Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

The relationship between no-flow interval and survival with favourable neurological outcome in out-of-hospital cardiac arrest: Implications for outcomes and ECPR eligibility

Andrew Guy[a,1,*], *Takahisa Kawano*[b,2], *Floyd Besserer*[c,1,3], *Frank Scheuermeyer*[d,1,4], *Hussein D. Kanji*[e,5], *Jim Christenson*[f,1,4], *Brian Grunau*[d,1,3,4]

[a] *Royal Columbian Hospital Emergency Department, 330 E Columbia St., New Westminster, BC V3L 3W7, Canada*
[b] *23-3 Shimoaigetsu, Eiheiji Town, Yoshida County, Fukui Prefecture, Japan*
[c] *University Hospital of Northern British Columbia Emergency Department, 1475 Edmonton St., Prince George, BC V2M 1S2, Canada*
[d] *St. Pauls Hospital Emergency Department, 1081 Burrard St., Vancouver, BC V6Z 1Y6, Canada*
[e] *Intensive Care Unit, Vancouver General Hospital, 899 West 12th St., Vancouver, BC V5Z 1M9, Canada*
[f] *Department of Emergency Medicine, Diamond Health Care Center 11th Floor, 2775 Laurel St., Vancouver, BC V5Z 1M9, Canada*

Abstract

Background: The "no flow" interval is the time from out-of-hospital cardiac arrest (OHCA) to cardiopulmonary resuscitation (CPR). Its prognostic value is important to define for prehospital resuscitation decisions, post-resuscitation care and prognostication, and extracorporeal cardiopulmonary resuscitation (ECPR) candidacy assessment.

Methods: We examined bystander-witnessed OHCAs without bystander CPR from two Resuscitation Outcomes Consortium datasets. We used modified Poisson regression to model the relationship between the no-flow interval (9-1-1 call to professional resuscitation) and favourable neurological outcome (Modified Rankin Score ≤ 3) at hospital discharge. Furthermore, we identified the no-flow interval beyond which no patients had a favourable outcome. We analysed a subgroup to simulate ECPR-treated patients (witnessed arrest, age < 65, non-asystole initial rhythm, and >30 min until return of circulation).

Results: Of 43,593 cases, we included 7299; 616 (8.4%) had favourable neurological outcomes. Increasing no-flow interval was inversely associated with favourable neurological outcomes (adjusted relative risk 0.87, 95% CI 0.85–0.90); the adjusted probability of a favourable neurological outcome decreased by 13% (95% CI 10–15%) per minute. No patients (0/7299, 0%; 1-sided 97.5% CI 0–0.051%) had both a no-flow interval >20 min and a favourable neurological outcome. In the hypothetical ECPR group, 0/152 (0%; 1-sided 97.5% CI 0–2.4%) had both a no-flow interval >10 min and a favourable neurological outcome.

Conclusions: The probability of a favourable neurological outcome in OHCA decreases by 13% for every additional minute of no-flow time until high-quality CPR, with the possibility of favourable outcomes up to 20 min.

* Corresponding author.
E-mail addresses: Andrew.guy@alumni.ubc.ca (A. Guy), kawano@u-fukui.ac.jp (T. Kawano), fbesserer@gmail.com (F. Besserer), frank.scheuermeyer@gmail.com (F. Scheuermeyer), hdkanji@gmail.com (H.D. Kanji), jim.christenson@ubc.ca (J. Christenson), Brian.grunau@ubc.ca (B. Grunau).
[1] Department of Emergency Medicine, University of British Columbia, Vancouver, Canada.
[2] University of Fukui Hospital, Fukui Prefecture, Japan.
[3] British Columbia Emergency Health Services, Canada.
[4] Centre for Health Evaluation & Outcome Sciences, Vancouver, BC. Canada.
[5] Division of Critical Care, University of British Columbia, Vancouver, Canada.

https://doi.org/10.1016/j.resuscitation.2020.06.009
Received 8 January 2020; Received in revised form 11 February 2020; Accepted 4 June 2020
Available online xxx
0300-9572/

Keywords: Cardiac arrest, Resuscitation, Cardiopulmonary resuscitation, Emergency medical services, Extracorporeal life support

Introduction

Non-traumatic out-of-hospital cardiac arrest (OHCA) affects approximately 365,000 people in North America annually[1,2]; however, only 5–19% of patients treated by emergency medical services survive to discharge with a favourable neurological outcome even in high performing centres focused on resuscitation process and outcomes.[3]

The "no-flow interval" is the time from cardiac arrest to initiation of cardiopulmonary resuscitation (CPR). The correlation between early CPR, whether by bystanders or professionals, and improved survival is well established.[4–6] Previous studies examining overall cohorts of EMS-treated OHCAs have shown that increasing periods without CPR are associated with worse patient outcomes.[7,8] These data included patients with EMS-witnessed arrests in whom immediate high-quality CPR is expected, as well as patients with bystander CPR in whom timing of CPR onset is uncertain and quality is variable. Therefore, the exact no-flow interval and CPR quality in these data are imprecise. Further, one of these studies[8] has been cited widely by scientific investigations[1,5,9] and public media campaigns,[2,10] however is based on data that is approximately 30-years old, and thus we deemed an evaluation with more recent data appropriate.

The prognostic value of the no-flow interval is important to prehospital providers and planners. EMS agencies may use no-flow interval in criteria to determine which cases are appropriate for withholding resuscitation,[11] but there is no evidence to support an absolute benchmark time. Second, programmes implementing extracorporeal cardiopulmonary resuscitation (ECPR) often include a no-flow interval limit (e.g. $<$10 min),[12,13] however, the optimal threshold is unclear. Third, hospital decisions to continue aggressive ICU care after return of spontaneous circulation (ROSC) are often made including the no-flow duration as a predictor of clinical futility.[14] None of these decision models is grounded in hard data from human studies.

For these reasons, we sought to define the impact of the no-flow interval on patient outcomes. We included patients with bystander-witnessed OHCA (9-1-1 call time used as a surrogate for the onset of cardiac arrest), however without any attempts at bystander resuscitation (therefore using the professional CPR time as the end of the no-flow interval). We hypothesized that increased no-flow interval would be associated with worse neurological outcomes, and that we could elucidate a threshold of no-flow interval above which no patients would have a favourable outcome. We repeated this analysis for a hypothetical cohort of patients to simulate the conditions for ECPR treatment.

Methods

Study setting and parent trials

This investigation was a secondary analysis of two combined datasets from two clinical trials implemented by the Resuscitation Outcomes Consortium (ROC), a network of 10 North American clinical sites covering 24 million people over 35,000 square miles. The *Prehospital Resuscitation Using an Impedance Valve* and *Early* vs *Delayed* trials ("PRIMED", 2006–2009)[15,16] and the *Continuous or Interrupted Chest Compressions during CPR* trial ("CCC", 2011–2015),[17] both enrolled consecutive adult, EMS-treated, non-traumatic OHCAs. The methods of both studies have been described previously.[18–20] Both trials had neutral results,[16,17,21] suggesting a low risk of bias from secondary analyses. This data is available upon request through the ROC.

ROC trial research staff prospectively and systematically abstracted prehospital data, including time-stamped diagnostics, treatments administered, patient characteristics, and prehospital outcomes through standardized EMS charting templates. Staff assessed survival and Modified Rankin Scale (mRS) at hospital discharge through chart review,[15,17] and were unaware of this post hoc analysis at the time of data collection.

The institutional ethics boards of Providence Health Care and the University of British Columbia approved this study (H17-03170).

Study design, selection of participants, and data collection

We examined all PRIMED and CCC cases. In order to create a cohort for which we would be able to calculate the no-flow interval, we excluded patients if the arrest was unwitnessed (not seen or heard), if CPR or an automated external defibrillator was administered by bystanders, if there was no time data of professional CPR initiation, or if the arrest was witnessed by EMS. There were no patients less than 18 years of age in the original parent datasets. In addition, we excluded cases with an obvious non-cardiac cause of arrest (as the relationship between no-flow interval and outcomes may be systematically different), or if outcome data on neurological status at hospital discharge was unavailable. To simulate the conditions of a hypothetical ECPR-treated group, we created a subgroup of those with age $\leq$65, non-asystole initial rhythm, and a prolonged period (over 30 min) of professional resuscitation until return of circulation. The authors had access to the full (de-identified) datasets for analysis.

Outcome measures and variable definitions

The primary endpoint was survival with favourable neurological outcome, defined as a Modified Rankin Scale $\leq$3 at hospital discharge.[22] Our primary independent variable of interest was no-flow interval, defined as the time interval from the bystander 9-1-1 call (recorded when the call is answered at the EMS dispatch centre and assumed to be the approximate arrest time) to initiation of EMS-performed CPR.

Data analysis

We used Microsoft Excel 2019 (Microsoft Corp, Redmond, WA, USA) and STATA version 13.1 (STATA Corp, College Station, TX, USA) for analysis. Categorical variables are reported as percentages (with 95% confidence intervals when appropriate). Continuous variables are reported as means with standard deviations (if normally distributed) or otherwise as medians with interquartile ranges (IQR). We reported patient characteristics of the full cohort, as well cases with no-flow intervals over 10 min to describe characteristics of those with prolonged low-flow periods.

We fit a multivariate Poisson regression model with a robust error variance, adjusting for Utstein pre-arrest co-variates known to be associated with outcomes in OHCA (age, sex, public location)[23,24] and study dataset (PRIMED or CCC) to estimate the association between no-flow interval (per minute) and a favourable neurological outcome at hospital discharge. We did not include bystander CPR as a co-variate since no patient had bystander CPR. We did not include initial cardiac rhythm in the analysis as previous data has shown that initial cardiac rhythm is dependent on the quantity of preceding no-flow duration.[23] We reported this model in the form of adjusted relative risk (aRR) with 95% CI. We tested the suitability of the model with the Pearson chi-squared goodness of fit test, and tested multicollinearity with variance inflation factor. To visualize the association between no-flow interval and outcome, we plotted the estimated probability of survival with favourable neurological outcome based on the model within 25 min of no flow interval. For both the full cohort and the ECPR subgroup, we reported the no-flow interval after which there were no favourable neurological outcomes.

To evaluate possible interaction, we repeated the main analysis stratified by the following subgroups: initial rhythm [shockable: ventricular fibrillation/ventricular tachycardia and automated external defibrillator-initiated shock; non-shockable: asystole, pulseless electrical activity, AED initiated no-shock and undetermined non-shockable] and sex. Within the ECPR subgroup, we assumed that there would be an insufficient sample size to develop a logistic regression model.

We divided patients into 2.5-min increments of no-flow time interval (based on previous studies),[7,25] and then obtained the proportion of patients with successful neurologic outcome in each increment. To explore the outcomes in the hypothetical ECPR cohort, we again obtained the proportion of successful outcomes in each increment of no-flow interval.

Results

Characteristics of study subjects

Of 43，593 consecutive EMS-treated OHCA in the parent studies, we included 7299 (17%) patients in the full cohort, and 152 (0.35%) patients in the hypothetical ECPR subgroup (Fig. 1).

Main results

Patient characteristics are shown in Table 1, including patients within the subgroup of potential ECPR eligible patients. We also separately characterized those patients with favourable neurological outcomes with a no-flow interval greater than 10 min. The median age was 70 (IQR 58-81), 66% were male, 17% occurred in a public location, 31% had a shockable initial rhythm, and ROSC was achieved in 45% of patients. The median no-flow interval was 8.0 min (IQR 6.4–10 min). Survival to hospital discharge was 11% overall, and 8.4% (95% CI 8.4–9.1%) had favourable neurological outcome.

Fig. 2 shows the proportion of cases with favourable neurological outcomes among successive 2.5-min no-flow categories. In the full cohort, there were no cases with both a no-flow interval exceeding 20 min and a favourable neurological outcome (0/7299, 0%; 1-sided 97.5% CI 0–0.051%).

In the adjusted analysis, each minute of no-flow interval was associated with a decreased probability of survival with favourable neurological outcome (aRR 0.87; 95% CI 0.85–0.90 per minute). The adjusted probability of a favourable neurological outcome decreased by 13% (95% CI 10–15%) per minute of no-flow interval. Pearson chi-squared goodness of fit test was not statistically significant. All variance inflation factors were below 10. Fig. 3 demonstrates the adjusted probability of a favourable neurological outcome as a function of no-flow interval. Results were similar when the analysis was performed within subgroups of initial shockable cardiac rhythm (aRR 0.89; 95% CI 0.86–0.92), initial non-shockable cardiac rhythm (aRR 0.91; 95% CI 0.87–0.96), female sex (aRR 0.88; 95% CI 0.84–0.93), and male sex (aRR 0.87; 95% CI 0.84–0.90).

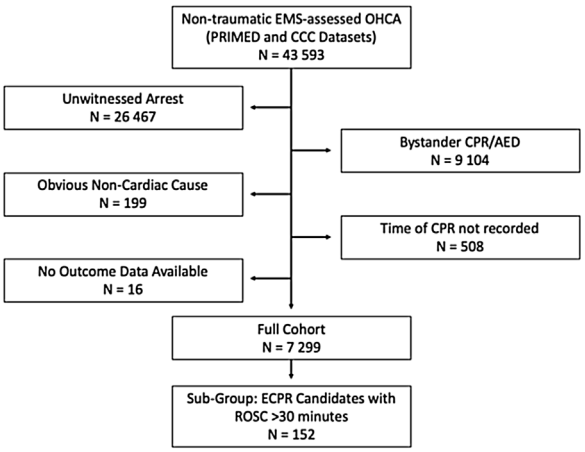

Fig. 1 – Study cohort and exclusions. EMS, emergency medical services; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; AED, automated external defibrillator; ECPR, extra-corporeal cardiopulmonary resuscitation.

For the 152 cases in the hypothetical ECPR subgroup (Table 1), the median no-flow interval was 8.3 min (IQR 6.6–10 min) and time to ROSC was 36 min (IQR 33–42 min). Overall, the rate of favourable neurological outcomes in this cohort was 9.9% (95% CI 5.6–15%). Fig. 4 shows the proportion of survivors with a favourable neurological outcome within 2.5-min no-flow intervals. No patients with a no-flow interval exceeding 10 min had a favourable neurological outcome (0/152, 0%; 97.5% CI 0–2.4%).

Discussion

We combined two large datasets in order to identify and analyse 7299 patients with out-of-hospital cardiac arrest who had an objective no-flow interval. Our data demonstrate that the probability of survival with a favourable neurologic outcome decreases by 13% per additional minute of no-flow interval. Importantly, we found that there were cases with favourable neurological outcome with no-flow intervals up to 20 min. These findings may help physicians, paramedics, and EMS planners by (1) demonstrating the relationship between no-flow interval and the probability of a favourable outcome, (2) showing that survival with a favourable neurological outcome is possible up to 20 min of no-flow interval, and (3) assisting with eligibility assessment for potential ECPR candidates. Decisions regarding initiating CPR, ECPR candidacy, and post-arrest prognostication will include other variables in addition to the no-flow interval, but our results—from data

Table 1 – Characteristics of 7299 patients with bystander witnessed arrests but no bystander resuscitation, along with a subgroup of ECPR eligible patients with prolonged (ROSC > 30 min) resuscitation, and patients with favourable neurological outcomes and no-flow interval > 10 min. *N*, number; ECPR, extracorporeal cardiopulmonary resuscitation; IQR, interquartile range; ROSC, return of spontaneous circulation; ALS, advanced life support; CABG, coronary artery bypass graft; ED, emergency department; EMS, emergency medicine services.

Variable	Full cohort, *N* = 7 299		ECPR eligible cohort, *N* = 152		Favourable outcome > 10 min no-flow, *N* = 66	
	N (% or IQR)	Missing	*N* (% or IQR)	Missing	*N* (% or IQR)	Missing
Age (years)	70 (58–81)	3	62 (55–70)	0	59 (51–70)	0
Male	4811 (65%)	1	102 (67%)	0	46 (70%)	1
Public location	1232 (16%)	8	29 (19%)	0	18 (27%)	1
ALS response	3925 (54%)	0	74 (49%)	0	64 (97%)	0
Use of advanced airway	6467 (87%)	5	145 (95%)	1	46 (70%)	1
Initial shockable rhythm	2274 (31%)	66	89 (58%)	0	32 (48%)	2
CPR to ROSC (min)	N/A	N/A	36 (32–41)	0	6.0 (3.5–11)	0
Initial ROSC prior to ED arrival	2313 (32%)	1476	98 (64%)	8	61 (92%)	0
Median no-flow Interval (min)	8 (6.4–10)	0	8.3 (6.6–10.5)	0	11 (11–12)	0
ROSC	3252 (44%)	56	152 (100%)	0	66 (100%)	0
Coronary angiography	N/A	N/A	N/A	N/A	30 (45%)	1
CABG	N/A	N/A	N/A	N/A	1 (2%)	3
Alive at discharge	802 (11%)	0	25 (16%)	0	66 (100%)	0
Favourable neurologic outcome at discharge	616 (8.4%)	0	15 (9.9%)	0	66 (100%)	0

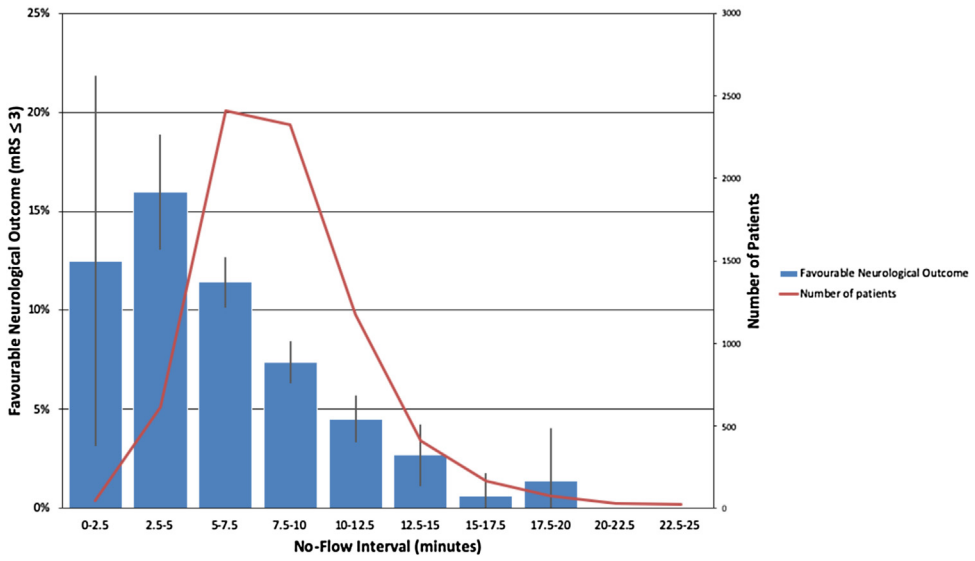

Fig. 2 – Proportion of cases with favourable neurological outcome in the full cohort, categorized by no-flow interval (with 95% confidence intervals). Each bar represents the percentage of patients with favourable outcome within each time period alone. The number of patients in each no-flow time period is represented by the red line.

more precise than previously described—can now be incorporated more objectively into patient management.

Remarkably, we found that in this cohort of patients without bystander CPR, overall survival was 11% and survival with favourable neurological outcomes over 8%. Further, while shorter no-flow intervals were associated with improved outcomes, there were still positive outcomes with no-flow intervals up to 20 min, which may help refine prognostic assessments in the prehospital and hospital environments. These results may provide a quality metric for EMS response, and a rationale for quality improvement initiatives to decrease EMS response times for suspected cardiac arrests. These should not be interpreted by the public and CPR training agencies as minimizing the importance of lay CPR since its relationship to survival is clearly established and this study shows that the shorter the time without CPR the better the outcome. However, it does show that even without optimum lay response, the patient can still survive with good neurologic function.

EMS systems have considerable variability in criteria for initiation and termination of resuscitation[26,27] and our data may assist EMS policy makers in these decisions. To illustrate, our local EMS system dictates that resuscitation may be withheld if “the patient has been unresponsive and without respirations and no CPR performed for

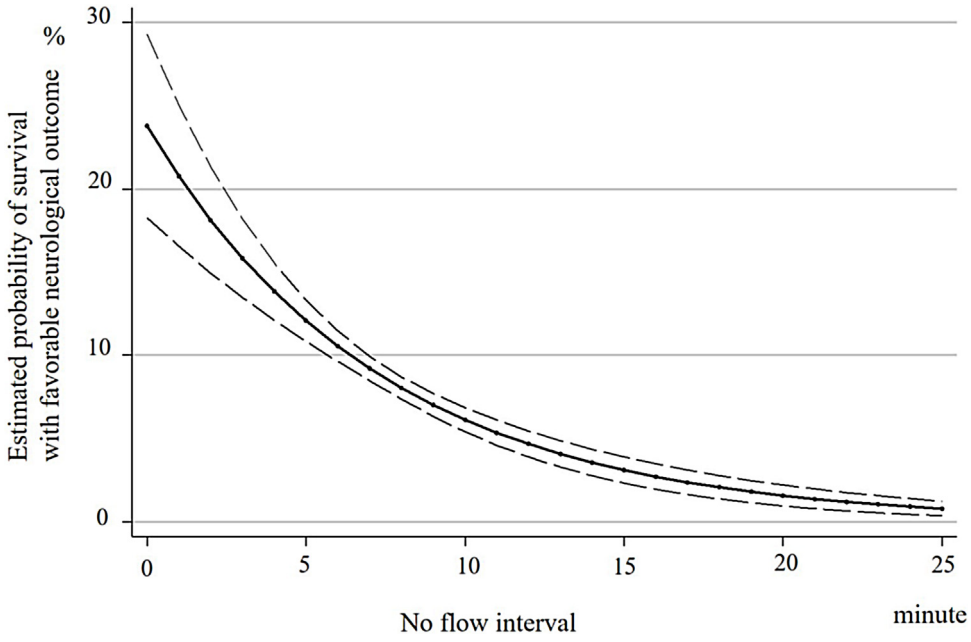

Fig. 3 – Adjusted probability of survival with favourable neurological outcome at hospital discharge as a function of no-flow interval in the full cohort (with 95% confidence intervals).

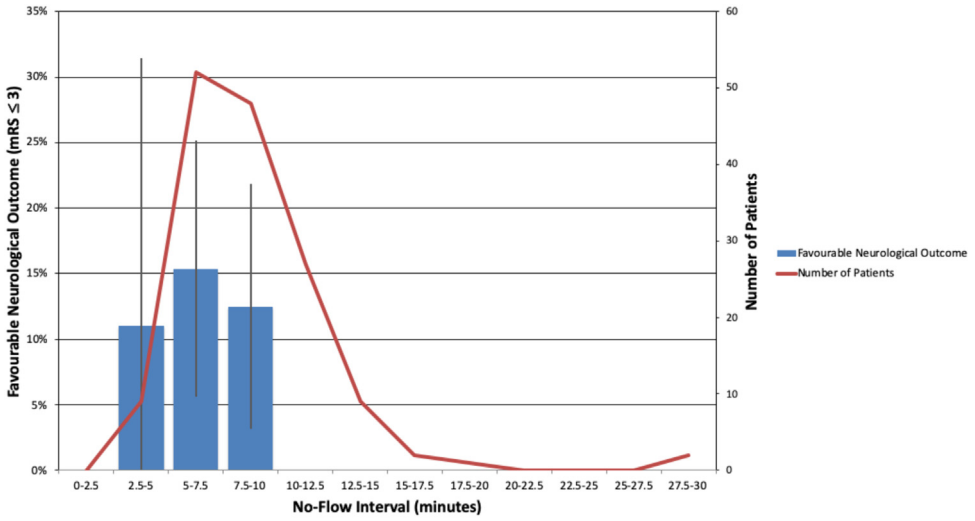

Fig. 4 – Proportion of cases with favourable neurological outcome in the ECPR eligible subgroup, categorized by no-flow interval (with 95% confidence intervals). Each bar represents the percentage of patients with favourable outcome within each time period alone. The number of patients in each no-flow time period is represented by the red line.

>15 minutes".[11] Unlike various termination of resuscitation rules that have used large cohorts to develop evidence-based guidelines for halting an in-progress resuscitation for futility, there are no corresponding guidelines advising EMS providers whether to initiate resuscitation or withhold efforts.[26–28] Our results show that favourable neurological outcome is possible after a no-flow interval up to 20 min. Perhaps with improvements in post ROSC resuscitative care, this could even be extended further. Our results indicate that EMS policies withholding resuscitation for those with no-flow intervals <20 min may require re-examination. This simple change could result in an increase in the proportion of patients who survive with good neurologic function.

ECPR is a resource-intensive treatment with low-quality of evidence suggesting favourable outcomes among carefully selected patients even after prolonged refractory OHCA.[29] No-flow interval often plays a role in candidacy assessment, with cut-off values typically below 5 or 10 min.[13,30] Given the low number of ECPR cases available to study, individual elements of ECPR eligibility criteria are based solely upon expert opinion. In view of the lack of evidence, we attempted to simulate the conditions of an ECPR-eligible treated patient—meeting specific criteria and having undergone a prolonged resuscitation —to examine the effect of no-flow interval. Our results suggest that ECPR cases with no-flow intervals >10 min are unlikely

to have positive outcomes. Knowledge of no-flow interval may also be useful consideration in deciding on use of other forms of mechanical circulatory support (e.g. Impella, ventricular assist devices), cardiac catheterization for angiography and percutaneous coronary intervention, as well as in neuroprognostication of post-cardiac arrest patients.

Our results support prior research. Larsen et al. analysed a cohort of OHCA patients with an initial VF rhythm and calculated an absolute 5.5% decline in survival per minute delay to CPR.[8] Subsequently, Adnet et al. described the inter-dependent relationship between no-flow interval and low-flow interval, after adjustment for baseline characteristics including initial rhythm.[7] They found that a no-flow interval greater than 12 min in association with a low-flow interval greater than 33 min yielded a probability of 30-day favourable neurological outcome of <1%. Our study is unique in isolating a large group of contemporary North American cases with witnessed arrests and no bystander CPR, from whom a reproducible no-flow interval could be calculated. Unlike other studies,[7,8] we excluded patients who had bystander CPR provided (for whom the time and quality of initial CPR is unclear) and EMS-witnessed arrests (for whom immediate CPR is assumed). Further, we did not adjust or limit our primary analysis to those with initial shockable rhythms: discovering a shockable rhythm on first rhythm analysis is associated with the preceding no-flow interval[25] and adjusting for this may obscure the true relationship.

Limitations

This was a retrospective analysis of prospectively collected data and conclusions are limited to association. Unmeasured variables could have influenced results. Although our study was conducted at multiple sites throughout North American, our observations may not be generalizable to other settings where patient characteristics and medical management differ. We created a specific study dataset (witnessed cardiac arrests without bystander CPR) that may have systematic differences from the overall study population, and thus results may not be generalizable. Due to changes in the 2010 AHA/ECC CPR Guidelines, there may have been differences in medical management between cases treated at different time periods, which may have affected our results.[31] The timing of the 9-1-1 call could have occurred either before, simultaneous with, or after the actual arrest. However, this uncertainty is also present for providers making patient management decisions; the time of 9-1-1 call is objective, available to clinicians, and the best and most consistent estimate of a clinically relevant no-flow interval. Our results may underestimate the possibility of survival due to prognostication bias. Once providers cease resuscitation due to a belief that it will be futile—due to prolonged no-flow-time, for example—unfavourable outcomes will be self-fulfilling. These patients would be classified as non-survivors, although some may have benefited if resuscitation attempts had been continued. Finally, the results stemming from our hypothetical ECPR cohort must be regarded cautiously given the assumptions in our model.

Conclusion

In a large population-based North American cohort of patients without bystander CPR, the probability of a favourable neurological outcome among OHCA cases decreases by 13% per additional minute from the 9-1-1 call until high quality CPR initiation, with the possibility of favourable outcomes up to 20 min.

Conflicts of interest

BG has received an honorarium for a speaking engagement with Stryker Corp. (Kalamazoo, MI).

Sources of funding

No commercial or academic financial support was provided to perform this specific study. BG is supported by the Michael Smith Foundation for Health Research. BG and FS are supported by the BC Emergency Medicine Network. The BC Cardiac Arrest Research Unit is supported by Heart and Stroke Foundation of Canada, the <GS0>BC Provincial Health Services Authority</GS4>, Providence Health Care, and the Canadian Institutes of Health Research.

Acknowledgements

We would like to acknowledge the original funding partners, staff, and EMS agencies of the Resuscitation Outcomes Consortium for their commitment to cardiac arrest research and quality improvement.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update. Circulation 2016;133:e29–e322, doi:http://dx.doi.org/10.1161/cir.0000000000000350.
2. Public Health Agency of Canada. Tracking heart disease and stroke in Canada. 2009. http://www.phac-aspc.gc.ca/publicat/2009/cvd-avc/pdf/cvd-avs-2009-eng.pdf.
3. Daya MR, Schmicker RH, Zive DM, et al. Out-of-hospital cardiac arrest survival improving over time: results from the Resuscitation Outcomes Consortium (ROC). Resuscitation 2015;91:108–15, doi:http://dx.doi.org/10.1016/j.resuscitation.2015.02.003.
4. Grunau B, Kawano T, Scheuermeyer F, et al. Early advanced life support attendance is associated with improved survival and neurologic outcomes after non-traumatic out-of-hospital cardiac arrest in a tiered prehospital response system. Resuscitation 2019;135:137–44, doi:http://dx.doi.org/10.1016/j.resuscitation.2018.12.003.
5. Hasselqvist-Ax I, Riva G, Herlitz J, et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. N Engl J Med 2015;372:2307–15, doi:http://dx.doi.org/10.1056/nejmoa1405796.
6. Wissenberg M, Lippert FK, Folke F, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013;310:1377–84, doi:http://dx.doi.org/10.1001/jama.2013.278483.
7. Adnet F, Triba M, Borron S, et al. Cardiopulmonary resuscitation duration and survival in out-of-hospital cardiac arrest patients. Resuscitation 2017;111:74–81, doi:http://dx.doi.org/10.1016/j.resuscitation.2016.11.024.
8. Larsen M, Eisenberg M, Cummins R, Hallstrom A. Predicting survival from out-of-hospital cardiac arrest: a graphic model. Ann Emerg Med 1993;22:1652–8. https://www.sciencedirect.com/science/article/pii/S0196064405813022%0Ahttp://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed3&NEWS=N&AN=1993319845.
9. Baeckgaard JS, Viereck S, Moller TP, Ersboll AK, Lippert F, Folke F. The effects of public access defibrillation on survival after out-of-

hospital cardiac arrest. Circulation 2017;136:954–65, doi:http://dx.doi.org/10.1161/CIRCULATIONAHA.117.029067.
10. Every Second Counts Rural and Community Access to Emergency Devices. 2013. https://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_301646.pdf.
11. Grunau B, Kawano T, Dick W, et al. Trends in care processes and survival following prehospital resuscitation improvement initiatives for out-of-hospital cardiac arrest in British Columbia, 2006–2016. Resuscitation 2018;125:118–25, doi:http://dx.doi.org/10.1016/j.resuscitation.2018.01.049.
12. Stub D, Bernard S, Pellegrino V, et al. Refractory cardiac arrest treated with mechanical CPR, hypothermia, ECMO and early reperfusion (the CHEER trial). Resuscitation 2015;86:88–94, doi:http://dx.doi.org/10.1016/j.resuscitation.2014.09.010.
13. Grunau B, Carrier S, Bashir J, et al. A comprehensive regional clinical and educational ECPR protocol decreases time to ECMO in patients with refractory out-of-hospital cardiac arrest. Can J Emerg Med 2017;19:424–33, doi:http://dx.doi.org/10.1017/cem.2017.376.
14. Temple A, Porter R. Predicting neurological outcome and survival after cardiac arrest. Contin Educ Anaesthesia, Crit Care Pain 2012;12:283–7, doi:http://dx.doi.org/10.1093/bjaceaccp/mks029.
15. Stiell IG, Nichol G, Leroux BG, et al. Early versus later rhythm analysis in patients with out-of-hospital cardiac arrest. N Engl J Med 2011;365:787–97, doi:http://dx.doi.org/10.1056/NEJMoa1010076.
16. Aufderheide TP, Nichol G, Rea TD, et al. A trial of an impedance threshold device in out-of-hospital cardiac arrest. N Engl J Med 2011;365:798–806, doi:http://dx.doi.org/10.1056/NEJMoa1010821.
17. Nichol G, Leroux B, Wang H, et al. Trial of continuous or interrupted chest compressions during CPR. N Engl J Med 2015;373:2203–14, doi:http://dx.doi.org/10.1056/nejmoa1509139.
18. Aufderheide TP, Kudenchuk PJ, Hedges J, et al. Resuscitation Outcomes Consortium (ROC) PRIMED cardiac arrest methods. Part 1: rationale and methodology for the impedance threshold device (ITD) protocol. Resuscitation 2008;78:179–85, doi:http://dx.doi.org/10.1038/jid.2014.371.
19. Stiell IG, Callaway CW, Davis D, et al. Resucitation Outcomes Consortium (ROC) PRIMED cardiac arrest trial methods. Part 2: Rationale and methodology for “analyze later” protocol. Resuscitation 2008;78:186–95, doi:http://dx.doi.org/10.1038/jid.2014.371.
20. Brown SP, Wang H, Aufderheide TP, et al. A randomized trial of continuous versus interrupted chest compressions in out-of-hospital cardiac arrest: rationale for and design of the Resuscitation Outcomes Consortium Continuous Chest Compressions Trial. Am Heart J 2015169:, doi:http://dx.doi.org/10.1016/j.ahj.2014.11.011 334–341.e5.
21. Stiell I, Nichol G, Leroux B, et al. Early vs later rhythm analysis in patients with out-of-hospital cardiac arrest. N Engl J Med 2011;365:787–97.
22. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the International Liaison Committee on Resusci. Circulation 2004;110:3385–97, doi:http://dx.doi.org/10.1161/01.CIR.0000147236.85306.15.
23. Reynolds JC, Frisch A, Rittenberger JC, Callaway CW. Duration of resuscitation efforts and functional outcome after out-of-hospital cardiac arrest: when should we change to novel therapies? Circulation 2013;128:2488–94, doi:http://dx.doi.org/10.1161/CIRCULATIONAHA.113.002408.
24. Stiell IG, Wells GA, DeMaio VJ, et al. Modifiable factors associated with improved cardiac arrest survival in a multicenter basic life support/defibrillation system: OPALS study phase I results. Ann Emerg Med 1999;33:44–50, doi:http://dx.doi.org/10.1016/S0196-0644(99)70415-4.
25. Tanguay-Rioux X, Grunau B, Neumar R, Tallon J, Boone R, Christenson J. Is initial rhythm in OHCA a predictor of preceding no flow time? Implications for bystander response and ECPR candidacy evaluation. Resuscitation 2018;128:88–92, doi:http://dx.doi.org/10.1016/j.resuscitation.2018.05.002.
26. Brooks SC, Schmicker RH, Cheskes S, et al. Variability in the initiation of resuscitation attempts by emergency medical services personnel during out-of-hospital cardiac arrest. Resuscitation 2017;117:102–8, doi:http://dx.doi.org/10.1016/j.resuscitation.2017.06.009.
27. Morrison LJ. Prehospital termination of resuscitation rule. Curr Opin Crit Care 2019;25:199–203, doi:http://dx.doi.org/10.1097/MCC.0000000000000614.
28. Morrison LJ, Visentin LM, Kiss A, et al. Validation of a rule for termination of resuscitation in out-of-hospital cardiac arrest. N Engl J Med 2006;355:478–87, doi:http://dx.doi.org/10.1056/NEJMoa052620.
29. Ortega-Deballon I, Hornby L, Shemie SD, Bhanji F, Guadagno E. Extracorporeal resuscitation for refractory out-of-hospital cardiac arrest in adults: a systematic review of international practices and outcomes. Resuscitation 2016;101:12–20, doi:http://dx.doi.org/10.1016/j.resuscitation.2016.01.018.
30. Le Guen M, Nicolas-Robin A, Carreira S, et al. Extracorporeal life support following out-of-hospital refractory cardiac arrest. Crit Care 2011;15:1–9, doi:http://dx.doi.org/10.1186/cc9976.
31. Field JM, Hazinski MF, Sayre MR, Part 1: Executive summary 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care 2010;122:640–56, doi:http://dx.doi.org/10.1161/CIRCULATIONAHA.110.970889.