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Statistical simulation

Optimizing extracorporeal cardiopulmonary resuscitation delivery for out-of-hospital cardiac arrest: a Monte Carlo simulation study ☆

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Abstract

Background: Extracorporeal cardiopulmonary resuscitation (ECPR) can improve outcomes in refractory out-of-hospital cardiac arrest (OHCA), but access is limited by geographic and system constraints. We aimed to compare the potential impact of different ECPR delivery strategies in an urban setting using simulation modeling.

Methods: We performed a Monte Carlo simulation using historical OHCA data (2015–2019) from Montreal's sole EMS. Each of 2000 iterations simulated 1240 annual OHCA cases using geospatial heatmaps. Patients meeting ECPR criteria (witnessed arrest, bystander CPR, age ≤ 70 years old) were included. We tested in-hospital models (2-, 3-, and 4-hospital), a rendezvous model, and two prehospital strategies: hospital-based deployment and an optimally located mobile team. Transport times were estimated using a machine learning model trained on real operational data. Outcomes included survival with favorable neurological outcome, proportion of patients achieving flow recovery at 60 min and low-flow time.

Results: On average, 255 patients were included per iteration. With in-hospital ECPR delivery, increasing from 2 to 4 hospitals modestly improved CPC 1–2 survival (25.3% vs 28.0%), flow recovery at 60 min (69.2% vs 75.1%), and low-flow interval (-2.4 min. Rendezvous yielded 28.8% CPC 1–2 survival, 77.3% flow-recovery at 60 min and -2.9 min low-flow time. Prehospital strategies had the greatest impact, improving CPC 1–2 survival (39.5% and 42.0%), flow-recovery at 60 min (99.7% and 100%), and low-flow time (-7.8 and -12 min) for hospital-based and optimally placed teams respectively.

Conclusion: In this simulation, prehospital ECPR strategies showed the potential to increase survival, improve flow recovery at 60 min, and reduce low-flow times in urban OHCA.

Keywords: Out-of-Hospital Cardiac Arrest, Prehospital, Extracorporeal Cardiopulmonary Resuscitation (ECPR), Monte Carlo Simulation, Low-flow time, Emergency medical system (EMS), Survival

Introduction

Out-of-hospital cardiac arrest (OHCA) is a major public health challenge, with over 60,000 cases annually in Canada, 300,000 in the U.S., and 150,000 in Europe.[1–4] Despite early defibrillation and high-quality cardiopulmonary resuscitation (CPR), many patients remain in refractory cardiac arrest.[5]

Extracorporeal cardiopulmonary resuscitation (ECPR), using extracorporeal membrane oxygenation (ECMO) to restore circulation, is recommended by the American Heart Association (AHA) for select patients with refractory OHCA (Class 2a).[6] However, its effec-

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tiveness is highly time-sensitive, with guidelines recommending initiation within 60 minutes of arrest to optimize neurological recovery.[7,8]

Integrating ECPR into emergency response systems presents logistical challenges. Early transport may compromise CPR quality and reduce the likelihood of spontaneous circulation (ROSC).[9–11] Studies suggest delaying transport until at least 16 min of professional resuscitation.[9] When adding EMS response times, scene interventions, patient extraction and transport time, achieving ECPR initiation within 60 min is challenging.[12] Expanding in-hospital ECPR coverage may reduce transport times and improve access, but requires substantial resources and risks diluting expertise.

As a potential solution, the Rendezvous model has been used: a single, expert ECMO team departs from a central ECPR center to perform cannulation at the closest receiving hospital.[13] This model preserves team expertise while extending regional coverage. However, it does not eliminate delays prior to ECMO initiation inherent to EMS activation, on-scene care, and transport. To address these limitations, some regions have explored prehospital ECPR, where ECMO cannulation is performed in the field.[14–17] By minimizing transport-related delays, prehospital ECPR could reduce low-flow times and increase the number of eligible patients.[12]

The optimal solution may vary from city to city depending on a host of factors including the geographical location and demography of OHCAs, number and location of ECMO centers and EMS characteristics. We therefore aimed to simulate the effect of different ECPR deployment strategies, including hospital-based models, a Rendezvous model, and prehospital models on the proportion of patients achieving flow recovery at 60 min, low-flow time, and survival with favorable neurological outcome (CPC 1–2) in patients with refractory OHCA in Montreal metropolitan area. The method we develop here could be applied in other cities using standard OHCA registry data to help determine the optimal system to be used.

Methods

Setting

This simulation study was based on historical data from Urgences-Santé, the EMS provider serving the urban regions of Montreal and Laval, with a combined population of approximately 2.4 million. The system operates with a two-tiered response: for cardiac arrest calls, first responders (firefighters), as well as primary care paramedics and, when criteria are met, advanced care paramedics, are dispatched to the scene. Within the Urgences-Santé coverage zone, four hospitals are ECMO-capable, two of which provide 24-hour ECPR coverage for out-of-hospital cardiac arrests. In the historical data, EMS would transport patients in refractory arrest to the nearest hospital. Recent updates to EMS protocols now allow ambulances transporting refractory OHCA patients to bypass closer hospitals if transport to an ECPR-capable center is feasible within 45 min of the 911 call (Fig. 1).

Patient population

Non-traumatic OHCA cases recorded between 2015 and 2019 by Urgences-Santé were used to define the simulated patient population. Each simulation iteration included 1240 OHCA cases, reflecting

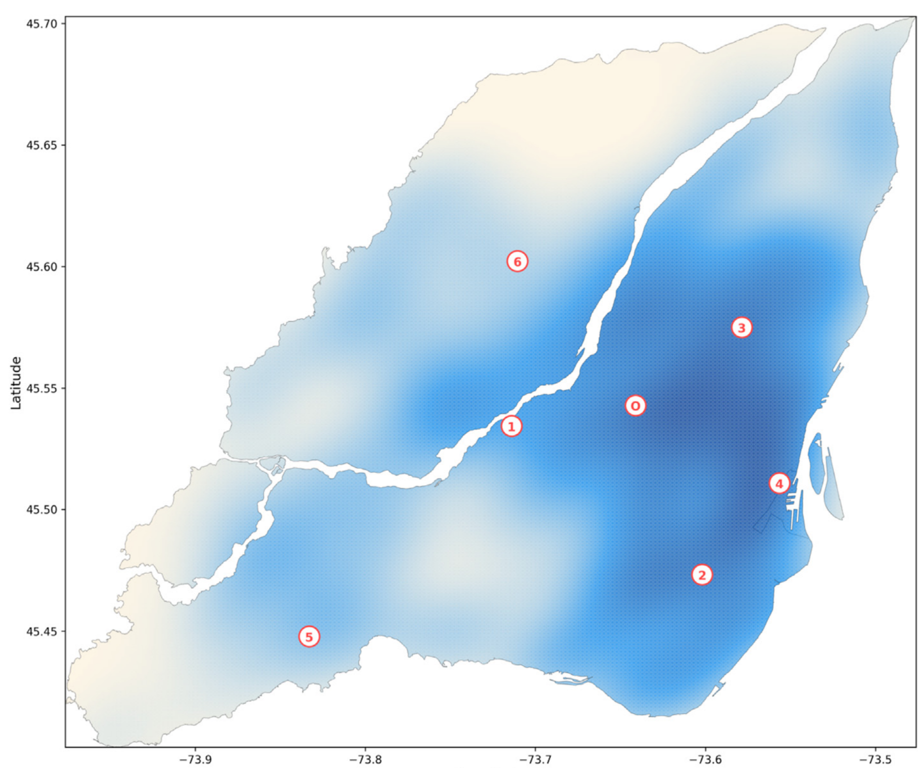

Fig. 1 – Out-of-hospital cardiac arrest (OHCA) density across the Urgences-Santé coverage area and geographic locations of key centers. ECMO-capable hospitals are shown as points 1, 2, 3, and 4. Rendezvous centers include hospitals 1, 2, 3, 5, and 6. The base hospital for the hospital-based prehospital (PH) ECPR team is Hospital 1. The optimal waiting zone for the optimally stationed prehospital (O-PH) team is marked as "O".

the average annual number of cardiac-origin OHCAs in the Urgences-Santé coverage area, based on data from our annually published Utstein registries. Individual patient characteristics were probabilistically assigned from distributions derived from historical data (Appendix A). Each simulated case was assigned a specific month, weekday, and hour based on observed temporal patterns. Additional simulated characteristics included patient age, witness status (paramedic, first responder, bystander providing CPR, bystander without intervention, or unwitnessed), and presence of first responders. Eligibility criteria for ECPR excluded patients over 70 years of age, unwitnessed OHCA and those without bystander CPR.

Outcomes

Primary outcome:

- **Survival with favorable neurological outcome at 6 months:** Defined as Cerebral Performance Category (CPC) 1 or 2 (assessed across all simulated patients, regardless of ECPR receipt).[18]

  Secondary outcomes:

- **Sub-60 min Flow Recovery:** An OHCA case in which either return of spontaneous circulation (ROSC) was achieved or ECMO was initiated within 60 min of the EMS call.
- **Low-flow interval:** Interval from time of the EMS call to either return of spontaneous circulation (ROSC) or ECMO initiation.

Statistical analysis

Monte Carlo simulation

We performed 2000 Monte Carlo iterations to evaluate different ECPR deployment strategies. To simulate geographic distribution, we generated a spatial incidence density heatmap using non-traumatic OHCA locations recorded between 2015 and 2019 by Urgences-Santé. Simulated cases were then probabilistically assigned geographic coordinates based on the spatial density distribution derived from this heatmap (Fig. 1). Individual patient characteristics were assigned from distributions derived from historical data, resulting in approximately 255 ECPR-eligible patients per iteration. ROSC occurrence and timing were simulated, and model-specific low-flow times were calculated. Simulations were conducted using Python v3.11.9, employing NumPy and SciPy libraries for statistical modeling.[19–21]

Tested models

Six deployment strategies were compared:

- **In-hospital strategy with 2, 3 or 4 sites:** An ambulance is dispatched to the scene, where initial resuscitation is initiated by first responders and paramedics. If no ROSC is achieved, the patient is transported to the nearest ECMO-capable hospitals (Hospitals 1, 2, 3 and 4). ECMO is initiated in-hospital following patient arrival.
- **Rendezvous strategy:** The patient undergoes standard prehospital management as detailed above. However, the ECPR team based at Hospital 1 is simultaneously dispatched to the nearest of five strategically located hospitals (1,2,3,5 and 6) closest to the patient. Once both the patient and the ECPR team have arrived, cannulation is performed and ECMO is initiated in-hospital by the ECPR team.
- **Prehospital (PH) strategy with a hospital-based team:** In this model, the ECPR team is based at Hospital 1. Upon receipt of a 911 call, the team is dispatched to the site of the Once on scene, the patient is cannulated and ECMO is initiated in the field.
- **Optimal position Prehospital (O-PH) ECPR strategy**: The prehospital team is stationed at an optimally selected location, not limited to hospitals. A two-step grid-based optimization was used: a coarse grid (0.02° resolution) over 10,000 simulated OHCA events, followed by a refined search (0.002°) to minimize average response time. Operations mirror the standard PH model.

  See Fig. 2 for complete description of each strategy.

Transport modeling

All transport times, including transport time from the scene to the hospital (In-hospital/Rendezvous), from Hospital 1 to the rendezvous hospital (Rendezvous), from Hospital 1 to the scene (PH) and from the optimal position to the scene (O-PH)) were estimated using the Open Source Routing Machine (OSRM)[22] and ambulance entrance coordinates of hospitals. Ambulance transport times were modeled using an XGBoost regression trained on historical EMS data, considering departure and arrival locations, OSRM-estimated travel times,[23] and temporal variables (month, weekday, hour) to account for variation in traffic.

Modeling of ROSC, low-flow time, ACLS duration, and survival outcomes

ROSC,[24] low-flow time (Table 1), and survival with favorable neurological outcome were modeled probabilistically based on published data and local parameters. Competing events (ROSC vs. ECMO) were simulated, and survival was determined as a function of low-flow time using survival model derived from Advanced cardiac life support (ACLS),[25] in-hospital ECPR[26–28] and prehospital ECPR[29–34] studies. Detailed modeling methods and sources are provided in Appendix B.

Comparison of outcomes

Each strategy was simulated over 2000 Monte Carlo iterations. For all outcomes, results were computed at the individual patient level within each iteration, then summarized across iterations as the mean of iteration-level values with 95 % confidence intervals (95%CI).

For each model, we calculated the proportion of patients achieving flow recovery within 60 min in each iteration, then reported the mean of these iteration-level values. Low-flow interval differences were assessed in patients who achieved flow recovery within 60 min in the 2-hospital model. For these patients, we compared their individual low-flow times across strategies, calculated the difference, and averaged these differences within each iteration. Results were summarized as the mean of iteration means. We identified patients who did not achieve flow recovery within 60 min in the 2-hospital model but did so in their respective strategy and computed their mean number per iteration and their average low-flow time, again summarizing results as the mean of means. Survival with favorable neurological outcome was calculated as the mean survival rate per iteration and reported as the mean of iteration means. ACLS without ECMO was included as

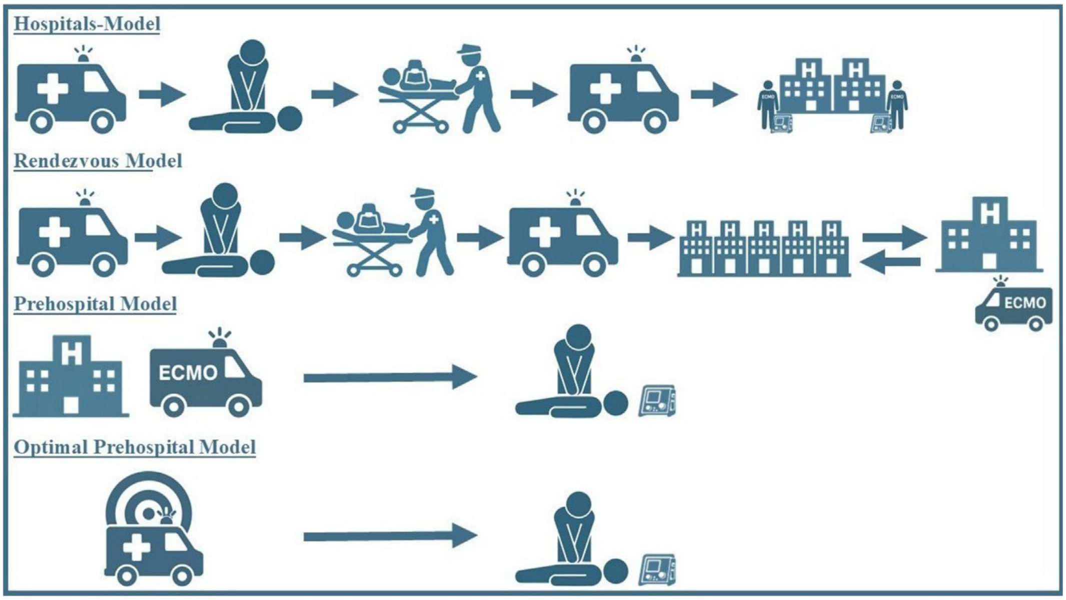

Fig. 2 – Visual representation of the ECPR deployment models evaluated. (1) In-hospital strategy with 2, 3 or 4 sites: An ambulance is dispatched to the scene (Response Time), where initial resuscitation is initiated by first responders and paramedics (Scene Time). If no ROSC is achieved, the patient is extracted from the scene (Extraction Time) and transported to the nearest ECMO-capable hospitals (Hospitals 1, 2, 3 and 4) (Transport Time). ECMO is initiated in-hospital following patient arrival and cannulation by the ECPR team (Door-to-ECMO Time). The total low-flow time in this model is the sum of these intervals. (2) Rendezvous strategy: The ECPR team is based at Hospital 1. Upon receipt of a 911 call, the ECPR team is dispatched (Dispatch Time) and transported to the nearest of five strategically located hospitals (1,2,3,5 and 6) closest to the patient (Team Transport Time). Simultaneously, the patient undergoes standard prehospital management as in the in-hospital strategy, including EMS dispatch, on-scene resuscitation (Scene Time), extraction (Extraction Time), and transport to the same receiving hospital (Patient Transport Time). Once both the patient and the ECPR team have arrived, cannulation is performed and ECMO is initiated in-hospital by the ECPR team (Door-to-ECMO Time). The total low-flow time in this model is calculated as the sum of the Door-to-ECMO Time and the longer of the patient or team arrival time. (3) Prehospital (PH) strategy with a hospital-based team: In this model, the ECPR team is based at Hospital 1. Upon receipt of a 911 call, the team is dispatched (Dispatch Time) and transported directly to the site of the OHCA (Team Transport Time). Once on scene, the patient is cannulated and ECMO is initiated in the field (Scene Time). The total low-flow time in this model is the sum of the dispatch, transport, and scene intervals. (4) Optimal position Prehospital (O-PH) ECPR strategy: The prehospital team is stationed at an optimally selected location, not limited to hospitals. A two-step grid-based optimization was used: a coarse grid (0.02° resolution) over 10,000 simulated OHCA events, followed by a refined search (0.002°) to minimize average response time. Operations mirror the standard PH model.

a comparator to contextualize outcomes across strategies. To test the impact of a more permissive window, we repeated this analysis using a 90-minute cut-off.

To assess the robustness of our findings given the assumption of independence among input variables (e.g., bystander status, age, location), we conducted a sensitivity analysis using the actual patient-level data from Urgences-santé. Real individual characteristics, arrest locations and time were used to simulate low-flow time and proportion of patients achieving flow recovery within 60 min outcomes across strategies. This allowed us to verify that the model's relative performance across strategies remained stable under more realistic conditions. To further test the effect of heterogeneity in survival estimates from the included literature, we created alternative survival models under optimistic and pessimistic scenarios by fitting the model using only the best or worst reported outcomes (Appendix C).

All analyses were performed using Python (Numpy and SciPy).[19–21] No p-values or null hypothesis tests were conducted, consistent with descriptive modeling approaches in Monte Carlo simulations.

Results

Patient population

Across 2000 Monte Carlo iterations, a total of 2,480,000 out-of-hospital cardiac arrests (OHCAs) were simulated using the spatial and temporal characteristics of the Urgences-Santé registry. After excluding patients over 70 years of age, unwitnessed arrests, and those without bystander CPR, a mean of 255 patients per iteration met ECPR eligibility criteria.

Transport modeling

The XGBoost transport model, trained on 3332 real-world EMS transports with 5-fold cross-validation, achieved a mean absolute error (MAE) of 1.55 min (SD: 2.45 min). OSRM-based routing esti-

Table 1 – Time intervals used for low-flow time modeling across ECPR strategies.

	Definition	Mean (min)	SD (min)	Sources
Hospital-Based				
Low-Flow time = Response Time + Scene Time + Extraction Time + Transport Time + Door-to-ECMO Time				
Response Time	Interval from EMS call to arrival at the scene	10.60	5.30	Cournoyer et al.[36]
Scene Time	On-scene resuscitation and preparation for transport	16.00	4.00	Grunau et al.[9]
Extraction Time	Patient's transport from the scene to the ambulance	6.10	5.86	Cournoyer et al.[36]
Door-to-ECMO Time	Interval from hospital arrival to ECMO initiation	15.01	9.44	CHEER[37], 2CHEER[38], Prague[27]
Prehospital				
Low-Flow Time = Dispatch Time + Transport time to the Scene + Scene Time				
Dispatch Time	Time from EMS call to prehospital ECPR team mobilization	4.60	1.67	Sub30[39]
Scene Time	On-scene resuscitation and ECMO initiation	23.00	3.75	CHEER3[32]
Rendezvous				
Time 1 [Patient Hospital Arrival Time] = Response Time + Scene Time + Extraction Time + Transport time to the Hospital				
Time 2 [ECPR Hospital Arrival Time] = Dispatch Time + Transport time to the Hospital				
Low-Flow Time = Maximum (Time 1 or Time 2) + Door-to-ECMO time				

Low-flow time was defined for each model using a combination of operational intervals based on published data. In the simulation, response time was set to 0 min for paramedic-witnessed arrests and adjusted as the difference between ambulance and first responder arrival times for first responder–witnessed arrests. All values represent means and standard deviations (SD) in minutes. ECMO = extracorporeal membrane oxygenation.

mates consistently overestimated real-world transport durations, with a mean OSRM-to-actual time ratio of 1.20. The model was subsequently retrained on the full dataset and used to estimate transport times in all simulations.

Survival with favorable neurological outcome

In the ACLS-only model (without ECMO access), 23 out of 255 patients survived with favorable neurological outcomes (8.9%). Survival increased to 65 patients (25.3%, 95%CI: 25.2–25.4) in the 2-hospital model, 70 patients (27.6%, 95%CI: 27.5–27.8) in the 3-hospital model, and 72 patients (28.0%, 95%CI: 27.9–28.1) in the 4-hospital model. In the Rendezvous model, 74 patients survived (28.8%, 95%CI: 28.7–29.0). Prehospital models achieved the highest survival, with 101 patients (39.5%, 95%CI: 39.3–39.6) in the PH ECPR model and 107 patients (42.0%, 95%CI: 41.8–42.1) in the O-PH model. (Table 2).

Flow recovery within 60 min

The mean number of ECPR-eligible patients per iteration who achieved flow recovery (defined as ROSC or ECMO initiation) within 60 min varied by deployment strategy (Table 3). In the 2-hospital model, 176 of 255 patients achieved flow recovery (69.2%, 95%CI: 69.1–69.3). This increased to 190 patients (74.4%, 95%CI: 74.2–74.5) in the 3-hospital model, 192 patients (75.1%, 95%CI: 75.0–75.3) in the 4-hospital model, and 197 patients (77.3%, 95%CI: 77.1–77.4) in the Rendezvous model. In the prehospital ECPR model, 254 patients achieved flow recovery (99.7%, 95%CI: 99.6–99.7), and in the optimized prehospital (O-PH) ECPR model, all 255 patients did (100.0%, 95%CI: 100.0–100.0).

Low-flow interval comparison

Mean low-flow intervals were significantly reduced in all models relative to the 2-hospital strategy (Table 4). Compared to the 2-hospital model, the 3-hospital model achieved a mean reduction of 2.0 min (95%CI: -2.0 to -2.0), the 4-hospital model a reduction of 2.4 min (95%CI: -2.4 to -2.4), and the Rendezvous model a reduction of 2.9 min (95%CI: -2.9 to -2.9). Reductions were substantially greater in the prehospital ECPR model (7.8 min, 95%CI: -7.9 to -7.8) and the O-PH model (12.0 min, 95%CI: -12.1 to -12.0).

Among patients not achieving flow recovery within 60 min by the 2-hospital model but successfully reached in other strategies, the mean low-flow times were 55.6 min (95%CI: 55.6–55.7) in the 3-hospital model, 55.8 min (95%CI: 55.8–55.9) in the 4-hospital model, and 55.6 min (95%CI: 55.6–55.6) in the Rendezvous model. For prehospital strategies, these times were markedly lower at 45.2 min (95%CI: 45.1–45.2) for the PH model and 40.5 min (95%CI: 40.5–40.6) for the O-PH model. (Table 4).

90-minute cut-off

Compared to the main 60-minute cut-off, extending the window to 90 min substantially increased flow recovery in the in-hospital strategies (from 69.2% to 99.2% in the 2-hospital model) but had minimal

Table 2 – Comparative Survival with CPC 1–2 Across ECPR Deployment Models.

Model	Mean Survivors/Iteration	Survival (%)	95% CI
ACLS	23/255	8.9	8.9–8.9
2 Hospitals	65/255	25.3	25.2–25.4
3 Hospitals	70/255	27.6	27.5–27.8
4 Hospitals	72/255	28.0	27.9–28.1
Rendezvous	74/255	28.8	28.7–29.0
PH ECPR	101/255	39.5	39.3–39.6
O-PH ECPR	107/255	42.0	41.8–42.1

Survival values reflect the mean number and percentage of patients achieving favorable neurological outcome (CPC 1–2) per iteration, across 2000 simulations.

Table 3 – Comparison of the proportion of patients achieving flow recovery at 60 min across deployment models.

Model	Mean Patients/ Iteration	Sub-60 min ROSC	Sub-60 min ECMO	Sub-60 min flow recovery (%)	95% CI
2 Hospitals	176/255	60	116	69.2	69.1–69.3
3 Hospitals	190/255	60	130	74.4	74.2–74.5
4 Hospitals	192/255	60	132	75.1	75.0–75.3
Rendezvous	197/255	60	137	77.3	77.1–77.4
PH ECPR	254/255	60	194	99.7	99.6–99.7
O-PH ECPR	255/255	60	195	100.0	100.0–100.0

Sub-60 min ROSC refers to patients who achieved return of spontaneous circulation through ACLS before 60 min. Sub-60 min ECMO refers to patients cannulated within 60 min. Flow recovery represents the combined total of patients achieving ROSC through ACLS or ECMO within 60 min.

Table 4 – Comparison of ECPR models by low-flow time and additional patient capture.

Model	*n* per iteration used for comparison	Mean Low-Flow Time Difference (min)	95 % CI	Additional patients	Mean Low-Flow Time (Additional patients) (min)	95 % CI
2 Hospitals	176	Reference				
3 Hospitals	176	-1.97	-1.98 to -1.96	13	55.6	55.6–55.7
4 Hospitals	176	-2.41	-2.43 to -2.40	15	55.8	55.8–55.9
Rendezvous	176	-2.89	-2.90 to -2.87	21	55.6	55.6–55.6
PH ECPR	176	-7.83	-7.87 to -7.79	78	45.2	45.1–45.2
O-PH ECPR	176	-12.01	-12.05 to -11.97	79	40.5	40.5–40.6

Time difference is relative to the 2-hospital model, which had a mean low-flow time of 51.71 min (95 %CI: 51.67–51.74). Additional patients reflect those newly eligible for ECPR within 60 min. Low-flow times are for these additional patients. Values represent means over 2000 iterations.

additional effect for prehospital ECPR (99.7–100.0%). The CPC 1–2 survival difference between deployment models narrowed slightly at 90 min (30.9% in the 2-hospital model vs 42.0% in the O-PH model). Detailed results are provided in Appendix D.

Sensitivity analysis

We conducted the sensitivity analysis using real-world patient characteristics, locations, and temporal patterns from 7134 OHCA cases recorded by Urgences-Santé. After excluding non-ECPR candidates, 823 patients remained.

The proportion of patients achieving flow recovery within 60 min was 41.8% in the 2-hospital model, increasing to 50.9% in the 3-hospital model, 52.2% in the 4-hospital model, and 53.4% in the Rendezvous model. Prehospital strategies achieved near-complete capture, with 99.5% in the PH model and 100.0% in the O-PH model.

In this cohort, 344 patients had a low-flow time of less than 60 min under the 2-hospital model and were included in the low-flow interval comparison. Among these patients, the mean low-flow time differences relative to the 2-hospital model were: –1.84 min (95%CI: –2.22 to –1.45) for the 3-hospital model, –2.71 min (95%CI: –3.11 to –2.32) for the 4-hospital model, and –2.21 min (95%CI: –2.65 to –1.78) for the Rendezvous model. Substantially larger reductions were observed in the prehospital models, with –6.23 min (95%CI: –7.29 to –5.18) in the PH model and –11.77 min (95%CI: –12.82 to –10.72) in the O-PH model.

Additional scenario testing

To test the impact of survival model assumptions, we also modeled survival under the most favorable and least favorable published survivals. Under a pessimistic pre-hospital ECPR survival model or an optimistic in-hospital ECPR model, the survival benefit associated with prehospital ECPR disappeared (Appendix C).

Discussion

In this simulation using historical OHCA data and spatial modeling, we found that prehospital ECPR models consistently outperformed hospital-based strategies across all key metrics. Compared to the 2-hospital model, the PH and O-PH ECPR models achieved the greatest reductions in low-flow time, near-universal 60-minute flow recovery, and higher predicted survival rates. These findings align with prior studies demonstrating that prehospital ECPR strategies can improve accessibility, reduce low-flow times, and, potentially, improve survival with favorable neurological outcomes.[12,17,16]

In comparison to a 2-hospital system, adding more in-hospital ECPR teams demonstrated only modest gains: it incrementally improved sub-60 min flow recovery rates and survival but with diminishing returns, while still leaving a substantial proportion of patients without timely access to ECPR. The Rendezvous model offered an intermediate solution by preserving cannulation expertise within a single team and improving access compared to fixed hospital models. However, it remained constrained by pre-cannulation delays inherent to EMS activation, on-scene resuscitation, and transport. In contrast, prehospital ECPR brought ECMO directly to the patient, minimizing low-flow time and maximizing eligibility without requiring expansion of in-hospital infrastructure or dilution of cannulation expertise.

While we primarily used a 60-minute flow recovery target, which is widely supported by expert consensus and many leading ECPR programs to balance survival benefit with the intensive resources required,[8] we also explored a more permissive 90-minute window to test the impact of extending eligibility. This supplementary analysis showed that extending the cut-off increased the number of patients achieving flow recovery for in-hospital strategies but had limited impact on survival with CPC 1-2 because of the extended cerebral ischemia before flow recovery. Maintaining a 60-min threshold aligns with the goal of prioritizing candidates most likely to benefit from this resource-intensive intervention while minimizing futile cannulation. Although extending the cut-off can increase the number of survivors for in-hospital models, this occurs largely by adding patients with longer low-flow times who contribute modestly to overall outcomes but consume considerable additional resources, potentially reducing cost-effectiveness.

Although the O-PH model achieved slightly better low-flow time differences and survival rates than the PH model, these marginal improvements must be weighed against significant operational and financial complexities. Implementing an optimally stationed mobile ECPR team would require dedicated personnel, strategic waiting zones, equipment staging, and complex logistical coordination. Furthermore, the dedicated nature of O-PH deployment reduces system flexibility and may limit cost-effectiveness. In this context, the PH model, based at a single ECMO center, may offer the optimal balance between improved access, increased survival, operational simplicity, and sustainability in large urban environments.

The resource implications of pH models must also be considered, given that hospital teams must leave their in-hospital duties to respond to a case in the community. This will not just be for cases eventually treated with ECMO, but also for false positive activations (i.e. cases the team is sent to but are not actually treated with ECPR). Given that ECMO teams must be immediately dispatched when a cardiac arrest is identified, there will be a proportion of cases who will achieve ROSC prior to ECMO initiation or are otherwise found to be ineligible. In comparison to the CHEER3 study, which reported only 10 ECPR cannulations among 358 confirmed OHCA cases, our projected cannulation rates appear higher.[32] However, CHEER3 included only 165 cases where resuscitation was initiated and was limited by exclusive daytime coverage (two days per week), pandemic-related reductions in incidence, stricter eligibility criteria (e.g., age < 65 years, transport time < 30 min), and a lower population density compared to our setting. Adjusting for their limited operational hours, CHEER3′s case volume would extrapolate to approximately 1453 resuscitated OHCAs annually, comparable to our region's reported 1587 cases. Their effective cannulation rate was 6%, whereas our model estimated 12%, likely due to less restrictive criteria (<70 years, <45-min transport). Notably, another trial (PRECARE) with criteria similar to ours reported a 10% cannulation rate.[35] These contextual differences suggest our projections are consistent with published experiences, though real-world implementation will ultimately determine their accuracy.

Prehospital ECPR also has the potential to address critical equity issues in OHCA care. In-hospital and Rendezvous models inevitably favor patients located closer to ECMO-capable hospitals, creating geographic disparities in access to life-saving interventions. Prehospital ECPR extends eligibility to patients who would otherwise be excluded due to prolonged transport times, enhancing geographic equity across urban regions. These insights further reinforce our focus on prehospital models as an approach to address the key limitations that contributed to the neutral results of the two most recent randomized trials, namely prolonged low-flow times and diluted cannulation expertise spread across multiple centers.[27,28] However, the benefits of ground-based prehospital ECPR may be limited in more remote or suburban areas where transport times remain prohibitive. Integration of Helicopter Emergency Medical Services (HEMS) into prehospital ECPR strategies could further expand equitable access by overcoming geographic barriers. The ongoing On-Scene trial will provide valuable insights into the feasibility, survival benefits, and logistical considerations associated with implementing HEMS-supported prehospital ECPR.[14]

Our simulation approach has multiple strengths. Cardiac arrest locations were based on real historical OHCA data, and transport times were modeled using OSRM-calculated driving routes adjusted for local ambulance performance. ROSC probabilities and survival projections were derived from published in-hospital and prehospital ECPR studies. All low-flow components were treated as probabilistic distributions, reflecting real-world variability. Additionally, modeling assumptions were intentionally designed to favor the performance of in-hospital ECPR and ACLS, including early transport initiation and idealized in-hospital cannulation times. The consistency between the sensitivity analysis results and the primary Monte Carlo simulation supports the internal validity of our model and suggests that its conclusions are stable across a range of realistic scenarios.

Nevertheless, certain limitations must be acknowledged. We assumed that the spatial distribution of witnessed OHCAs mirrored that of potential ECPR candidates, which may not perfectly reflect real-world selection. Transport times, although adjusted to regional performance, were still based on modeled rather than live operational data. Survival was modeled only as a function of low-flow time without adjusting for other key patient-level predictors such as presenting rhythm, comorbidities, functional status, or signs of life during CPR, which are known to strongly influence real-world outcomes. Therefore, our survival figures should be interpreted as potential estimates driven by modeled time differences alone and not as precise patient-level predictions. Additionally, the reported 95% confidence intervals are highly reduced by the large number of Monte Carlo iterations and do not account for parameter uncertainty in the underlying survival models. To explore this uncertainty, we also tested optimistic and pessimistic scenarios, which showed that the survival advantage of prehospital ECPR over in-hospital ECPR diminished under less favorable assumptions. While all simulations carry assumptions, the consistency between modeled parameters and real-world benchmarks suggests that any differences in implementation are likely to be modest. Future studies should explore these factors through prospective trials to evaluate operational logistics, refine survival predictions, and assess the cost-effectiveness of different deployment strategies in practice.

Conclusion

This simulation study suggests that prehospital ECPR strategies could potentially improve the proportion of patients achieving flow recovery at 60 min, reduce low-flow times, and increase survival for patients with refractory OHCA. Among the models evaluated, a hospital-based prehospital (PH) ECPR team achieved near-universal access while maintaining operational feasibility, offering an optimal balance between improved outcomes and system sustainability.

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used ChatGPT to review syntax and orthograph to improve readability and language. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

CRediT authorship contribution statement

Lawrence Leroux: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Brian Grunau:** Writing – review & editing, Methodology. **Pierre Lecuyer:** Writing – review & editing, Methodology. **Nathaniel B. Dennis-Benford:** Writing – review & editing. **Lionel Lamhaut:** Writing – review & editing. **Sheldon Cheskes:** Writing – review & editing. **Alexis Cournoyer:** Writing – review & editing. **Yiorgos Alexandros Cavayas:** Writing – review & editing, Writing – original draft, Supervision, Methodology, 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

Simulated patient characteristics assigned in the Monte Carlo model.

Characteristic	Mean	SD
Age (years)	68.3	16.0
First responder attendance (%)	59.3	0.58*
First responder arrival time (min)	6.31	3.7
Non-intervening bystanders (%)	61.96	0.58*
Intervening bystanders:		
Arrest in front of paramedics or first responders (%)	29.8	0.87*

All characteristics were probabilistically assigned to each. simulated patient based on regional data from the. Urgences-Santé registry (2015–2019).[36]

*: calculated using Wald interval.

Appendix B

ROSC and Low-flow time modeling

ROSC occurrence was modeled probabilistically using a minute-by-minute distribution derived from Nagao et al.[24] and scaled to match our 23.7% local ROSC rate.[36] For each model and simulated patient, ROSC and ECMO initiation were treated as competing events. Patients who achieved ROSC before the projected ECMO time were excluded from ECPR. Those without ROSC by the time ECMO would have been initiated were deemed ECMO-eligible and assumed to be cannulated. Low-flow time was calculated by summing multiple simulated time intervals, each sampled from a normal distribution based on published means and standard deviations (Table 1). For witnessed arrests by paramedics dispatch time was set to zero. For unwitnessed arrests, dispatch time was drawn from a distribution based on historical means and standard deviations.[36]

Survival with favorable neurological outcome modeling

Individual survival outcomes were stochastically sampled based on modeled survival probabilities. For patients with ROSC (without ECMO), we used Goto et al. data[25] to model the time-dependent probability of survival with favorable neurological outcome. For the in-hospital and Rendezvous ECPR models, survival probability as a function of low-flow time was modeled using published survival rates and the corresponding low-flow time means and confidence intervals extracted from three in-hospital ECPR cohorts.[26–28] For prehospital ECPR models, survival was similarly modeled using reported survival percentages and associated low-flow time means and confidence intervals from published prehospital ECPR studies.[29–34] Survival was modeled solely as a function of low-flow time; individual patient characteristics such as comorbidities or initial rhythm were not incorporated, due to lack of available data. In the in-hospital, Rendezvous, and prehospital models, patients with low-flow times exceeding 60 min were considered not cannulated and assigned a survival probability of 0%, consistent with existing literature on outcomes following prolonged conventional CPR.[7] This 60-minute cutoff ensured that comparisons between deployment strategies were restricted to a clinically relevant timeframe. We used stochastic sampling to simulate individual outcomes and the iteration-level survival rate for each strategy was then calculated as the proportion of survivors among all simulated patients.

Data Sources for the Hospital and Prehospital ECPR Survival Model

First Author	Sample Size	CPC Assessment Timing	CPC 1–2 N (%)	Low-Flow Time (mean ± SD)
Hospital Models				
Yannopoulos (2017)[26]	14	6 months	6 (42.9%)	59 ± 28
Belohlavek (2021)[27]	92	6 months	20 (21.7%)	61 ± 11.1*
Suverein (2022)[28]	33	6 months	5 (15.2%)	74 ± 17.8*
Prehospital Models				
Lamhaut (2017)**[29]	46	ICU discharge or 28 days	2 (4,3%)	83 ± 26,9
Petermichl (2021)[30]	69	Hospital discharge	17 (24,6%)	48 ± 9,3
Pozzi (2022)[31]	30	Hospital discharge	7 (23,3%)	71 ± 15,4
Richardson (2023)[32]	10	Hospital discharge	4 (40%)	50 ± 8,5
Trummer (2024)[33]	14	3 months	6 (42,9%)	37 ± 20
Khoury (2024)[34]	114	1 year	24 (21,1%)	76 ± 18,5

* Estimated from median and IQR.

** Only patients from Period 1 were selected due to dataset overlap between Period 2 and Khoury et al. (2024).

ACLS model survival:

$$PredictedSurvivalRate = e^{-\left(\frac{t}{7.1162}\right)^{0.7965}}$$

Hospital model survival:

$$PredictedSurvivalRate = 0.7000e^{-\left(\frac{t}{59.6314}\right)^{2.0000}}$$

Prehospital model survival:

$$PredictedSurvivalRate = 0.6000e^{-\left(\frac{t}{70.0177}\right)^{2.0000}}$$

Appendix C

Optimist Hospital model survival:

$$PredictedSurvivalRate = 0.7000e^{-\left(\frac{t}{84.2000}\right)^{2.0000}}$$

Pessimist Hospital model survival:

$$PredictedSurvivalRate = 0.7000e^{-\left(\frac{t}{56.4000}\right)^{2.0000}}$$

Optimist Prehospital model survival:

$$PredictedSurvivalRate = 0.6000e^{-\left(\frac{t}{78.5000}\right)^{2.0000}}$$

Pessimist Prehospital model survival:

$$PredictedSurvivalRate = 0.6000e^{-\left(\frac{t}{50.9000}\right)^{2.0000}}$$

Table C1 – Comparative Optimist and Pessimist Survival with CPC 1–2 Across ECPR Deployment Models.

Model	Survival (%)
Optimist 2 Hospitals	42.5
Pessimist 2 Hospitals	28.9
Optimist 3 Hospitals	43.7
Pessimist 3 Hospitals	30.5
Optimist 4 Hospitals	43.9
Pessimist 4 Hospitals	30.7
Optimist Rendezvous	44.3
Pessimist Rendezvous	31.2
Optimist PH ECPR	42.2
Pessimist PH ECPR	30.6
Optimist O-PH ECPR	44.3
Pessimist O-PH ECPR	33.8

Survival values reflect the mean number and percentage of patients achieving favorable neurological outcome (CPC 1–2) per iteration, across 2000 simulations.

Appendix D

Table D1 – Comparative Survival with CPC 1-2 Across ECPR Deployment Models.

Model	Mean Survivors/ Iteration	Survival (%)	95% CI
ACLS	23/255	8.9	8.9–8.9
2 Hospitals	79/255	30.9	30.9–31.0
3 Hospitals	83/255	32.4	32.4–32.5
4 Hospitals	83/255	32.7	32.7–0.32.8
Rendezvous	85/255	33.2	33.1–33.2
PH ECPR	101/255	39.6	39.5–39.6
O-PH ECPR	107/255	42.0	42.0–42.0

Survival values reflect the mean number and percentage of patients achieving favorable neurological outcome (CPC 1–2) per iteration, across 2000 simulations.

Table D2 – Comparison of the proportion of patients achieving flow recovery at 90 min across Deployment Models.

Model	Mean Patients/ Iteration	Sub-90 min ROSC	Sub-90 min ECMO	Sub-90 min flow recovery (%)	95% CI
2 Hospitals	253/255	60	193	99.2	99.2–99.2
3 Hospitals	254/255	60	194	99.5	99.5–99.5
4 Hospitals	254/255	60	194	99.5	99.5–99.6
Rendezvous	254/255	60	194	99.7	99.7–99.7
PH ECPR	255/255	60	195	100.0	100.0–100.0
O-PH ECPR	255/255	60	195	100.0	100.0–100.0

Sub-90 min ROSC refers to patients who achieved return of spontaneous circulation through ACLS before 90 min. Sub-90 min ECMO refers to patients cannulated within 90 min. Flow recovery represents the combined total of patients achieving ROSC through ACLS or ECMO within 90 min.

Table D3 – Comparison of ECPR Models by Low-Flow Time.

Model	Mean *n* per iteration	Mean Low-Flow Time Difference (min)	95% CI
2 Hospitals	253	Reference	
3 Hospitals	253	−2.27	−2.28 to −2.26
4 Hospitals	253	−2.69	−2.70 to −2.67
Rendezvous	253	−3.43	−3.44 to −3.42
PH ECPR	253	−12.74	−12.78 to −12.70
O-PH ECPR	253	−17.08	−17.12 to −17.05

Time difference is relative to the 2-hospital model, which had a mean low-flow time of 57.03 min (95% CI: 57.00–57.07). Values represent means over 2000 iterations.

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