



Extracorporeal Cardiopulmonary Resuscitation for Refractory Cardiac Arrest: Patient Selection Under Extreme Time Pressure

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Introduction

Extracorporeal cardiopulmonary resuscitation (ECPR) substitutes a mechanical circuit for the heart and lungs when conventional resuscitation has failed, buying time for a reversible cause of arrest to be identified and treated. The concept is mechanically straightforward; the clinical question is whether it can be deployed fast enough, and in the right patients, to translate that physiological rescue into a meaningful chance of neurologically intact survival. Three randomized trials published within three years of each other have now tested this question directly, with results that diverge more than the shared underlying technology might suggest.

This review sets those three trials, their pooled meta-analysis, and a separate review of selection-criteria variability side by side, to ask what the accumulated evidence actually supports about who should receive ECPR and how quickly.

Out-of-hospital cardiac arrest remains one of the most lethal emergencies a health system encounters, and conventional resuscitation alone leaves most such patients without a meaningful chance of neurologically intact survival once an initial round of advanced life support has failed. ECPR was conceived precisely for this population: patients for whom the underlying cause of arrest may be reversible, but only if circulation can be restored before irreversible neurological injury accumulates. Whether that promise is realized in practice, rather than only in physiological principle, is the

question this review sets out to answer using the best available randomized evidence.

Material and Methods

This is a narrative review drawing on the three published randomized trials of ECPR for refractory out-of-hospital cardiac arrest, their pooled meta-analysis, and a systematic review of selection-criteria variability, identified through the sources cited above and citation tracking between them, without a pre-registered protocol or systematic search string. All percentages, odds ratios, risk ratios, and p-values reported here are taken directly from the cited sources; none has been invented, estimated, or extrapolated.

Figures and tables in this review restate, rather than reanalyze, the outcomes reported by each source: no individual-patient data were available to the authors, and no new statistical test was performed on any of the pooled or trial-level estimates presented. Where a source reported a result only as a range or as an indexed abstract without full methodological detail, that limitation is noted explicitly alongside the corresponding finding rather than resolved by assumption.

Results

A single-center trial stopped early for a large effect

The ARREST trial randomized 30 patients with refractory ventricular fibrillation or tachycardia arrest at a single US center to early ECMO-facilitated resuscitation or standard advanced cardiac life support [1]. Survival to hospital discharge was 43% (6 of 14) in the early-ECMO group versus 7% (1 of 15) in the standard group, and the trial was stopped early after meeting its prespecified efficacy stopping rule (posterior probability of benefit 0.9861) [1]. Figure 1 sets this comparison out directly. A sixfold difference from 30 patients at one experienced center is a striking result, but also the kind of early-stopped, single-site finding that later, larger trials often narrow.

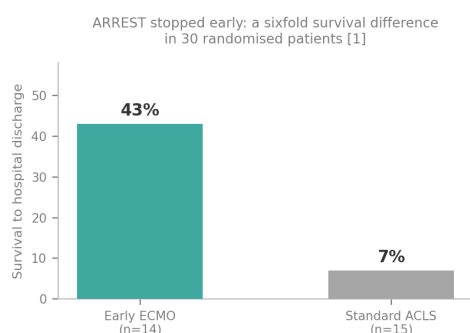


Figure 1: Survival to hospital discharge, early ECMO strategy versus standard ACLS, ARREST trial [1].

A larger multi-center trial narrowly missed its primary endpoint

The Prague OHCA trial randomized 256 analyzed patients (of a planned 285, also stopped early) across multiple Czech centers to a hyperinvasive strategy (intra-arrest transport plus ECPR) or standard resuscitation [2]. The primary outcome, 180-day survival with favourable neurologic outcome, was numerically higher with the invasive strategy (31.5% vs 22.0%) but did not reach statistical significance (OR 1.63, 95% CI 0.93-2.85, $P=0.09$) [2]. A secondary endpoint, 30-day neurological recovery, did reach significance (30.6% vs 18.2%, OR 1.99, 95% CI 1.11-3.57, $P=0.02$) [2]. Figure 2 sets both endpoints out together. This primary-miss/secondary-hit pattern recurs across this literature and should temper how confidently either result is read in isolation.

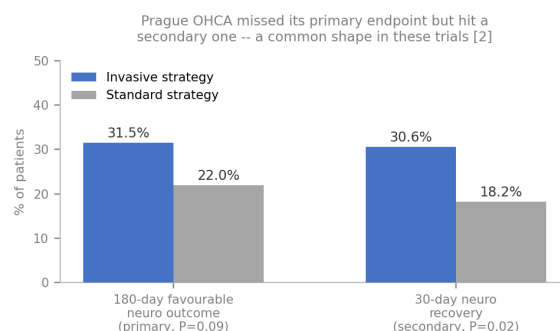


Figure 2: Primary (180-day) and secondary (30-day) neurologic outcomes, invasive versus standard strategy, Prague OHCA trial [2].

The largest and most recent trial found almost no benefit, and more harm

The INCEPTION trial, conducted across multiple Dutch centers, randomized patients to ECPR ($n=70$ analyzed) or conventional CPR ($n=62-64$ depending on the outcome) [3]. The primary outcome, 30-day survival with favourable neurologic outcome, was 20% with ECPR versus 16% with conventional CPR, a difference that did not approach significance (OR 1.4, 95% CI 0.5-3.5, $P=0.52$) [3]. Serious adverse events were markedly more common with ECPR: major bleeding occurred in 16% versus 3%, and lower-limb ischemia in 6% versus 0% [3]. Figure 3 sets both the primary outcome and this safety asymmetry out together. Unlike ARREST and Prague OHCA, INCEPTION found not just an absence of benefit but a measurable procedural cost.

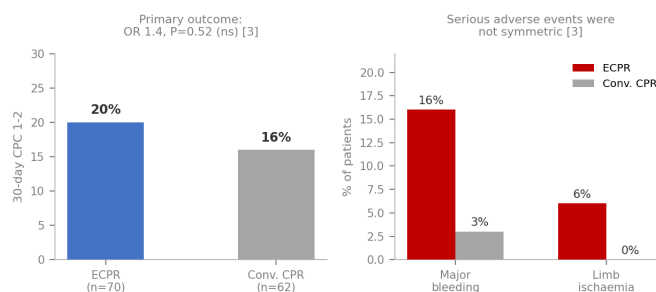


Figure 3: Primary 30-day outcome and serious adverse events, ECPR versus conventional CPR, INCEPTION trial [3].

Pooled across all three trials, the direction is consistent but not significant

A meta-analysis pooling all three trials (418 patients total) found risk ratios favouring ECPR at both the shortest reported follow-up (RR 1.47, 95% CI 0.91-2.40, $P=0.12$) and at 6 months (RR 1.48, 95% CI 0.88-2.49, $P=0.14$), alongside a non-significant reduction in in-hospital mortality (RR 0.89, 95% CI 0.74-1.07, $P=0.23$) [4]. Figure 4 sets both pooled estimates out together. The consistent direction of effect across three independently conducted trials is itself informative, even though no individual estimate, nor the pooled one, crosses conventional statistical significance.

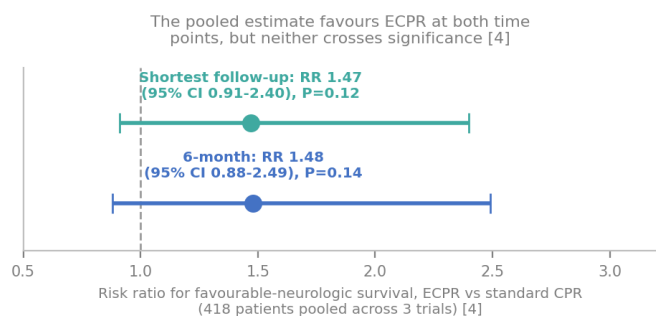


Figure 4: Pooled risk ratio for favourable-neurologic survival, ECPR versus standard care, at shortest follow-up and 6 months, meta-analysis of 3 trials [4].

Time to flow, not any single eligibility criterion, is what the evidence tracks

A systematic review of 67 ECPR studies published between January 2000 and June 2021 found that selection criteria vary substantially by study design: 84% of prospective studies applied an age criterion versus 73% of retrospective studies, with a lower median patient age (52 vs 56 years) and a longer median arrest-to-ECMO-flow time (74 vs 57 minutes) in prospective cohorts [5]. Across all 67 studies, a meta-regression found arrest-to-ECMO-flow time to be an independent predictor of survival ($\beta = -0.023$, $p < 0.001$) [5]. Figure 5 sets this directional finding out. The same review found pooled favourable-neurologic survival differed sharply by arrest setting: 16% for out-of-hospital arrest versus 28% for in-hospital arrest [5]. Figure 6 sets both the criteria-variability pattern and this setting-based difference out together.

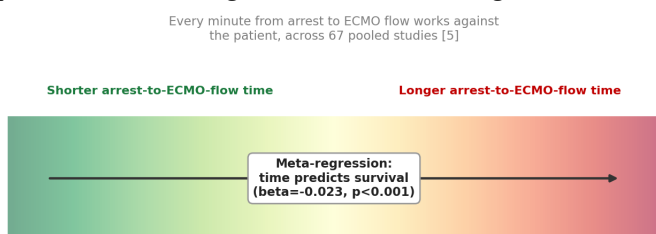


Figure 5: Direction of the meta-regression finding: arrest-to-ECMO-flow time predicts survival across 67 pooled ECPR studies [5].

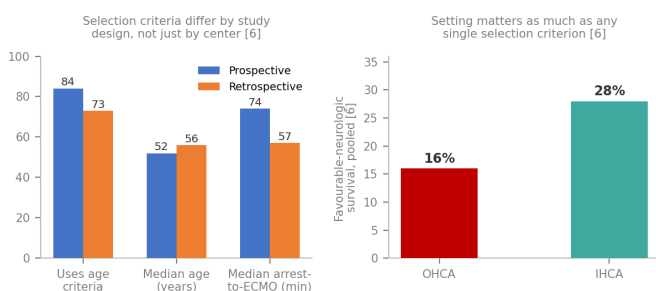


Figure 6: Selection-criteria variability by study design, and pooled favourable-neurologic survival by arrest setting (OHCA versus IHCA) [5].

Discussion

Read individually, these three trials could support almost any position: ARREST argues ECPR transforms outcomes, INCEPTION argues it adds risk without benefit, and Prague OHCA sits ambiguously between the two depending on which endpoint is emphasized. Read together with the meta-analysis, a more coherent picture emerges: a consistent direction of benefit that no individual trial, nor the pooled estimate, has yet demonstrated with statistical confidence. The selection-criteria review offers a plausible reason why the trials disagree as much as they do -- arrest-to-ECMO-flow time is an independent predictor of outcome, and the three trials differed in the intensity of the prehospital and in-hospital systems built around achieving that flow quickly. INCEPTION's excess bleeding and limb-ischemia complications are a reminder that ECPR is not a risk-free intervention even when it is not helping.

The practical implication is that ECPR's value is likely concentrated in systems that can reliably achieve short arrest-to-flow times in carefully selected patients, rather than being a uniform benefit available wherever the equipment exists. Building that system, not merely acquiring the equipment, appears to be the harder and more consequential problem.

That system includes a standing cannulation team available around the clock, a prehospital or emergency-department workflow that can identify eligible patients within minutes rather than after prolonged conventional resuscitation, and an intensive-care pathway equipped to manage the downstream complications of ECMO support itself, including the excess bleeding and limb ischemia INCEPTION recorded. None of the three trials was designed to isolate how much of the observed variation in benefit is attributable to this surrounding system rather than to the ECMO circuit itself, which is why the selection-criteria review's focus on arrest-to-flow time, a marker of system performance as much as of patient selection, is a useful complement to reading the trials in isolation.

Study limitations

This is a narrative review, not a systematic review with a pre-registered protocol, and it draws on only three randomized trials, all of out-of-hospital refractory ventricular fibrillation or tachycardia arrest -- the findings may not generalize to other rhythms, to in-hospital arrest, or to systems with different baseline emergency-medical-services infrastructure. ARREST's dramatic effect size comes from a single center with only 30 patients and should be weighted accordingly against the two larger, more equivocal trials. The selection-criteria review's meta-regression is observational across heterogeneous studies, not a controlled comparison of time thresholds, so its beta coefficient describes an association rather than a proven causal lever, and the full author list for reference 5 could not be independently confirmed beyond its indexed abstract. Finally, none of the three trials was adequately powered individually to detect the modest effect size the pooled meta-analysis suggests, so the true effect of ECPR versus standard resuscitation remains genuinely uncertain.

Conclusion

The randomized evidence for ECPR in refractory cardiac arrest is directionally consistent but individually inconclusive, and the clearest signal to emerge across the underlying literature is not which trial to believe but that time from arrest to ECMO flow independently predicts outcome. Patient selection under extreme time pressure is therefore not only a triage question about who is eligible, but a systems question about whether a given center can deliver flow fast enough, for the selected patient, to make the intervention's theoretical benefit real.

Trial	N	Primary outcome	ECPR	Control	Result
ARREST [1]	30	Survival to discharge	43%	7%	Stopped early
Prague OHCA [2]	256	180-d favourable neuro	31.5 %	22.0 %	P=0.09
INCEPTION [3]	134	30-d favourable neuro	20%	16%	P=0.52

Table 1: Design, size, and primary-outcome result of the three randomized ECPR trials reviewed here [1-3].

Characteristic	Prospective studies	Retrospective studies
Applied an age criterion	84%	73%
Median patient age	52 years	56 years
Median arrest-to-flow time	74 minutes	57 minutes

Table 2: Selection-criteria and timing differences between prospective and retrospective ECPR studies, pooled across 67 studies [5].

The same 67-study review found pooled favourable-neurologic survival of 16% for out-of-hospital

arrest versus 28% for in-hospital arrest, a further reminder that arrest setting itself, independent of any selection criterion applied within it, shapes what a given protocol can realistically achieve [5].

Taken together, the pooled three-trial meta-analysis (RR 1.47 at shortest follow-up and RR 1.48 at 6 months, neither reaching significance) and the 67-study meta-regression (arrest-to-flow time an independent predictor of survival, $\beta = -0.023$, $P < 0.001$) point in the same direction from two different bodies of evidence: the trials that most consistently moved the needle were not distinguished by which eligibility criterion they used, but by how quickly the selected patient actually reached ECMO flow once that criterion was met [3-5].

Adverse event (INCEPTION)	ECPR	Conventional CPR
Major bleeding	16%	3%
Lower-limb ischemia	6%	0%

Table 3: Serious procedural adverse events reported in the only one of the three trials to measure them systematically, INCEPTION [3].

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