

Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

Time of on-scene resuscitation in out of-hospital cardiac arrest patients transported without return of spontaneous circulation



Corina de Graaf*, Stefanie G. Beesems, Rudolph W. Koster

Amsterdam UMC, Academic Medical Center, Heart Center, Department of Cardiology, Meibergdreef 9, Amsterdam, The Netherlands

Abstract

Background: In out-of-hospital cardiac arrest (OHCA), return of spontaneous circulation (ROSC) on scene occurs only in a minority of patients. The optimal duration of resuscitation on scene before transport with ongoing cardiopulmonary resuscitation (CPR) is unknown.

Purpose: To determine the time of resuscitation on scene ("time on scene") and survival in patients transported with ongoing CPR in the Netherlands.

Methods: Data on OHCA patients (>18 years) without ROSC on scene, where resuscitation was started between January 1, 2012 and December 31, 2016 in the Amsterdam Resuscitation Study (ARREST) database were analyzed. Time on scene was related to 30-day survival.

Results: Of the 5871 OHCA patients where resuscitation was started, 2437 did not achieve ROSC on scene. Of these, 655 patients were transported with ongoing CPR and 606 (93%) had complete rhythm data. At the moment of transport, 199 (33%) patients had a shockable rhythm, 299 (49%) pulseless electrical activity (PEA) and 108 (18%) asystole as rhythm. Twenty-nine patients (4%) were alive at 30 days. Patients who survived 30 days had a higher proportion of a shockable first monitored rhythm (89% vs. 52%, $p < 0.001$). Survivors had a significantly shorter time on scene (20 min vs. 26 min, $p = 0.004$), with the highest survival rate (8%) in patients transported within 20 min. In a multivariable model time on scene (OR 0.94; 95%CI 0.89–0.99) was independently associated with 30-day survival.

Conclusion: In OHCA patients transported with ongoing CPR the survival rate significantly declines when time on scene increases.

Keywords: Out-of-hospital cardiac arrest (OHCA), Return of spontaneous circulation (ROSC), Cardiopulmonary resuscitation (CPR), Advanced life support (ALS), Emergency medical services (EMS), Transport with ongoing CPR, Time of resuscitation on scene, Survival, Rhythm at moment of transport

Introduction

In out-of-hospital cardiac arrest (OHCA) patients, advanced life support does result in return of spontaneous circulation (ROSC) on scene in a minority of patients, ranging between 15% and 45%.^{1–5} Survival of patients transported with ongoing CPR is low, but there is sufficient evidence that transport is not futile (above a 1% futility rate⁶) and should be considered.^{1,4,7} While the termination of resuscitation

guidelines apply to approximately 30% of patients with OHCA, many patients that do not meet these criteria, do not achieve ROSC on scene.^{8,9} Positive patient and process characteristics associated with survival to hospital discharge in patients transported with ongoing CPR are bystander-witnessed arrest, initial shockable rhythm, public location and emergency medical services (EMS) witnessed arrest.^{1,3,5}

What is the optimal moment to decide to initiate transport with ongoing CPR? According to the European Resuscitation Council

* Corresponding author at: Amsterdam UMC, Academic Medical Center, Department of Cardiology, Room XT4-110, P.O. Box 22660, 1100 DD Amsterdam, The Netherlands.

E-mail address: c.degraaf@amc.uva.nl (C. de Graaf).

<http://dx.doi.org/10.1016/j.resuscitation.2019.03.030>

Received 20 December 2018; Received in revised form 5 March 2019; Accepted 19 March 2019

0300-9572/© 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

(ERC) guidelines in 2015 the decision to transport with ongoing CPR should be weighed after 10 min of passed on-scene resuscitation, however this time is not supported with data.¹⁰ The American Heart Association (AHA) guidelines of 2010 recommend optimizing care on scene to achieve ROSC rather than transport with ongoing CPR, but give no specific guidance when to transport to the hospital if ROSC is not achieved.¹¹ The AHA guideline is not updated on this topic in 2015.

Currently, it is unclear at what time in the resuscitation process the decision to transport a patient with ongoing CPR should be made. Emergency medical services (EMS) have to take in account the risk of transporting an unstable patient in a moving vehicle who may have achieved ROSC if resuscitation efforts on scene had continued longer. The aim of this study is to determine the relation between time on scene and survival in patients transported with ongoing CPR, in a system in which extracorporeal cardiopulmonary resuscitation (ECPR) was not yet implemented.

Methods

Study setting and design

This study was performed using data from the Amsterdam Resuscitation Study (ARREST). The ARREST study is an ongoing prospective registry of all-cause OHCA in North-Holland, a province of the Netherlands. The registry was established to identify the determinants of outcome of OHCA.^{12,13} The study region covers an area of 2404 km² and had a population of 2.8 million in 2015.¹⁴ All adult OHCA patients (>18 years) without ROSC on scene, between January 1, 2012 to December 31, 2016, were included. Exclusion

criteria were (transient) ROSC prior to transport and unknown survival status. Patients with complete data considering the first monitored rhythm, the rhythm at the start of transport and rhythm at hospital arrival were analyzed to identify the different rhythms and survival. The medical ethics review board of the Amsterdam UMC, Academic Medical Center, approved the study (nr. W18_231 # 18.276).

EMS system in the study region

In a medical emergency, the national emergency number will be dialed and if the dispatcher suspects an OHCA, two EMS teams are dispatched. Each ambulance is equipped with a manual defibrillator and manned with a driver, who is qualified to perform Basic Life Support (BLS), and a paramedic, who is qualified to perform Advanced Life Support (ALS). In addition, first responders, equipped with an automated external defibrillator (AED), are dispatched. These first responders are firefighters, police officers and/or citizen-responders, trained in BLS and AED use. Also, many public areas in the study region have AEDs and every individual in the study region is allowed to use these AEDs.

In the study region three dispatch centers participated, each with one EMS agent. The EMS follows a national protocol for cardiac arrest based on the European guidelines.^{15,16} In the national protocol it is stated, when a patient despite resuscitation efforts does not achieve ROSC, EMS can consider termination of resuscitation after 20 min of ALS in case of a non-shockable rhythm and in the absence of a reversible cause. Early transport is to be considered early in the process e.g., after 10 min of ALS without ROSC in patients with ventricular fibrillation (VF), ventricular tachycardia (VT) or treatable cause, but at what precise moment a

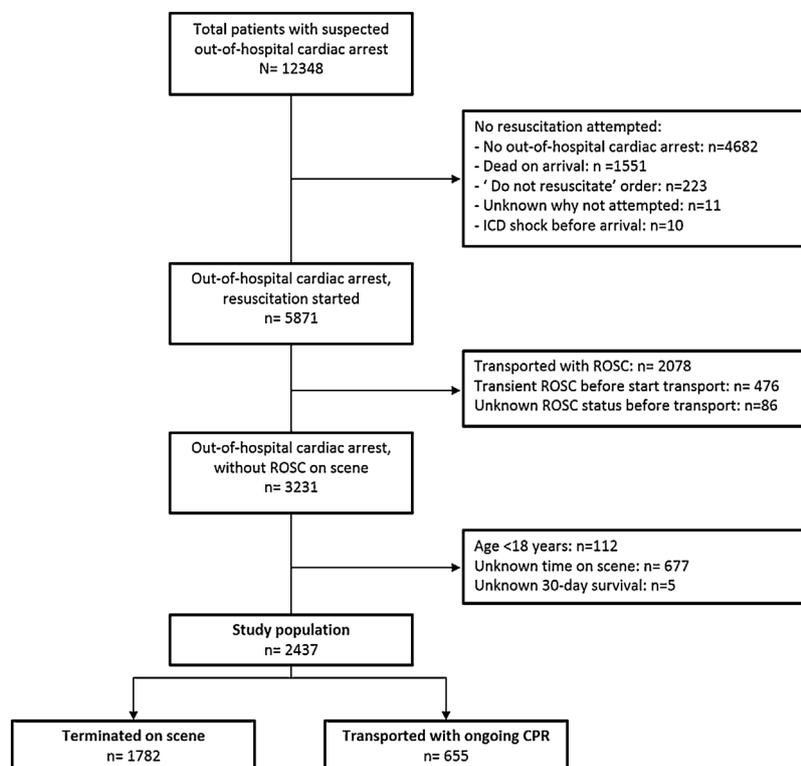


Fig. 1 – Flowchart of patient inclusion. In 5871 cases EMS personnel attempted to resuscitate of which 3231 without ROSC on scene, including 2437 patients aged ≥ 18 years with complete survival data (died on scene: $n = 1782$; transported with ongoing CPR: $n = 655$). Years 2012–2016 in the Netherlands.

decision to transport with ongoing CPR should be initiated is not described in the national protocol and the ERC Guidelines, nor what specific criteria are involved in such a decision. Physicians are not part of the standard dispatched EMS team and the paramedic is qualified and legally allowed to make termination of resuscitation decisions without consulting a physician in the pre-hospital setting. During the study period, in two of the three participating regions a mechanical CPR device was available in the ambulance. There were no hospitals in the region that used ECPR as a treatment strategy in OHCA patients.

Data collection

If a resuscitation is attempted by EMS, EMS routinely sends the continuous electrocardiography (ECG) from their manual defibrillator and EMS run report to the ARREST study center. In addition, the paramedic also answers a pre-determined set of questions considering specifics of the patient and condition before and during transport. If an AED was connected before the ambulance defibrillator, ARREST study personnel visited the AED site shortly after OHCA to collect the AED ECG recording. The ECG from the EMS manual defibrillator and AED were stored and analyzed with dedicated software. Clock drift of defibrillators and AEDs was corrected to standardized times for each recording. Data were registered using the Utstein templates for resuscitation registries.¹⁷ Data from the EMS manual defibrillator and AED ECG were analyzed to document the first monitored rhythm, the

rhythm at moment of transport, time of the first defibrillation and time of first mechanical CPR compression (if mechanical CPR was used).

Time intervals and definitions

Time-stamped data on emergency call at dispatch center, EMS arrival on scene, EMS departure from scene and arrival at the emergency department (ED) were collected to create time intervals. EMS arrival on scene was defined as the moment the EMS manual defibrillator was connected to the patient. The 'time on scene' of EMS was the interval between EMS arrival on scene and departure of the ambulance from the scene. In cases of EMS witnessed arrests, 'time on scene' was the interval between collapse and departure of the ambulance from the scene. If the resuscitation was terminated on scene, 'time on scene' was the interval between EMS arrival and disconnection of the EMS manual defibrillator at the moment of termination. 'The 'total prehospital time' was the time between the emergency call at the dispatch center and the arrival at the ED. Information considering (transient) ROSC was collected from the EMS report and defined as: a palpable pulse or a measurable blood pressure.

Outcome

The outcome of this study was overall 30-day survival, based on information from the National Civil Registry.

Table 1 – Baseline characteristics of OHCA patients who died on scene and patients transported with ongoing CPR.

	No ROSC and died on scene N = 1782	No ROSC and transported N = 655	p-Value	Missing n (%)
Pre-OHCA factors				
Age, years, mean (SD)	68 (15)	63 (15)	<0.001	–
Sex, n (%)			<0.001	–
Male	1193 (67%)	518 (79%)		
Female	589 (33%)	137 (21%)		
Resuscitation parameters				
First monitored rhythm, n (%) ^a			<0.001	38 (1.6%)
Shockable (VF/VT)	236 (13%)	345 (54%)		
Not shockable	1524 (87%)	294 (46%)		
Presumed cause, n (%)			<0.001	–
Cardiac	1645 (92%)	577 (88%)		
Not cardiac	137 (8%)	78 (12%)		
Location of arrest, n (%)			<0.001	1
Residential	1495 (84%)	397 (61%)		(<0.01%)
Public	286 (16%)	258 (39%)		
Witnessed arrest, n (%)			<0.001	19 (0.8%)
Not witnessed	826 (47%)	133 (21%)		
EMS witnessed	62 (3%)	87 (13%)		
Bystander witnessed	880 (50%)	430 (66%)		
Bystander CPR, n (%) ^b			0.89	16 (0.7%)
Bystander CPR	1370 (81%)	452 (81%)		
No Bystander CPR	322 (19%)	109 (19%)		
Time intervals				
Call to first defibrillation, minutes, median (IQR 25,75) ^c	12 (9,23)	10 (8,17)	<0.001	10 (1.5%)
Response time, minutes, median (IQR 25,75)	12 (10,15)	12 (9,15)	0.002	3 (<0.01%)
Time on scene, minutes, median (IQR 25,75)	23 (17,28)	25 (19,32)	<0.001	–

CPR – cardiopulmonary resuscitation; VF/VT – ventricular fibrillation/tachycardia; EMS – emergency medical services; SD – standard deviation; IQR – inter-quartile range; ED – emergency department. Percentages shown are column percentages.

^a In case of EMS witnessed, first monitored rhythm is rhythm at collapse.

^b If not EMS witnessed.

^c If shockable rhythm.

Statistical analysis

Categorical variables were presented as percentages and continuous variables as mean and standard deviation (SD) or as median and interquartile range (IQR) depending on the data distributions. Chi-square statistics were used to compare categorical data. For continuous data unpaired t-test or Mann-Whitney U test was used when appropriate. A multivariable logistic regression model was used to investigate independent associations between time on scene and 30-day survival. A stepwise-forward approach was used with variables significantly associated in univariate analysis (p-value <0.05). In the model, the number of events per variable was 10.¹⁸ Consequently, in this study a maximum of 3 variables were allowed in the model. Associations were reported as odds ratio with 95% confidence intervals (CI) and associated p values. The Hosmer-Lemeshow test was used to test the model for goodness of fit. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS statistics 24 (IBM Corporation, Armonk, NY).

Results

Out of 12,348 patients with suspected OHCA in the study period, 5871 had attempted resuscitation by EMS. Of these, 3231 patients did not achieve ROSC on scene of which, after exclusion, 2437 patients were

included for analysis. In 1782 patients the resuscitation was terminated on scene and 655 patients were transported with ongoing CPR (Fig. 1).

Baseline patient and process characteristics

Patient and process characteristics of patients without ROSC on scene are shown in Table 1. Patients who were transported with ongoing CPR were significantly younger, had a higher proportion of shockable first monitored rhythm, had their arrest more often in public locations, and the arrest was more often witnessed, compared to patients without ROSC and a resuscitation that was terminated on scene. In patients who were not transported, the median time on scene before termination of resuscitation was 23 (IQR 17, 28) min. Patients transported with ongoing CPR had a median time on scene of 25 (IQR 19, 32) min before the start of transport. The regional EMS agencies with mechanical CPR devices utilized it in 83% of the cases, with a median connection time of 3 min after EMS arrival.

First monitored rhythm, rhythm at moment of transport and rhythm at ED arrival

Of all patients transported with ongoing CPR, 606 (93%) had complete data on the time of first monitored rhythm, the rhythm at moment of transport and rhythm at ED arrival. The rhythms at different stages in

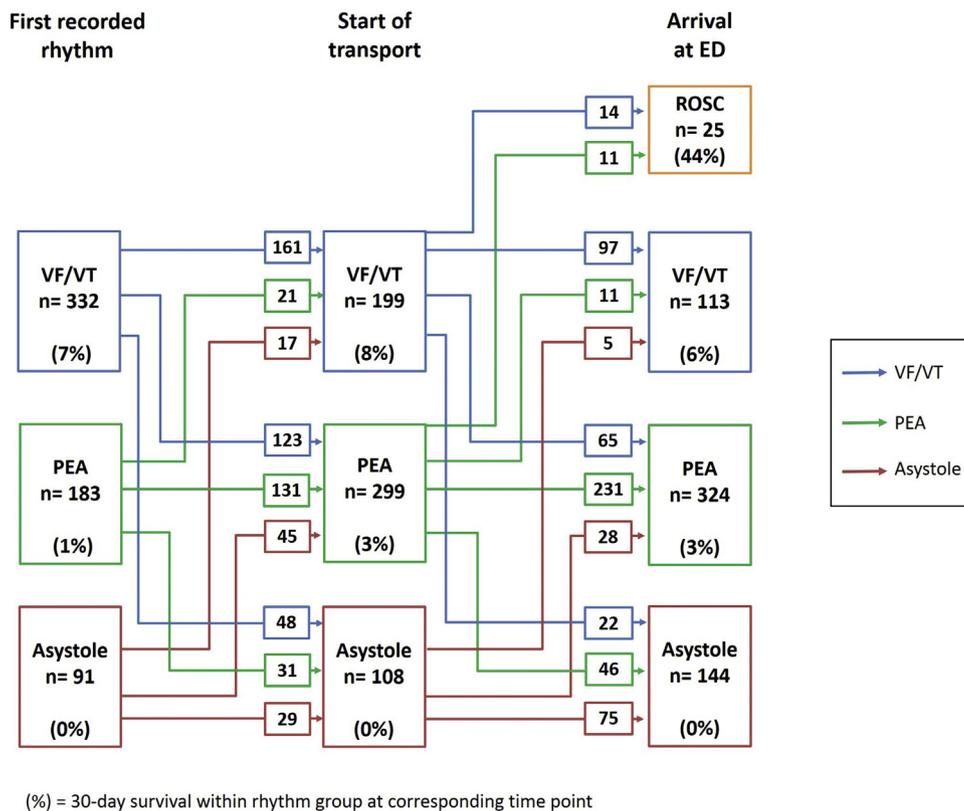


Fig. 2 – Rhythm and 30-day survival at different time points during resuscitation of patients transported with ongoing CPR. Of the 655 patients transported with ongoing CPR, 609 (95%) had complete data on rhythm at EMS arrival, moment of transport at arrival at ED. The arrows correspond with the number of cases and rhythms indicated with the color. (For example: of the 332 cases with a shockable VF/VT rhythm as first recorded rhythm, 161 also had a shockable VF/VT rhythm at moment of transport). Survival is calculated within each rhythm group at the different time points. (For example: of 199 patients with a shockable rhythm (VF/VT) at moment of transport 16 (8%) survived).

the resuscitation are illustrated in Fig. 2. At the moment of transport, 199 (33%) patients had VF/VT, 299 (49%) pulseless electrical activity (PEA) and 108 (18%) asystole as rhythm. At ED arrival 25 patients (4%) had ROSC, leaving 113 (19%) with VF/VT, 324 (53%) with PEA and 144(24%) with asystole.

Outcome

Of the 655 transported patients, 544 died in the emergency room, 111 (17%) were admitted to the hospital and 29 (4%) survived 30 days. Patient and process characteristics of survivors vs non-survivors are shown in Table 2. Patients who survived 30 days had a higher proportion of a shockable first monitored rhythm (89% vs. 52%, $p < 0.001$) and a higher proportion of shockable rhythm at moment of transport (63% vs.31%, $p = 0.001$) compared to patients who died. Fig. 2 shows the survival within the rhythm groups and corresponding rhythms of patients at the time of first monitored rhythm, the moment of transport and ED arrival. During transport 25 of 606 (4%) patients achieved ROSC, and 44% of these patients survived. In patients, transported with ongoing CPR, at every time point a shockable rhythm resulted in the highest survival, 7% at moment of first monitored rhythm, 8% at start of transport and 6% at ED arrival respectively. PEA

at the moment of first monitored rhythm was associated with a survival of 1% and a survival of 3% at moment of transport and ED arrival. None of the patients with asystole at any time point survived.

Time on scene and 30-day survival

Patients who survived had a significant shorter time on scene (20 min vs. 26 min, $p = 0.003$). Fig. 3 shows there was a significant trend between time spent on scene and 30-day survival (p for trend = 0.014). In a multivariable model (Table 3) time on scene was independently associated with 30-day survival (OR 0.94; 95%CI 0.89–0.99); for every minute longer time on scene before transport, the odds of 30-day survival decreased by 6%. First rhythm VF/VT and response time were also independently associated with 30-day survival. Rhythm at transport VF/VT was not independently associated with 30-day survival in the multivariable model.

Discussion

Our study showed that in OHCA patients transported with ongoing CPR the survival rate significantly declined when time on scene

Table 2 – Characteristics of surviving and non-surviving patients transported with ongoing CPR.

	Died N=626	30-day survival N = 29	p-Value	Missing n (%)
Pre-OHCA factors				
Age, years, mean (SD)	63 (15)	61 (14)	0.34	–
Sex			0.34	–
Male, n (%)	493 (79%)	25 (86%)		
Female, n (%)	133 (21%)	4 (14%)		
Resuscitation parameters				
First monitored rhythm, n (%) ^a			<0.001	16 (2.4%)
Shockable (VF/VT)	320 (52%)	25 (89%)		
Not shockable	291 (48%)	3 (11%)		
Presumed cause, n (%)			0.15	–
Cardiac	549 (88%)	28 (97%)		
Not cardiac	77 (12%)	1 (3%)		
Location of arrest, n (%)			0.54	–
Residential	381 (61%)	16 (55%)		
Public	245 (39%)	13 (45%)		
Witnessed arrest, n (%)			0.06	5 (0.8%)
Not witnessed	131 (21%)	2 (7%)		
Witnessed	490 (79%)	27 (27%)		
CPR before EMS arrival			0.10	2 (0.3%)
No bystander CPR	100 (16%)	9 (31%)		
EMS witnessed	83 (13%)	4 (14%)		
Bystander CPR	436 (71%)	16 (55%)		
Rhythm at moment of transport, n (%)			0.001	33 (5.0%)
Shockable (VF/VT)	187 (31%)	17 (63%)		
Not shockable	408 (69%)	10 (37%)		
Time intervals				
Call to first defibrillation, minutes, median (IQR 25,75) ^b	10 (8,17)	9 (6,12)	0.06	10 (1.5%)
Response time, minutes, median (IQR 25,75)	12 (9,15)	10 (8,14)	0.008	–
Time on scene, minutes, median (IQR 25,75)	26 (20,32)	20 (15,26)	0.003	–
Transport time to ED, minutes, median (IQR 25,75)	8 (5,12)	8 (6,14)	0.45	13 (2.0%)
Total prehospital time, minutes, median (IQR 25,75)	47 (39,55)	45 (36,51)	0.02	13 (2.0%)

CPR – cardiopulmonary resuscitation; VF/VT – ventricular fibrillation/tachycardia; EMS – emergency medical services; SD – standard deviation; IQR – interquartile range; ED – emergency department. Percentages shown are column percentages.

^a In case of EMS witnessed, first monitored rhythm is rhythm at collapse.

^b If shockable rhythm.

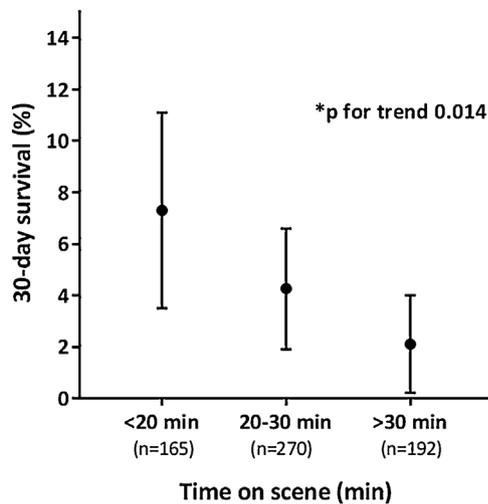


Fig. 3 – Time on scene intervals and 30-day survival of patients transported with ongoing CPR. Of 178 patients which were transported within 20 min of time on scene, 13 (7%) survived. Of the 282 patients transported after 20–30 min, 12 (4%) survived and of 195 patients transported after 30 min, 4 (2%) survived.

increased. Patients with a shockable rhythm as first monitored rhythm and patients with a shockable rhythm at the moment of transport had the highest probability to survive 30 days.

The overall survival of patients transported with ongoing CPR in this study was 4% which is higher than the accepted limit of medical futility.⁶ This is in accordance with previous studies which found survival rates of 3.6% and 6%.^{1,7} The highest survival rate was found in patients transported within 20 min of on-scene resuscitation and patients with a shockable first monitored rhythm. Furthermore, time on scene was independently associated with 30-day survival. This suggests that a shorter time on scene is associated with a higher probability of survival.

In our study besides time on scene, a first monitored rhythm VF/VT was associated with better 30-day survival in the patients transported without ROSC, which is consistent with the guidelines.¹⁰ Yates et al found a survival rate of 1.3% in patients transported with ongoing CPR; all survivors had a shockable first rhythm.⁴ Our study showed that patients with a shockable rhythm had the highest chances of 30-day survival with a survival rate at moment of first monitored rhythm and moment of transport of respectively 7% and 8%, but patients with PEA

had a survival rate of respectively 1% and 3%. There were no patients with asystole that survived to 30 days.

Although transport should be considered, transporting a patient with ongoing CPR is associated with interruptions in CPR and possible lower survival rate.^{19–21} This could be a factor why paramedics may choose to stay longer on scene in non-public locations where moving the patient into an ambulance with ongoing CPR may be challenging. In addition, manual CPR in a moving ambulance reduces the quality of CPR and is potentially harmful to the paramedic.^{22,23} To facilitate and support earlier transport in patients without ROSC, the quality of CPR and safety of the paramedics during transport needs to be ensured. The use of mechanical CPR could facilitate this and accelerate the decision to transport with ongoing CPR.^{22,24}

At the beginning of resuscitation, it is not known which patients will achieve ROSC and at what time. In our study 5% of all transported patients without ROSC had ROSC at hospital arrival, suggesting they could have achieved ROSC on scene before start of transport if EMS had continued their resuscitation on scene. Earlier studies describe that in OHCA patients, the first 10–15 min of standard ALS strategies are most effective and after 15 min the probability of survival with good neurologic outcome decreases.^{25,26} In our study there were insufficient patients transported within 10 or 15 min to analyze the potential benefit of earlier initiation of transport than 20 min.

There is a need for novel treatment strategies for patients who do not respond to conventional resuscitation after the first 15 min. The use of ECPR in OHCA is a new strategy, which improves the chances of survival in a selected group of OHCA patients.²⁷ Although randomized studies are lacking, the use of ECPR may be a beneficial therapy, especially when there is a short low-flow time and early ECPR initiation.^{28–30} Grunau et al. suggests that the window to transport for ECPR is between 8 to 24 min, with 16 min as the optimal moment to transport balancing the risks between early transport with ongoing CPR and the possibility of achieving ROSC on scene.²⁵ Our study suggests that a delay to transport for more than 20 min is already associated with lower survival.

Limitations

First, the precise reason for the decision to transport patients with ongoing CPR and terminate CPR in others was not documented. A selection mechanism could be present that our analysis did not detect. Second, this study did not include data considering hospital care and 30-day survival could be affected by interventions such as coronary revascularisation.^{31,32} Finally, due to the observational character of this prospective cohort, only an association and not causality between time on scene and survival could be determined. Therefore, our study

Table 3 – Multivariable logistic stepwise forward regression of variables associated with 30-day survival.

	Unadjusted		Adjusted	
	OR (95% CI)	p-Value	OR (95% CI) ^a	p-Value
Time on scene	0.93 (0.89–0.98)	0.004	0.94 (0.89–0.99)	0.02
First rhythm: VF/VT	7.58 (2.26–25.36)	0.001	10.52 (2.36–43.96)	0.002
Response time	0.88 (0.80–0.98)	0.02	0.85 (0.76–0.96)	0.007
Rhythm at transport: VF/VT	3.71 (1.67–8.26)	0.001	–	–

Hosmer and Lemeshow test P 0.55.

OR – odds ratio; CI – confidence interval; ROSC – return of spontaneous circulation; VF/VT – ventricular fibrillation/tachycardia.

^a Variables put in model stepwise forward: first rhythm, response time, time on scene, rhythm at moment of transport.

does not answer the question if an even earlier decision on scene to transport without ROSC would have resulted in even higher survival.

Future research

It remains unclear why a patient is transported with ongoing CPR in some situations, but the resuscitation is terminated in others. Future qualitative studies will explore medical and non-medical factors that are not specified in the ambulance guidelines and that appear to contribute to the decision.

Conclusion

In OHCA patients transported with ongoing CPR the survival rate significantly declines when time on scene increases. Patients transported within 20 min of time on scene have the highest survival rate, this suggests the decision to transport with ongoing CPR needs to be made early in the resuscitation process.

Funding

The ARREST database is maintained by an unconditional grant of Physio Control Inc., part of Stryker, Redmond, WA.

Conflict of interest

Author CG received a speaker's fee from Stryker. RWK is the recipient of the funding for maintaining the ARREST database.

Acknowledgements

We thank all dispatch centers, ambulance services and first responders for their cooperation in the ongoing data collection. We are greatly indebted to Paulien Homma, Remy Stieglis and Sandra de Haas for their support in the data collection.

REFERENCES

- Drennan IR, Lin S, Sidalak DE, Morrison LJ. Survival rates in out-of-hospital cardiac arrest patients transported without prehospital return of spontaneous circulation: an observational cohort study. *Resuscitation* 2014;85:1488–93.
- Hawkes C, Booth S, Ji C, et al. Epidemiology and outcomes from out-of-hospital cardiac arrests in England. *Resuscitation* 2017;110:133–40.
- Stub D, Nehme Z, Bernard S, Lijovic M, Kaye DM, Smith K. Exploring which patients without return of spontaneous circulation following ventricular fibrillation out-of-hospital cardiac arrest should be transported to hospital? *Resuscitation* 2014;85:326–31.
- Yates EJ, Schmidbauer S, Smyth AM, et al. Out-of-hospital cardiac arrest termination of resuscitation with ongoing CPR: an observational study. *Resuscitation* 2018;130:21–7.
- Zive D, Kowicz K, Schmidt T, et al. Variation in out-of-hospital cardiac arrest resuscitation and transport practices in the Resuscitation Outcomes Consortium: ROC Epistry-Cardiac Arrest. *Resuscitation* 2011;82:277–84.
- Schneiderman LJ. Defining medical futility and improving medical care. *J Bioeth Inq* 2011;8:123–31.
- Eisenburger P, Havel C, Sterz F, et al. Transport with ongoing cardiopulmonary resuscitation may not be futile. *Br J Anaesth* 2008;101:518–22.
- Morrison LJ, Verbeek PR, Vermeulen MJ, et al. Derivation and evaluation of a termination of resuscitation clinical prediction rule for advanced life support providers. *Resuscitation* 2007;74:266–75.
- Morrison LJ, Verbeek PR, Zhan C, Kiss A, Allan KS. Validation of a universal prehospital termination of resuscitation clinical prediction rule for advanced and basic life support providers. *Resuscitation* 2009;80:324–8.
- Bossaert LL, Perkins GD, Askitopoulou H, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 11. The ethics of resuscitation and end-of-life decisions. *Resuscitation* 2015;95:302–11.
- Morrison LJ, Kierzek G, Diekema DS, et al. Part 3: ethics: 2010 American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010;122:970905.
- Bardai A, Berdowski J, van der Werf C, et al. Incidence, causes, and outcomes of out-of-hospital cardiac arrest in children. A comprehensive, prospective, population-based study in the Netherlands. *J Am Coll Cardiol* 2011;57:1822–8.
- Blom MT, Beesems SG, Homma PC, et al. Improved survival after out-of-hospital cardiac arrest and use of automated external defibrillators. *Circulation* 2014;130:1868–75.
- Centraal Bureau Statistiek: Bevolking, geslacht, leeftijd en burgerlijke staat per regio januari 2015, 2016. (Accessed 22 August 2016, at <http://statline.cbs.nl/Statweb/publication/?DM=SLNL&PA=03759NED&D1=0&D2=129&D3=1-128,130-797&D4=27&HDR=T&STB=G2,G1,G3&VW=T>).
- in' t VC, van EP, Rombouts M, et al. Landelijk Protocol Ambulancezorg Versie 8, 2014. 3/1/2014.
- Perkins GD, Handley AJ, Koster RW, et al. European Resuscitation Council Guidelines for resuscitation 2015: section 2. Adult basic life support and automated external defibrillation. *Resuscitation* 2015;95:81–99.
- 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 Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385–97.
- Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol* 1996;49:1373–9.
- Cheskes S, Schmicker RH, Christenson J, et al. Perishock pause: an independent predictor of survival from out-of-hospital shockable cardiac arrest. *Circulation* 2011;124:58–66.
- Christenson J, Andrusiek D, Everson-Stewart S, et al. Chest compression fraction determines survival in patients with out-of-hospital ventricular fibrillation. *Circulation* 2009;120:1241–7.
- Krurup NH, Terkelsen CJ, Johnsen SP, et al. Quality of cardiopulmonary resuscitation in out-of-hospital cardiac arrest is hampered by interruptions in chest compressions—a nationwide prospective feasibility study. *Resuscitation* 2011;82:263–9.
- Fox J, Fiechter R, Gerstl P, et al. Mechanical versus manual chest compression CPR under ground ambulance transport conditions. *Acute Card Care* 2013;15:1–6.
- Olasveengen TM, Wik L, Steen PA. Quality of cardiopulmonary resuscitation before and during transport in out-of-hospital cardiac arrest. *Resuscitation* 2008;76:185–90.
- Gyory RA, Buchle SE, Rodgers D, Lubin JS. The efficacy of LUCAS in prehospital cardiac arrest scenarios: a crossover mannequin study. *West J Emerg Med* 2017;18:437–45.
- Grunau B, Reynolds J, Scheuermeyer F, et al. Relationship between time-to-ROSC and survival in out-of-hospital cardiac arrest ECPR

- candidates: when is the best time to consider transport to hospital? *Prehosp Emerg Care* 2016;1–8.
26. 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.
 27. Holmberg MJ, Geri G, Wiberg S, et al. Extracorporeal cardiopulmonary resuscitation for cardiac arrest: a systematic review. *Resuscitation* 2018;131:91–100.
 28. Debaty G, Babaz V, Durand M, et al. Prognostic factors for extracorporeal cardiopulmonary resuscitation recipients following out-of-hospital refractory cardiac arrest. A systematic review and meta-analysis. *Resuscitation* 2017;112:1–10.
 29. Chen YS, Lin JW, Yu H-Y, Ko W-J, 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;372:554–61.
 30. 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.
 31. Cha WC, Lee SC, Shin SD, Song KJ, Sung AJ, Hwang SS. Regionalisation of out-of-hospital cardiac arrest care for patients without prehospital return of spontaneous circulation. *Resuscitation* 2012;83:1338–42.
 32. McKenzie N, Williams TA, Ho KM, et al. Direct transport to a PCI-capable hospital is associated with improved survival after adult out-of-hospital cardiac arrest of medical aetiology. *Resuscitation* 2018;128:76–82.