ORIGINAL CONTRIBUTIONS

INCIDENCE OF REARREST AFTER RETURN OF SPONTANEOUS CIRCULATION IN OUT-OF-HOSPITAL CARDIAC ARREST

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Background. Return of spontaneous circulation (ROSC) occurs in 35.0 to 61.0% of emergency medical services (EMS)-treated out-of-hospital cardiac arrests (OHCAs); however, not all patients achieving ROSC survive to hospital arrival or discharge. Previous studies have estimated the incidence of some types of rearrest(RA) at 61.0 to 79.0%, and the electrocardiogram (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 National Heart, Lung, and Blood Institute (NHLBI) -sponsored Resuscitation Outcomes Consortium (ROC) provided cases from a population-based cardiac arrest surveillance program, ROC Epistry. Only OHCA cases of nontraumatic etiology with available and adequate ECG files were included. We analyzed defibrillator–monitor ECG tracings (Philips MRX), patient care reports (PCRs), and defibrillator audio recordings from EMS-treated cases of OHCA spanning the period from October 2006 to December 2008. We identified ROSC and RA through interpretation of ECG tracings and audio recordings. Rearrest 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.** Return of spontaneous circulation occurred in 329 of 1,199 patients (27.4% [95.0% confidence interval (CI): 25.0–30.0%]) treated for cardiac arrest. Of these, 113 had ECG tracings that were available and adequate for analysis. Rearrest occurred in 41 patients (36.0% [95.0% CI: 26.0–46.0%]), with a total of 69 RA events. Survival to hospital discharge in RA cases was 23.1% (95.0% CI: 11.1–39.3%), compared with 27.8% (95.0% CI: 17.9–39.6%) in cases without RA. Counts of RA events by type were as follows: 17 VF (24.6% [95% CI: 15.2–36.5%]), 20 pulseless VT (29.0% [95.0% CI: 18.7–41.2%]), 26 PEA (37.0% [95.0% CI: 26.3–50.2%]), and six asystole (8.8% [95.0% CI: 3.3–18.0%]). Rearrest was not predictive of survival to hospital discharge; however, initial EMS rhythm was predictive of RA shockability. The overall median (interquartile range) 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 38.0%. The most common type of RA was PEA. Shockability of first EMS rhythm was found to predict subsequent RA rhythm shockability. **Key words** sudden cardiac death; ventricular fibrillation; cardiac arrest; rearrest; 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 emergency medical services (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 35.0% to 61.0%.[2–4] A number of factors are responsible for this disparity, including neurologic pathology, in-hospital complications, and spontaneous rearrest (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 nonperfusing electrocardiogram (ECG) rhythm. The incidence and characteristics of RA before reaching the hospital have not been thoroughly studied. Reported incidences of RA range from 61.0% to 79.0%.[5–7] 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 refibrillation in particular. However, refibrillation 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, nontraumatic cardiac arrest from the Pittsburgh Regional Clinical Center of the NHBLI-sponsored Resuscitation Outcomes Consortium (ROC) Epistry–Cardiac Arrest database, a population-based surveillance program, from October 2006 through December 2008. The EMS systems that compose the ROC source agencies have been described in detail previously.[9,10] Systems included in this study were staffed by advanced life support (ALS) providers and served a primarily urban area with a population of approximately 300,000 over an area of 56 square miles. We included all Pittsburgh-area Epistry cases of nontraumatic cardiac arrest within the available date range that met the in-

clusion criteria of having available and adequate (i.e., readable) Philips MRX (Amsterdam, The Netherlands) data files and ROSC reported on patient care reports (PCRs). Philips MRX monitor data files include continuously recorded compression, impedance, end-tidal carbon dioxide (ETCO$_2$), multiple-lead ECG tracings, and continuous audio. Case data also included demographic and health status variables, including age, gender, 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. Cardiopulmonary resuscitation (CPR) delivery and ROSC were considered mutually exclusive. We defined RA events as the initiation of nonperfusing 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 nonperfusing rhythm evident in the ECG. Rearrest classifications were VF, pulseless VT, asystole, and PEA. Any event in which an RA 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 because of discrepancies between audible EMS commentary and 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, whereas 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 nonpulsatile 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
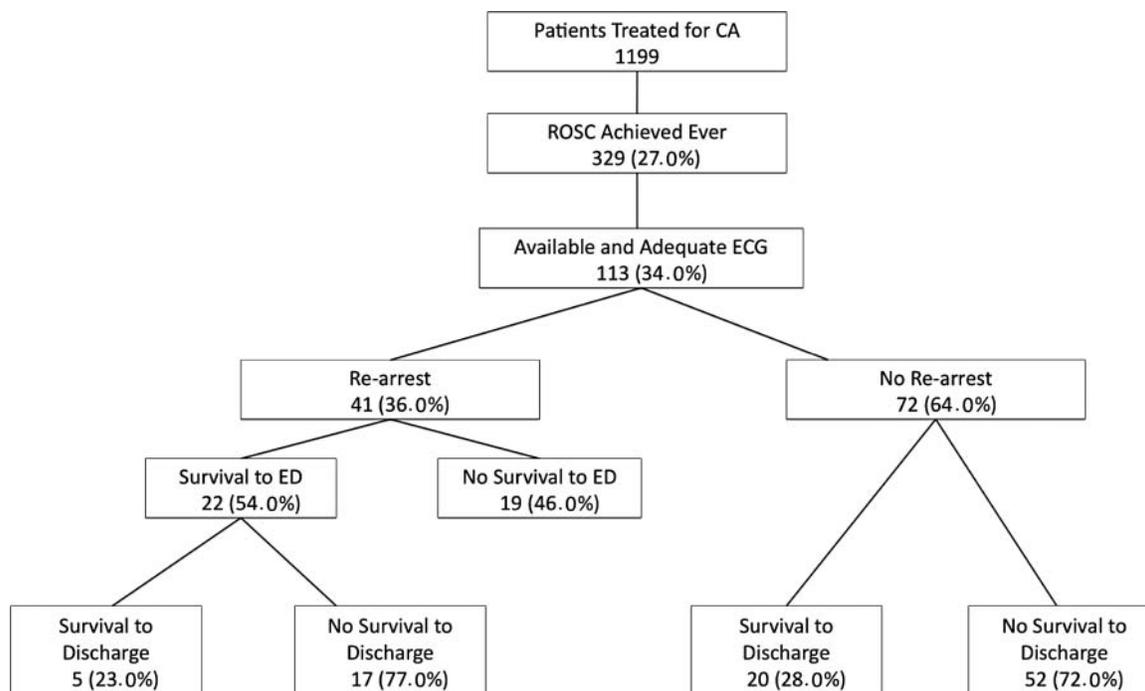
FIGURE 1. Case collection. CA = cardiac arrest; ECG = electrocardiogram; ED = emergency department; ROSC = return of spontaneous circulation.

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 (IQRs) stratified by RA rhythm.

We used a number of statistical techniques to analyze the data. Proportions were compared using Pearson's chi-square test. Medians were compared using the Kruskal-Wallis test. In order to investigate the predictive 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, gender, age, and number of RAs. The results of the logistic regression analyses are reported as odds ratios (ORs) with 95.0% confidence intervals (CIs). 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 LP, College Station, TX).

RESULTS

Return of spontaneous circulation occurred in 329 of 1,199 EMS-treated OHCA patients (27.4% [95.0% 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. The median age in this population was 68 (57–79) years, and the proportion of female patients was 43.0% (95.0% CI: 34.0–53.0%). Among this sample, the most common initial rhythm noted by EMS was asystole. Sample characteristics, including age, gender, initial rhythm, and RA status, are listed in Table 1.

TABLE 1.   Age, Gender, Rhythm, and Status Variables

	Total	Cases with RA	Cases without RA	p-Value
N	113	41	72	—
Age, median (IQR)	68 (57–79)	67 (54–74)	70.5(59–80.5)	0.237
Gender—female,% (95.0% CI)	43.4(34.1–53.0)	34.1(20.1–50.6)	48.6(36.7–60.7)	0.136
Initial rhythms,% (95.0% 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 the ED, % (95.0% CI)	83.2(75.0–89.6)	53.7(37.4–69.3)	100	—
Survival to hospital discharge,% (95.0% CI)	26.1(18.2–35.3)	23.1(11.1–39.3)	27.8(17.9–39.6)	0.590

CI = confidence interval; ED = emergency department; IQR = interquartile range; PEA = pulseless electrical activity; RA = rearrest; VF/VT = ventricular fibrillation/ventricular tachycardia.
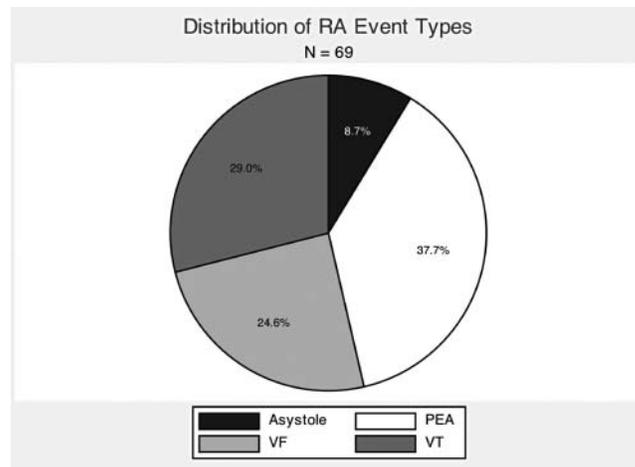
FIGURE 2. Percentages of rearrest (RA) types. PEA = pulseless electrical activity; VF = ventricular fibrillation; VT = ventricular tachycardia.

Forty-one patients (36.0% [95.0% CI: 26.0–46.0%]) had an 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).

The distribution of RA events by type is shown in Figure 2. Out of 69 RA events, we observed 17 VFs (24.6% [95% CI: 15.2–36.5%]), 20 pulseless VTs (29.0% [95% CI: 18.7–41.2%]), 26 PEAs (37.7% [95.0% CI: 26.3– 50.2%]), and six asystoles (8.7% [95.0% CI: 3.3–18.0%]). When dichotomized as shockable and nonshockable, the proportion of shockable RA events was 54.0% (95.0% CI: 42.0–65.0%). 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 rhythm after RA.

In univariate logistic regression models, neither RA, gender, nor age was predictive of survival to hospital discharge (RA: p = 0.591; gender: p = 0.814; age: p = 0.884). However, an initial shockable ECG rhythm was strongly predictive of survival to hospital discharge relative to nonshockable rhythm (OR: 10.04 [95.0% 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 (OR: 0.10 [95.0% CI: 0.02, 0.42]). Additionally, an initial shockable EMS ECG rhythm was predictive of subsequent shockable first RA (OR: 12.44 [95.0% CI: 2.39, 67.56]), and a nonshockable first EMS rhythm was predictive of nonshockable first RA (OR: 0.13 [95.0% 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 nonshockable first RA, to which it was related (OR: 9.14 [95.0% 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 (OR: 7.00 [95.0% 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) minutes. Median (IQR) times from ROSC to first RA when stratified by RA type were as follows: PEA 5.9 (2.7–10.6); pulseless VT 6.0 (2.8–9.1); VF 1.0 (0.5–3.4); and 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 five events, observer time was longer, with an average discrepancy of 3.2 minutes (range: 2–5.4).

DISCUSSION

Rearrest 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 with those of previous studies because of our expanded interest in not just refibrillation, but RA of all manifesting rhythms, in addition to multiple methodologic differences between our study and previous studies. However, focusing on

TABLE 2. Characteristics of Subsequent Rearrests by Initial Emergency Medical Services Rhythm

| | RA Rhythm (First/All) | |
	Shockable First RA % (95.0% CI)	Shockable RA Total % (95.0% 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)
Nonshockable	37.5(18.8–59.4)	41.7(22.1–63.4)

CI = confidence interval; EMS = emergency medical services; PEA = pulseless electrical activity; RA = rearrest; VF/VT = ventricular fibrillation/ventricular tachycardia.

shockable rhythms, we may be able to make some comparisons. Russell et al., for instance, found a 61.0% rate of VF recurrence, which would classify as a VF-type RA by our study criteria.[11] Koster et al. reported a somewhat higher rate of 79.0% VF recurrence.[8] 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 after ROSC. For first RA only, this rate decreases to 36.8%. It is not clear what is responsible for this discrepancy, although we note two potential factors. In the Koster study, presence or absence of pulses did not play a direct role in defining RA. Our study was dependent on inference to pulses, and so it may be that we were considering different denominators in judging demarcations between RA and non-RA periods. In the Russell study, analyses were focused on patients receiving primarily BLS interventions, whereas the patients 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 patients.

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 proportions of shockable and nonshockable events. While this is encouraging for the prospect of RA treatment, the nearly 50.0% of RA cases with nonshockable 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 nonshockable initial rhythms tended to have RAs that are nonshockable. 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 postresuscitation 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 nonshockable rhythms are likely not limited to initial rhythms. It could also be that those with nonshockable rhythms have experienced more prolonged cardiac arrest, making it more difficult to generate good reperfusion during CPR.[12] These may be cases in which patients with initially nonshockable 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 indicate 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.[13] However, potential solutions may involve not only reactive treatments such as antiarrhythmic administration, but also proactive strategies such as pretransport stabilization periods, aggressive use of drugs, and resumption of mechanical chest compression immediately upon RA.[14] The utility of a pretransport 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" 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.

LIMITATIONS AND FUTURE RESEARCH

This study has several limitations. First, because of the relatively small number of ECGs available, our CIs 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 nontraumatic). 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 were 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 nonrefibrillation RA and non-VF initial rhythms in the interest of providing a more complete epidemiologic picture of this phenomenon. Future studies may operationalize or expand our research in a manner more consistent with defined resuscitation research guidelines.

CONCLUSIONS

Rearrest occurred in 38% of nontraumatic 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.

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