort and 34/35 (97.1%) survivors who completed follow-up. We found that 27/108 (25.0%) of patients had a good functional outcome and 81/108 (75.0%) had a poor functional outcome at 6-months, the majority of whom had died [74/81 (91.4%)]. Of the survivors, 27/34 (79.4%) had a good functional outcome and 7/34 (20.6%) had a poor functional outcome (moderate to severe disability) at six months (Fig. 1).

Patients reported a median of 4.5 (2–6) complications at six-month follow-up. The most frequently reported complications were reduced lower limb sensation [23/35 (65.7%)], lower limb weakness [19/35 (54.3%)], memory problems [18/35 (51.4%)], anxiety [14/35 (40.0%)], and shortness of breath [12/35 (34.3%)] (eTable 6).

3.3. Comparison between baseline and six month outcomes

Baseline disability and health status were reported for 32/35 (91.4%) patients who completed the six month follow-up. The mean WHODAS percentage score was significantly higher at six months than at baseline (25.58 ± 23.39% vs 6.45 ± 12.32%; mean difference [95% CI] −19.13 [−28.49 to −9.77]; $p < 0.001$), indicating increased disability. An increase in disability was reported across most domains of the WHODAS (eFig. 1). Overall, the severity of disability increased from baseline to six months with 18/32 (56.3%) of patients reporting new disability (increase WHODAS percentage score >10%). Patients rated their level of financial distress higher at six months than at baseline (3.5 out of 10 [1, 6] vs 1.5 out of 10 [0, 5]; median difference [95% CI] 0 [0 to 2]; $p = 0.013$). There were 13/32 (40.6%) who were newly unemployed at six months and the proportion of patients unemployed due to health reasons was 4/32 (12.5%) at baseline and 19/34 (55.9%) (Percentage difference 43.8% [95% CI 23.4%–64.1%]; $p < 0.001$) at 6 months (eTable 7).

Table 3
Functional outcomes at six months of patients who completed the follow-up interview.

Functional outcomes	Total, n = 35
Modified Rankin Scale Score[a]; median (IQR)	1 (1–3)
Good functional outcome[b]; n/N (%)	27/34 (79.4)
Lawton IADL Score[a]; median (IQR)	8 (5–8)
Barthel Index Score[a]; median (IQR)	100 (90–100)
WHODAS % Score[a]; mean ± SD	25.58 ± 13.39
EQ-5D-5L Index Value[a]; mean ± SD	0.73 ± 0.23
EQ VAS Score[a]; mean ± SD	64.72 ± 24.39

Data are n/N (%), median (IQR), or mean ± SD. All available data were reported; some categories have denominators that are not the full sample size owing to missing data (eTable 5).
Abbreviations. IADL: instrumental activities of daily living; WHODAS: World Health Organization Disability Assessment Schedule; VAS: visual analogue scale.
[a] Functional outcome measures and scoring are described in appendix eTable 1.
[b] Good functional outcome is defined as a modified Rankin scale (mRs) score of 0–3.

Health status was worse at six months than at baseline (mean EQ-5D-5L index value 0.73 ± 0.23 vs. 0.89 ± 0.14; mean difference [95% CI] 0.17 [0.07 to 0.26]; $p = 0.003$ and EQ visual analogue scale score 64.72 ± 24.39 vs. 78.41 ± 22.55; mean difference [95% CI] 13.73 [2.61 to 24.85]; $p = 0.03$). Patients reported more problems with mobility, self-care, and usual activities at six months than at baseline (eTable 8 and eFig. 2).

4. Discussion

4.1. Key findings

In this secondary analysis of EXCEL registry data, we found approximately one in eleven patients recorded in the registry received ECPR following an IHCA. Almost all IHCAs that received

ECPR occurred in patients with minimal frailty and fewer comorbidities, witnessed with immediate CPR, two-thirds were non-shockable, and half occurred on the first day of hospital admission. Approximately one-third of patients who received ECPR following IHCA survived to hospital discharge. At six months, most survivors had a good functional outcome; however, patients reported greater disability, poorer health status, new unemployment, and financial stress compared with baseline, and ongoing complications were common.

4.2. Comparisons with previous studies

The survival rates and functional outcomes observed in our cohort are consistent with those reported in existing registry data.[11,22,23] However, there are significant variability in reported outcomes, which may be attributed to differing selection criteria across studies.[24] Currently, there is no consensus regarding appropriate selection criteria, and it is unclear which patients may benefit from ECPR.[13]

A significant proportion of our patients exhibited non-shockable rhythms, predominantly pulseless electrical activity, which is noteworthy given that current guidelines typically recommend ECPR primarily for shockable rhythms.[13,14] Despite these guidelines, our registry data indicate that a clinical inclination to initiate ECPR in cases of non-shockable rhythms, highlighting a discrepancy between guideline recommendations and clinical practice. This divergence is supported by Pabst et al. (2018), who suggest that the current data are insufficient to categorically exclude patients with non-shockable rhythms from ECPR eligibility.[25]

Our cohort were relatively young of age and functionally independent but subjected to prolonged CPR prior to ECPR initiation, showing a one-third survival rate to hospital discharge. The outcome is particularly significant given the typically poor prognosis associated with prolonged CPR.[10,26–29] Recent studies support this observation, suggesting that ECPR may confer a survival benefit over conventional CPR in prolonged resuscitation efforts.[30–33] However, the absence of comprehensive comparative studies, particularly large-scale randomised controlled trials, leaves a substantial gap in definitive evidence supporting ECPR over conventional methods.[32]

Although the mRS classified most survivors as having a 'good functional outcome', our study revealed that survivors experienced worsened disability and health status compared with their baseline. This finding raises questions about the long-term benefits and burdens of ECPR, prompting a comparison with outcomes of IHCA patients not treated with ECPR. Our previous work,[10] among other studies, provides valuable insights into the recovery trajectories of IHCA patients undergoing conventional CPR, indicating that these patients often face significant long-term impairments aligning with the challenges observed in our cohort.[34–36]

While the mRS provides a standardised, valid, and reliable assessment of functional outcome, it is a measure of global disability that may not adequately represent the health challenges most important to patients.[37] To gain a more comprehensive understanding of patients' long-term recovery and quality of life, it is crucial to expand our evaluation methods. Incorporating patient-reported outcomes, detailed functional assessments, and qualitative information from patient and caregiver interviews can provide a more holistic view of patient experience and the complexities of cardiac arrest and ECPR survivorship.[38]

It remains unclear how much of the observed morbidity is directly attributable to the ECPR intervention versus the underlying IHCA or the complexities of the ICU admission. The high prevalence of long-term complications presents a similar dilemma—disentangling the effects attributable to ECPR from those stemming from IHCA or ICU treatments is challenging. This complexity is echoed in the broader literature, where direct comparisons of long-term functional outcomes and health-related quality of life between IHCA patients treated with and without ECPR are scarce.[32]

4.3. Implications for clinical practice

An important finding of our study is how infrequently ECPR is utilised in Australia following IHCA. Amongst 22 hospitals over 3.5 years, only 113 patients received ECPR following an IHCA (1.5 patients/hospital/year). In a prospective study of IHCA amongst 7 hospitals in Australia, we found that 23 patients from 7 hospitals (3.3 patients/hospital/year) may have been eligible for ECPR, but did not receive it.[29] This highlights the challenges of deploying ECPR for IHCA, and the requirements for training for this infrequent event.[39]

Our study contributes to the growing body of evidence that ECPR may be a viable intervention for selected patients following IHCA, especially in settings where there are sufficient resources, such as high-volume ECMO centres. We found that ECPR is being considered for a wider range of patients than those traditionally identified by existing guidelines, including those with non-shockable rhythms. This may reflect evolving clinical practices and acknowledges the complexities involved in the decision-making around and management of IHCA.

Our data show that approximately one-third of ECMO cannulations occurred outside usual working hours (0800–1800). This finding highlights a significant logistical challenge, particularly in lower-volume centres, where after-hours cannulation may not be feasible. The reliance on in-hours cannulation could limit the availability of ECPR in these settings, underscoring the need for strategic planning and resource allocation to ensure access to ECPR when and where it is most needed.

The significant variability in long-term functional outcomes and the high incidence of complications observed in our study underscores the need for a comprehensive, multidisciplinary approach to post-discharge care. Developing integrated care pathways that include physical, cognitive, and psychological rehabilitation could be crucial in enhancing the quality of life for survivors, reducing long-term disability, and ensuring that survivors receive the support necessary to optimise their outcomes.

4.4. Areas for further research

While our study provides valuable insights into the six-month functional outcomes of IHCA patients treated with ECPR, additional research is needed to further characterise the long-term outcomes of these patients. Future studies with larger sample sizes and longer follow-up periods are warranted to validate our findings. Conducting studies that compare the outcomes of ECPR and conventional CPR approaches, alongside exploring the impact of different post-resuscitation care strategies, such as targeted temperature management and neuroprotective therapies, would be instrumental in guiding clinical decision-making and optimising patient care pathways.

There is an urgent need to identify patient characteristics that indicate when ECPR may be more beneficial than continued conventional CPR, particularly for those who do not respond quickly to advanced life support. This could be explored through registries that capture natural variations in patient outcomes following both CPR and ECPR.

Establishing standardised selection criteria that reflect real-world clinical decision-making will help clarify the current ambiguities surrounding ECPR eligibility and enhance its application in

clinical practice, ensuring that the potential benefits of ECPR are accessible to those most likely to benefit. Additionally, qualitative research exploring both patient and caregiver perspectives on ECPR and its long-term consequences could provide deeper understanding of the experiences of IHCA survivors, thus informing more comprehensive approaches to care delivery.

4.5. Study strengths and limitations

A key strength of our study was the use of prospectively collected data from a high-quality, binational registry, which captures over 90% of all ECMO incidences in Australia,[20] enhancing the external validity and generalisability of our findings. Additionally, we report patient-reported outcome measures used at six-month follow-up that are validated tools included in the core outcome set for cardiac arrest and ECMO, allowing for meaningful comparisons with other studies. Despite these strengths, our study has several limitations. The secondary use of data and the potential for selection bias inherent in follow-up studies must be acknowledged. The absence of a comparator group, due to the EXCEL registry not capturing data on all IHCAs where resuscitation was attempted, contributes to selection bias and limits the contextualisation of the observed survival rate. Our relatively small sample size, particularly at the six-month follow-up, limits the statistical power of our analysis and our ability to detect significant differences in comparisons between some baseline and follow-up outcomes. This small sample size, both overall and within individual hospitals, also restricts our ability to explore potential associations between ECMO patient volume, patient characteristics (such as age, comorbidity, or initial rhythm), and survival outcomes or functional status. Some patients were lost to follow-up, and not all patients completed the entire follow-up interview, resulting in missing data for some outcome measures. Baseline disability and health status were assessed retrospectively at the six-month follow-up, introducing the possibility of recall bias. Finally, as with any observational study, our results cannot establish a causal relationship between the use of ECPR following an IHCA and six-month functional outcomes, and all analyses should be considered exploratory.

5. Conclusion

In conclusion, from our secondary analysis of EXCEL registry data, we found one in three patients who received ECPR following IHCA were alive at six months and most had a good functional outcome. However, survivors reported higher levels of disability and a worse health status at six months compared with the baseline and ongoing complications were common. This information provides the necessary epidemiologic background and patient-centred outcomes to support the conduct of more in-depth studies of ECPR use and survivorship following IHCA.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Carol Hodgson reports a relationship with National Health and Medical Research Council that includes: funding grants. Carol Hodgson reports a relationship with National Heart Foundation of Australia that includes: funding grants. Corresponding author leads the binational EXCEL registry, is on the executive committee of the International ECMO Network (ECMONet) and is an associate editor of Critical Care Resuscitation – Prof. Carol Hodgson. Co-author is on the editorial board of Critical Care Resuscitation – Prof. Ary Serpa Neto If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

EXCEL Study Management Committee (Appendix A).
ANZICS Clinical Trials Group (CTG) (Appendix B).
International ECMO Network.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ccrj.2024.08.008.

Credit authorship contribution statement

G. Pound: Concept and study design, Visualization, Data acquisition, Statistical analysis and data interpretation, Writing - original draft preparation, Project administration. *D. Jones:* Concept and study design, Visualization, Validation, Writing - review & editing, Supervision, Project administration. *G. M. Eastwood:* Concept and study design, Visualization, Validation, Writing - review & editing, Supervision, Project administration. *E. Paul:* Statistical analysis and data interpretation, Writing - review & editing. *A. Serpa Neto:* Statistical analysis and data interpretation, Writing - review & editing. *C.L. Hodgson:* Concept and study design, Visualization, Validation, Writing - review & editing, Supervision, Project administration. All authors read and approved the final manuscript.

References

[1] Jones DA, Pound G, Eastwood GE, Hodgson CL. Estimate of annual in-hospital cardiac arrests in Australia. Crit Care Resusc 2021;23(4):427.
[2] Key NCAA statistics. Available at: https://www.icnarc.org/audit/ncaa/reporting/ [Accessed 10 April 2024].
[3] Jerkeman M, Sultanian P, Lundgren P, Dworeck C, Helleryd E, Nielsen N, et al. Trends in survival after cardiac arrest: a Swedish nationwide study over 30 years. Eur Heart J 2022;43(46):4817–29.
[4] Australia and New Zealand Cardiac Arrest Outcome and Determinants of ECMO (ANZ-CODE) Investigators. The epidemiology of in-hospital cardiac arrests in Australia: a prospective multicentre observational study. Crit Care Resusc 2019;21(3):180–7.
[5] Holmberg MJ, Ross CE, Fitzmaurice GM, Chan PS, Duval-Arnould J, Grossestreuer AV, et al. Annual incidence of adult and pediatric in-hospital cardiac arrest in the United States. Circ Cardiovasc Qual Outcomes 2019;12(7):e005580.
[6] Andersen LW, Holmberg MJ, Lofgren B, Kirkegaard H, Granfeldt A. Adult in-hospital cardiac arrest in Denmark. Resuscitation 2019;140:31–6.
[7] Hessulf F, Herlitz J, Lundgren P, Aune S, Myredal A, Engdahl J, et al. Temporal variation in survival following in-hospital cardiac arrest in Sweden. Int J Cardiol 2023;381:112–9.
[8] Tirkkonen J, Skrifvars MB, Parr M, Tamminen T, Aneman A. In-hospital cardiac arrest in hospitals with mature rapid response systems - a multicentre, retrospective cohort study. Resuscitation 2020;149:109–16.
[9] Witten L, Gardner R, Holmberg MJ, Wiberg S, Moskowitz A, Mehta S, et al. Reasons for death in patients successfully resuscitated from out-of-hospital and in-hospital cardiac arrest. Resuscitation 2019;136:93–9.
[10] Pound GM, Jones D, Eastwood GM, Paul E, Hodgson CL. Long-term functional outcome and quality of life following in-hospital cardiac arrest-a longitudinal cohort study. Crit Care Med 2022;50(1):61–71.
[11] Richardson AS, Schmidt M, Bailey M, Pellegrino VA, Rycus PT, Pilcher DV. ECMO Cardio-Pulmonary Resuscitation (ECPR), trends in survival from an international multicentre cohort study over 12-years. Resuscitation 2017;112:34–40.
[12] Abrams D, MacLaren G, Lorusso R, Price S, Yannopoulos D, Vercaemst L, et al. Extracorporeal cardiopulmonary resuscitation in adults: evidence and implications. Intensive Care Med 2022;48(1):1–15.
[13] Richardson ASC, Tonna JE, Nanjayya V, Nixon P, Abrams DC, Raman L, et al. Extracorporeal cardiopulmonary resuscitation in adults. Interim guideline

consensus statement from the extracorporeal life support organization. ASAIO J 2021;67(3):221–8.
[14] Soar J, Maconochie I, Wyckoff MH, Olasveengen TM, Singletary EM, Greif R, et al. 2019 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations: summary from the basic life support; advanced life support; pediatric life support; neonatal life support; education, implementation, and teams; and first aid task forces. Circulation 2019;140(24):e826–80.
[15] Haywood K, Whitehead L, Nadkarni VM, Achana F, Beesems S, Bottiger BW, et al. COSCA (Core Outcome Set for Cardiac Arrest) in adults: an advisory statement from the International Liaison Committee on Resuscitation. Circulation 2018;137(22):e783–801.
[16] Hodgson CL, Fulcher B, Mariajoseph FP, Burrell AJC, Pellegrino V, Brodie D, et al. A core outcome set for research in patients on extracorporeal membrane oxygenation. Crit Care Med 2021;49(12):e1252–4.
[17] Shin TG, Jo IJ, Sim MS, Song Y, Yang J, Hahn J, et al. Two-year survival and neurological outcome of in-hospital cardiac arrest patients rescued by extracorporeal cardiopulmonary resuscitation. Int J Cardiol 2013;168(4):3424–30.
[18] Blumenstein J, Leick J, Liebetrau C, Kempfert J, Gaede L, Gross S, et al. Extracorporeal life support in cardiovascular patients with observed refractory in-hospital cardiac arrest is associated with favourable short and long-term outcomes: a propensity-matched analysis. Eur Heart J Acute Cardiovasc Care 2016;5(7):13–22.
[19] Spangenberg T, Schewel J, Dreher A, Meincke F, Bahlmann E, Van Der Schalk H, et al. Health related quality of life after extracorporeal cardiopulmonary resuscitation in refractory cardiac arrest. Resuscitation 2018:73–8.
[20] Hodgson CL, Higgins AM, Bailey MJ, Anderson S, Bernard S, Fulcher BJ, et al. Incidence of death or disability at 6 months after extracorporeal membrane oxygenation in Australia: a prospective, multicentre, registry-embedded cohort study. Lancet Respir Med 2022;10(11):1038–48.
[21] Nolan JP, Berg RA, Andersen LW, Bhanji F, Chan PS, Donnino MW, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry Template for In-Hospital Cardiac Arrest: a consensus report from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia). Resuscitation 2019;144:166–77.
[22] Extracorporeal Life Support Organization. ECLS Registry Report: International Summary – October 2023. https://www.elso.org/registry/internationalsummaryandreports/internationalsummary.aspx [Accessed 17 April 2024].
[23] Gravesteijn BY, Schluep M, Disli M, Garkhail P, Dos Reis Miranda D, Stolker R, et al. Neurological outcome after extracorporeal cardiopulmonary resuscitation for in-hospital cardiac arrest: a systematic review and meta-analysis. Crit Care 2020;24(1):505.
[24] Koen J, Nathanaël T, Philippe D. A systematic review of current ECPR protocols. A step towards standardisation. Resusc Plus 2020;3:100018.
[25] Pabst D, Brehm CE. Is pulseless electrical activity a reason to refuse cardiopulmonary resuscitation with ECMO support? Am J Emerg Med 2018;36(4):637–40.
[26] Okubo M, Komukai S, Andersen LW, Berg RA, Kurz MC, Morrison LJ, et al. Duration of cardiopulmonary resuscitation and outcomes for adults with in-hospital cardiac arrest: retrospective cohort study. BMJ 2024;384:e076019.
[27] Goodarzi A, Khatiban M, Abdi A, Oshvandi K. Survival to discharge rate and favorable neurological outcome related to gender, duration of resuscitation and first document of patients in-hospital cardiac arrest: a systematic meta-analysis. Bull Emerg Trauma 2022;10(4):141–56.
[28] Pound G, Jones D, Eastwood GM, Paul E, Hodgson CL. Survival and functional outcome at hospital discharge following in-hospital cardiac arrest (IHCA): a prospective multicentre observational study. Resuscitation 2020;155:48–54.
[29] Pound G, Eastwood GM, Jones D, Hodgson CL. Potential role for extracorporeal membrane oxygenation cardiopulmonary resuscitation (E-CPR) during in-hospital cardiac arrest in Australia: a nested cohort study. Crit Care Resusc 2023;25(2):90–6.
[30] Bian Y, Pan Y, Zheng J, Zheng W, Qin L, Zhou G, et al. Extracorporeal versus conventional cardiopulmonary resuscitation for in-hospital cardiac arrest: a propensity score matching cohort study. Crit Care Med 2024;52(6):e268–78.
[31] Low CJW, Ling RR, Ramanathan K, Chen Y, Rochwerg B, Kitamura T, et al. Extracorporeal cardiopulmonary resuscitation versus conventional CPR in cardiac arrest: an updated meta-analysis and trial sequential analysis. Crit Care 2024;28(1):57.
[32] Miraglia D, Miguel LA, Alonso W. Extracorporeal cardiopulmonary resuscitation for in- and out-of-hospital cardiac arrest: systematic review and meta-analysis of propensity score-matched cohort studies. J Am Coll Emerg Physicians Open 2020;1(4):342–61.
[33] Chen YS, Lin JW, Yu HY, Ko WJ, Jerng JS, Chang WT, et al. Cardiopulmonary resuscitation with assisted extracorporeal life-support versus conventional cardiopulmonary resuscitation in adults with in-hospital cardiac arrest: an observational study and propensity analysis. Lancet 2008;372(9638):554–61.
[34] Larsson I-M, Wallin E, Rubertsson S, Kristofferzon M-L. Health-related quality of life improves during the first six months after cardiac arrest and hypothermia treatment. Resuscitation 2014;85(2):215–20.
[35] Tong JT, Eyngorn I, Mlynash M, Albers GW, Hirsch KG. Functional neurologic outcomes change over the first 6 months after cardiac arrest. Crit Care Med 2016;44(12):e1202–7.
[36] Raina KD, Rittenberger JC, Holm MB, Callaway CW. Functional outcomes: one year after a cardiac arrest. Biomed Res Int 2015;2015:283608.
[37] Rittenberger JC, Raina K, Holm MB, Kim YJ, Callaway CW. Association between cerebral performance category, modified Rankin scale, and discharge disposition after cardiac arrest. Resuscitation 2011;82(8):1036–40.
[38] Sawyer KN, Camp-Rogers TR, Kotini-Shah P, Del Rios M, Gossip MR, Moitra VK, et al. Sudden cardiac arrest survivorship: a scientific statement from the American Heart Association. Circulation 2020:E654–85.
[39] Dennis M, Shekar K, Burrell AJ. Extracorporeal cardiopulmonary resuscitation for refractory cardiac arrest in Australia: a narrative review. Med J Aust 2024;220(1):46–53.