Published in final edited form as:

Prehosp Emerg Care. 2010 ; 14(4): 413–418. doi:10.3109/10903127.2010.497902.

Incidence of Re-arrest after Return of Spontaneous Circulation in Out-of-Hospital Cardiac Arrest

David D. Salcido,

University of Pittsburgh

Amanda M. Stephenson,

University of Pittsburgh

Joseph P. Condle,

University of Pittsburgh

Clifton W. Callaway, and

University of Pittsburgh

James J. Menegazzi

University of Pittsburgh

Abstract

BACKGROUND—Return of spontaneous circulation (ROSC) occurs in approximately 30% of EMS-treated out-of-hospital cardiac arrests (OHCA), however not all patients achieving ROSC survive to hospital arrival or discharge. The incidence of re-arrest (RA) before reaching the hospital is unknown, and the ECG waveform characteristics of prehospital RA rhythms have not been previously described.

OBJECTIVES—We sought to determine the incidence of RA in OHCA, to classify RA events by type, and to measure the time from ROSC to RA. We also conducted a preliminary analysis of the relationship between first EMS-detected rhythms and RA, as well as the effect of RA on survival.

METHODS—The Pittsburgh Regional Clinical Center of the NHLBI-sponsored Resuscitation Outcomes Consortium (ROC) provided cases from a population-based cardiac arrest surveillance program, ROC Epistry. Only OHCA cases of non-traumatic etiology with available and adequate ECG files were included. We analyzed defibrillator-monitor ECG tracings (Philips MRX), patient care reports (PCR) and defibrillator audio recordings from EMS-treated cases of OHCA spanning the period 2006 – 2008. We identified ROSC and RA through interpretation of ECG traces and audio recordings. RA events were categorized as ventricular fibrillation (VF), pulseless ventricular tachycardia (VT), asystole, and pulseless electrical activity (PEA) based on ECG waveform characteristics. Proportions of RA rhythms were stratified by first EMS rhythm and compared using Pearson's Chi Square test. Logistic regression was used to test the predictive relationship between RA and survival to hospital discharge.

RESULTS—ROSC occurred in 329/1199 patients (27.4% {95% CI: 25.0–30.0}) treated for CA. Of these, 113 had ECG tracings that were available and adequate for analysis. RA occurred in 41 patients (36.0%, {95% CI: 26–46%}), with a total of 69 RA events. Survival to hospital discharge in RA cases was 23.1% (11.1–39.3) compared to 27.8% (17.9–39.6) in cases without RA. RA event counts by type were: 17 VF (24.6%, {95% CI: 15.2–36.5%}), 20 pulseless VT (29.0%,

Corresponding author: James J. Menegazzi, Ph.D., Iroquois Building, Suite 400A, 3600 Forbes Avenue, Pittsburgh, PA 15261, Phone: 412-647-7992 menegazzijj@upmc.edu, Fax: 412-647-6999.

Presented at the American Heart Association Resuscitation Science Symposium November 14, 2009 Orlando, FL

{95% CI: 18.7–41.2%}), 26 PEA (37%, {95% CI: 26.3–50.2%}), and 6 asystole (8.8%, {95% CI: 3.3–18.0%}). RA was not predictive of survival to hospital discharge, however initial EMS rhythm was predictive of RA shockability. The overall median time from ROSC to RA among all events was 3.1 (1.6–6.3) minutes.

CONCLUSION—In this sample, the incidence of RA was 38%. Of cases experiencing RA 54% survived to hospital arrival. A time window on the order of minutes may be available for intervention prior to RA.

Keywords

sudden cardiac death; ventricular fibrillation; cardiac arrest; emergency medical services; cardiopulmonary resuscitation; defibrillation

INTRODUCTION

In the treatment of out-of-hospital cardiac arrest (OHCA), achieving return of spontaneous circulation (ROSC) alone does not define success. The ultimate goal of resuscitation is to achieve downstream survival to hospital discharge. The significance of this distinction is evident in the disparity between published rates of survival to hospital discharge and ROSC. A meta-analysis of published studies reporting outcomes after EMS-treated OHCA indicates that the median rate of survival to hospital discharge is 6.4%.¹ However, the reported incidence of ROSC in OHCA, while variable, is generally dramatically higher, ranging from 35% to 61%.^{2,3} There are a number of factors responsible for this disparity, including neurologic pathology, in-hospital complications, and spontaneous re-arrest (RA) prior to hospital arrival.

In the prehospital setting, RA functionally refers to the loss of pulses after they have been restored and can include any non-perfusing electrocardiographic rhythm. The incidence and characteristics of RA before reaching the hospital have not been thoroughly studied. Reported incidences of RA range from 61% to 79%.^{5,6,7} Furthermore, at least one study indicated that with each subsequent RA, successful ROSC becomes less likely.⁸ These limited findings provide compelling grounds for further investigation.

Previous studies of RA have adhered to Utstein criteria for cardiac arrest research and focused on refrillation in particular. However, refrillation is just one subset of RA and by definition requires an initial recorded rhythm of ventricular fibrillation (VF) or ventricular tachycardia (VT). Studies focusing on this criterion consequently have excluded RA following initial rhythms of pulseless electrical activity (PEA) or asystole, which may represent a substantial portion of RA. In the present study, we sought to determine the incidence of RA occurring after any initial arrest rhythm and manifesting in any RA rhythm. We also sought to conduct a preliminary analysis of the relationship between first EMS-detected rhythms and RA, as well as the effect of RA on survival.

METHODS

This study was conducted with approval from the Institutional Review Board of the University of Pittsburgh. We obtained cases of EMS-treated, non-traumatic cardiac arrest from the Pittsburgh Regional Clinical Center of the Resuscitation Outcomes Consortium (ROC) Epistry-Cardiac Arrest database from October 2006 through December 2008. The EMS systems that comprise the ROC source agencies have been described in detail previously.¹⁰ Systems included in this study were staffed by ALS providers and served a primarily urban area with a population of approximately 300,000 over an area of 56 sq mi. We included all Pittsburgh area Epistry cases of non-traumatic cardiac arrest within the

available date range that met the inclusion criteria of having available and adequate (i.e. readable) Philips MRX (Amsterdam, The Netherlands) data files and ROSC reported on Patient Care Reports (PCR). Philips MRX monitor data files include continuously recorded compression, impedance, end-tidal carbon dioxide (ETCO₂), multiple lead ECG traces, and continuous audio. Case data also included demographic and health status variables including: age, sex, initial EMS-detected ECG rhythm, and survival to hospital discharge status obtained directly from the Epistry database.

We screened each case for RA by visual and audio analysis of continuous defibrillator data files, using PCRs for clarification of events when the audio recording was insufficient or unavailable. In order to qualify as RA, the suspected RA event was required to follow ROSC. We defined ROSC as pulses explicitly and verbally identified by medics in the audio recording channel and/or ECG findings indicative of pulses corroborated by PCR. CPR delivery and ROSC were considered mutually exclusive. We defined RA events as the initiation of non-perfusing ECG rhythms and/or loss of pulses noted in the audio recording. Resumption of CPR and additional defibrillation attempts were interpreted independently as indicators of loss of pulses. Identified RA events were classified by the presenting non-perfusing rhythm evident in the ECG. RA classifications were VF, pulseless ventricular tachycardia (VT), asystole, and pulseless electrical activity (PEA). Any event in which a re-arrest occurred with significant, patterned electrical activity that was not VF or VT was placed in the PEA category. We report these results as raw counts of RA events stratified by RA rhythm and percentages of the total RA event count.

We also calculated the time from ROSC to each RA event, i.e. the treatment window of each event, by the following formula:

$$\text{Time to RA}_i = \text{Time of RA}_i - \text{Time of ROSC}_i$$

The exact moment of some events could not be determined due to discrepancies between audible EMS commentary vs. ECG findings. For example, on an ECG tracing that shows a rescue shock followed by immediate CPR (without pulse check) followed immediately by a positive pulse check, the moment of ROSC as determined by an ECG observer would be immediately after the shock that ultimately restored pulses, while the EMS crew audibly noted ROSC at a later time (after the period of CPR). We call these the Observer Time of ROSC and the EMS Time of ROSC, respectively. Similarly, there were multiple cases in which we observed a non-pulsatile rhythm such as VF or asystole earlier than it was recognized by the EMS crew. We call these the Observer time of RA and the EMS time of RA, respectively. In order to reconcile the discrepancies between these times, we computed their averages and then calculated the ROSC-to-RA time based on the average EMS/Observer ROSC and RA times. We report these results in minutes to one decimal place with interquartile ranges (IQR) stratified by RA rhythm.

We used a number of statistical techniques to analyze the data. Proportions were compared using the Chi Squared test. Medians were compared using the Kruskal-Wallis test. In order to investigate the relationship between RA and survival to hospital discharge, we utilized univariate logistic regression with the binary outcome of survival and a single dichotomous predictor of RA (yes/no), followed by multivariate logistic regression incorporating additional covariates including initial EMS rhythm, sex, age, and number of RAs. The results of the logistic regression analyses are reported as odds ratios with 95% confidence intervals. An alpha level of 0.05 was used as the criterion of statistical significance for all tests, and all statistical calculations were performed using Stata 11 (StataCorp, College Station, TX).

RESULTS

ROSC occurred in 329/1199 EMS-treated OHCA patients (27.4% {95% CI: 25.0–30.0%}). Figure 1 shows the case selection breakdown for this study. Of those with ROSC, 113 had ECG tracings that were available and adequate for analysis. Median age in this population was 68 (57–79) and proportion female was 43% (95% CI: 34–53%). Among this sample, the most common initial rhythm noted by EMS was asystole. An enumeration of sample characteristics including age, sex, initial rhythm and RA status are listed in Table 1. Forty-one patients (36%, {95% CI: 26–46%}) had a RA event prior to hospital arrival. A total of 69 individual RA events were detected for a median RA frequency of 1 (range: 1–6).

Distribution of RA events by type are shown in Figure 2. Out of 69 RA events, we observed 17 VF (24.6%, {95% CI: 15.2–36.5%}), 20 pulseless VT (29.0%, {95% CI: 18.7–41.2%}), 26 PEA (37%, {95% CI: 26.3–50.2%}), and 6 asystole (8.8%, {95% CI: 3.3–18.0%}). When dichotomized as shockable and nonshockable, the proportion of shockable RA events was 54% (95% CI: 42–65%). Table 2 shows the proportion of shockable RA rhythms by initial EMS rhythm. A majority of patients originating in a shockable rhythm (VF/VT) also had an initial shockable ECG after RA.

In univariate logistic regression models neither RA, sex, nor age were predictive of survival to hospital discharge (RA: $p = 0.591$, Sex: $p = 0.814$, Age: $p = 0.884$). However, an initial shockable ECG rhythm was strongly predictive of survival to hospital discharge relative to non-shockable rhythm (Odds Ratio: 10.04 {95% CI: 3.79, 26.58}) in a univariate logistic model, and an initial ECG rhythm of asystole was highly predictive of not surviving to hospital discharge relative to all other rhythms (Odds Ratio: 0.10 {95% CI: 0.02, 0.42}). Additionally, initial shockable EMS ECG rhythm was predictive of subsequent shockable first RA (Odds Ratio: 12.44 {95% CI: 2.39, 67.56}), and non-shockable first EMS rhythm was predictive of non-shockable first RA (Odds Ratio: 0.13 {95% CI: 0.03, 0.57}). In light of these results, we also investigated whether a shockable first RA was associated with survival to hospital discharge relative to a non-shockable first RA, to which it was related (Odds Ratio: 9.14 {95% CI: 1.01, 82.44}, $p = 0.049$). However, the occurrence of a shockable RA at any time among cases with RA was not predictive of survival (Odds Ratio: 7.00 {95% CI: 0.78, 63.12}).

The overall median (IQR) time from ROSC to RA among all events was 3.1(1.6–6.3) minutes. Looking at only first RAs, the median time from ROSC to RA was 3.8(1.6–7.5). Median (IQR) times from ROSC to first RA when stratified by RA type were: PEA 5.9(2.7–10.6); pulseless VT 6.0(2.8–9.1); VF 1.0(0.5–3.4); asystole 3.6(2.5–30.4). In 19 instances of RA, we found a discrepancy between observer ROSC-to-RA time and EMS ROSC-to-RA time. In 14 of these events, EMS time was longer than observer time with a median discrepancy of 2.6 (0.7–4.9). In 5 events, observer time was longer with an average discrepancy of 3.2 minutes (range: 2–5.4).

DISCUSSION

RA following ROSC is known to be a common occurrence in OHCA, although a general rate of RA has not been established. Our study provides one estimate of RA indicating that more than a third of all patients with ROSC lost pulses prior to hospital arrival. It is not easy to directly compare this rate to previous studies due to our expanded interest in not just refrillation, but RA of all manifesting rhythms, in addition to multiple methodological differences between our study and previous studies. However, focusing on shockable rhythms, we may be able to make some comparisons. Russell, for instance, found a 61% rate of VF recurrence, which would classify as a VF-type RA by our study criteria⁹. Koster

reported a somewhat higher rate of 79% VF recurrence⁸. In our study, if we consider only those cases with initial EMS rhythm of VF/VT, we find a nearly 39.5% rate of VF or VT type RA at any point post-ROSC. For first RA only, this rate reduces to 36.8%. It is not clear what is responsible for this discrepancy, although we will note two potential factors. In Koster's study, presence or absence of pulses did not play a direct role in defining RA. Our study was dependent upon inference to pulses, and so it may be that we were considering different denominators in judging demarcations between RA and non-RA periods. In Russel's study, analyses were focused on cases receiving primarily BLS interventions, while the cases in our study received care from an ALS agency. It may be that the recurrence of VF or other RA rhythms was reduced by the expanded level of care available to our cases.

Our results also provided an estimate of the distribution of RA event types, to our knowledge a novel finding. These results indicated a near even split between the proportion of shockable and non-shockable events. While this is encouraging for the prospect of RA-treatment, the nearly 50% of RA cases with non-shockable rhythms present a therapeutic challenge to EMS. Perhaps this finding will call further attention to the dearth of effective treatments for PEA and asystole. In line with these findings, we also demonstrated that RA patients with shockable initial rhythms tended to have RAs that are shockable, whereas RA patients with non-shockable initial rhythms tended to have RAs that are non-shockable. This finding seems to make physiologic sense, assuming that the relationship between the etiology of a cardiac arrest and its initial presenting rhythm does not change over the course of resuscitation and post-resuscitation care.

Our results concerning survival to hospital discharge suggest some potential for predicting long term outcomes related to RA, if not treatment, then prevention. Unexpectedly, RA itself was not predictive of survival. While we did observe an absolute difference in survival of 4.7% between those with and without RA, our sample was too small to determine whether this difference was due to chance. Certain RA rhythms were associated with survival, which makes intuitive sense; the difficulties associated with resuscitation from non-shockable rhythms are likely not limited to initial rhythms. It could also be that those with non-shockable rhythms have experienced more prolonged cardiac arrest, making it more difficult to generate good reperfusion during CPR.¹³ These may be cases in which patients with initially non-shockable rhythms who do have ROSC were barely on the cusp of getting pulses back and thus could not sustain ROSC.

Finally, the time-to-RA data that we report here indicates that there is a therapeutic window on the order of minutes, not seconds, during which paramedics could potentially intervene to prevent RA from occurring. The nature of these interventions and perhaps more importantly, the signals for their initiation, remain to be determined. However, potential solutions may involve not only reactive treatments such as antiarrhythmic administration, but also proactive strategies such as pre-transport stabilization periods, aggressive use of drugs, and resumption of mechanical chest compression immediately upon RA.¹⁴ The utility of a pre-transport stabilization period could hinge on the relationship, if any, between the process of transporting a patient and the impact transport has on immediate care and monitoring. This would not necessarily require additional ALS caregivers, as this has not been shown to improve care, but would involve a paradigm shift in their treatment strategy.^{15,16} It may be better to "stay and stabilize" rather than to "hurry to hospital".

An ancillary finding of this study showed that discovery of RA was often delayed at the EMS level by a matter of minutes, relative to discovery by a detached observer with access to the same data. While we did not analyze the relationship of this phenomenon to transport or the relationship between ROSC-to-RA time and survival outcomes, it does suggest that the on-scene or in-transit environment can obscure an obvious change in patient status.

This study has several limitations. First, due to the relatively small number of ECGs available, our confidence intervals were wide. The cases that we did analyze represented only a third of the total number of cases with ROSC within the study period, so it is entirely possible that the figures that we have observed could differ from the actual values. That said, we did observe that the primary determinant of ECG availability was recency, and we do not believe that this factor would have significantly altered our findings. Second, we used sample data from a particular geographic area with EMS protocol, organization, and expertise that is likely to be specific to this locale and therefore may not be generalizable everywhere. Moreover, as a retrospective study, this analysis does not control for behavioral inconsistency among EMS personnel, including any deviations from protocol or inconsistent administration of medications. Comorbidities of the patients were not considered, nor were the etiologies of the initial cardiac arrests (apart from being non-traumatic). In addition, while we attempted to provide objective assessments of all clinical endpoints, the constraints of prehospital research imposed some necessity for subjective judgment, particularly when audio data was not available. The vast majority of subjectivity was confined to judgments of the presence of a pulse, and future research would benefit from the adoption of sensitive paramedic-independent carotid pulse monitors with recording capability. Lastly, while we recognize the utility of the Utstein criteria, it was necessary to expand these criteria to include non-refibrillation RA and non-VF initial rhythms in the interest of providing a more complete epidemiological picture of this phenomenon. Future studies may operationalize or expand our research in a manner more consistent with defined resuscitation research guidelines.

CONCLUSIONS

RA occurred in 38% of non-traumatic cases of OHCA. The most common type of RA rhythm was PEA, followed by pulseless VT, then VF and finally asystole. Shockability of initial EMS cardiac arrest rhythm was found to predict subsequent RA rhythm shockability. The median time to RA was 3.1 minutes.

Acknowledgments

FUNDING/SUPPORT

This study was supported by a cooperative agreement (5U01 HL077863) with the National Heart, Lung and Blood Institute in partnership with the National Institute of Neurological Disorders and Stroke, The Canadian Institutes of Health Research (CIHR)–Institute of Circulatory and Respiratory Health, Defense Research and Development Canada, the Heart and Stroke Foundation of Canada, and the American Heart Association.

References

1. Nichol G, Stiell IG, Laupacis A, Ba'Pham De Maio V, Wells G. A cumulative meta-analysis of the effectiveness of defibrillator-capable emergency medical services for victims of out-of-hospital cardiac arrest. *Ann Emerg Med.* 1999; 34(4.1):517–525. [PubMed: 10499952]
2. Gräsner JT, Meybohm P, Fischer M, Bein B, Wnent J, Franz R, Zander J, Lemke H, Bahr J, Jantzen T, Messelken M, Dörge V, Böttiger BW, Scholz J. A national resuscitation registry of out-of-hospital cardiac arrest in Germany—a pilot study. *Resuscitation.* 2009 Feb; 80(2):199–203. [PubMed: 19081171]
3. Grmec S, Krizmaric M, Mally S, Kozelj A, Spindler M, Lesnik B. Utstein style analysis of out-of-hospital cardiac arrest--bystander CPR and end expired carbon dioxide. *Resuscitation.* 2007 Mar; 72(3):404–14. [PubMed: 17161518]
4. Nichol G, Thomas E, Callaway C, Hedges J, Powell J, Aufderheide T, Rea T, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA.* 2008; 300:1423. [PubMed: 18812533]

5. White R, Russell J. Refibrillation, resuscitation and survival in out-of-hospital sudden cardiac arrest victims treated with biphasic automated external defibrillators. *Resuscitation*. 2002; 55:17–23. [PubMed: 12297349]
6. van-Alem A, Post J, Koster R. VF recurrence: characteristics and patient outcome in out-of-hospital cardiac arrest. *Resuscitation*. 2003; 59:181–188. [PubMed: 14625108]
7. Martens P, Russell J, Wolcke B, Paschen H, Kuisma M, Gliner B, Weaver WD, Bossaert L, Chamberlain D, Schneider T. Optimal Response to Cardiac Arrest study: Defibrillation waveform effects. *Resuscitation*. 2001; 49:233–243. [PubMed: 11719116]
8. Koster R, Walker R, Champan F. Recurrent ventricular fibrillation during advanced life support care of patients with prehospital cardiac arrest. *Resuscitation*. 2008; 78:252–257. [PubMed: 18556106]
9. Russell J, White R, Crone W. Analysis of the ventricular fibrillation waveform in refibrillation. *Crit Care Med*. 2006; 34(12, suppl)
10. Davis DP, Garberson LA, Andrusiek DL, Hostler D, Daya M, Pirrallo R, Craig A, Stephens S, Larsen J, Drum AF, Fowler R. A descriptive analysis of Emergency Medical Service Systems participating in the Resuscitation Outcomes Consortium (ROC) network. *Prehospital Emergency Care*. Oct–Dec; 2007 11(4):369–82. [PubMed: 17907019]
11. Morrison LJ, Nichol G, Rea TD, Christenson J, Callaway CW, Stephens S, Pirrallo RG, Atkins DL, Davis DP, Idris AH, Newgard C. ROC Investigators. Rationale, development and implementation of the Resuscitation Outcomes Consortium Epistery-Cardiac Arrest. *Resuscitation*. Aug; 2008 78(2):161–9. [PubMed: 18479802]
12. Tereshchenko L, Fetis B, Domitrovich P, Lindsay B, Berger R. Prediction of Ventricular Tachyarrhythmias by Intracardiac Repolarization Variability Analysis. *Circ Arrhythmia Electrophysiol*. 2009; 2:276–284.
13. Reynolds JC, Salcido DD, Menegazzi JJ. Coronary Perfusion Pressure and Return of Spontaneous Circulation after Prolonged Cardiac Arrest. *Prehospital Emergency Care*. Jan; 2010 14(1):78–84. [PubMed: 19947871]
14. Gonzales L, Langlois J, Parker C, Yost D. Combined Interventions May Improve Success When Treating Sudden Cardiac Arrest. *Prehospital Emergency Care*. Apr; 2010 14(2):222–228. [PubMed: 20144018]
15. Martin-Gill C, Guyette FX, Rittenberger JC. Effect of Crew Size on Objective Measures of Resuscitation for Out-of-Hospital Cardiac Arrest. *Prehospital Emergency Care*. Apr; 2010 14(2): 229–234. [PubMed: 20128704]
16. Eschmann NM, Pirrallo RG, Aufderheide TP, Lerner EB. The Association between Emergency Medical Services Staffing Patterns and Out-of-Hospital Cardiac Arrest Survival. *Prehospital Emergency Care*. Jan; 2010 14(1):71–77. [PubMed: 19947870]

Fig 1.
Case Collection

Fig 2.
Percentages of Re-arrest Types

Table 1

Age, Sex, Rhythm, and Status Variables

	Total	RA Cases	No-RA	p-value
N	113	41	72	--
Age (Median(IQR))	68 (57–79)	67 (54–74)	70.5 (59–80.5)	0.237
Female (% {95% CI})	43.4 (34.1–53.0)	34.1 (20.1–50.6)	48.6 (36.7–60.7)	0.136
Initial Rhythms (% {95% CI})				
VF/VT	33.6 (25.0–43.1)	39.0 (24.2–55.5)	30.6 (20.2–42.5)	0.360
PEA	29.2 (21.0–38.5)	26.8 (14.2–42.9)	30.6 (20.2–42.5)	0.675
Asystole	35.4 (26.6–45.0)	31.7 (18.1–48.1)	37.5 (26.4–49.7)	0.536
Unknown	1.8 (0.2–6.2)	2.4 (0.0–1.3)	1.4 (0–0.75)	0.648
Pulses at ED (% {95% CI})	83.2 (75.0–89.6)	53.7 (37.4–69.3)	100	--
Survival to Hospital Discharge (% {95% CI})	26.1 (18.2–35.3)	23.1 (11.1–39.3)	27.8 (17.9–39.6)	0.590

Table 2

Characteristics of Subsequent RAs by Initial EMS Rhythm

	RA Rhythm (First/All)	
	Shockable First RA (% {95%CI})	Shockable RA Total (% {95%CI})
Initial EMS Rhythm	--	--
VF/VT	87.5 (61.7–98.4)	93.8 (69.8–99.8)
PEA	45.5 (16.7–76.7)	45.5 (16.7–76.6)
Asystole	30.8 (9.1–61.4)	38.5 (13.9–68.4)
Non-Shockable	37.5 (18.8–59.4)	41.7 (22.1–63.4)