Temporal Differences in Out-Of-Hospital Cardiac Arrest

Incidence and Survival

Running title: Bagai et al.; Temporal variability in OHCA

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Abstract

**Background**—Understanding temporal differences in the incidence and outcomes of out-of-hospital cardiac arrest (OHCA) has important implications for developing preventative strategies and optimizing systems for OHCA care.

**Methods and Results**—We studied 18,588 OHCAs of presumed cardiac etiology in patients ≥18 years who received resuscitative efforts by emergency medical services (EMS) and were enrolled in the Cardiac Arrest Registry to Enhance Survival (CARES) from 10/01/2005–12/31/2010. We evaluated temporal variability in OHCA incidence and survival to hospital discharge. There was significant variability in the frequency of OHCA by hour of the day (p<0.001), day of the week (p<0.001), and month of the year (p<0.001), with the highest incidence occurring during the daytime, from Friday to Monday, in December. Survival to hospital discharge was lowest for OHCA occurring overnight (2301-0700h; 7.1%) versus daytime (0701-1500h; 10.8%) versus evening (1501-2300h; 11.3%) (p<0.001), and during the winter (8.8%) versus spring (11.1%) versus summer (11.0%) versus fall (10.0%) (p<0.001). There was no difference in survival to hospital discharge between OHCA occurring on weekends and weekdays (9.5% vs. 10.4%, p=0.06). After multivariable adjustment for age, sex, race, witness status, layperson resuscitation, first monitored cardiac rhythm and EMS response time, compared with daytime and spring, survival to hospital discharge remained lowest for OHCA occurring overnight (OR 0.81, 95% CI 0.70–0.95, p=0.008) and during the winter (OR 0.81, 95% CI 0.70–0.94, p=0.006), respectively.

**Conclusions**—There is significant temporal variability in the incidence of and survival after OHCA. The relative contribution of patient pathophysiology, likelihood of being observed, pre-hospital and hospital based resuscitative factors deserves further exploration.

**Key words:** cardiac arrest, epidemiology, mortality, heart arrest, Out-of-hospital cardiac arrest
Out-of-hospital cardiac arrest (OHCA) occurs in more than 300,000 individuals in the United States each year and remains associated with very high mortality and morbidity.\(^1\,^2\) Successful resuscitation requires implementing a “chain of survival” with both pre-hospital and hospital-based links, including activation of the emergency medical services (EMS) system, early cardiopulmonary resuscitation (CPR), defibrillation as appropriate, advanced life support measures, and post-resuscitation care in the receiving hospital.\(^3\) Prior studies have suggested temporal variability in OHCA occurrence,\(^4\,\,^{10}\) and a few have suggested temporal differences in survival;\(^8\,\,^{11}\,\,^{12}\) however, mechanisms for these findings are poorly understood. These epidemiologic studies are limited by lack of details on patient and arrest characteristics, and on pre-hospital care and outcomes. Further understanding of the temporal variability of OHCA occurrence and outcomes is important to develop preventative strategies and optimize resource planning for pre- and in-hospital response to cardiac arrest, with the aim of improving patient survival.

In this study, we utilized OHCA data from the Cardiac Arrest Registry to Enhance Survival (CARES) Registry, which is a large diverse United States population surveillance database of OHCA episodes. We investigated temporal variability by time of day, day of week, and month of year, in the incidence and outcomes of OHCA. We also explored potential mechanisms that may explain this variability.

**Methods**

**Study Population**

The CARES Registry is a central repository of OHCA data from over 70 EMS agencies and 340 hospitals throughout the United States (Figure 1). The registry serves as a quality improvement
project and allows EMS agencies to compare key performance indicators to improve OHCA care. Methods for data collection and a complete description of the registry population have been previously reported. In brief, CARES includes data on persons who have an OHCA event of a presumed cardiac etiology (based on the care providers’ clinical judgment), and who receive resuscitative efforts (e.g., CPR and/or defibrillation) by EMS. Patients with obvious signs of death (e.g., rigor mortis or dependent lividity) or for whom a “do not resuscitate” order is respected are not included. Non-cardiac etiologies (e.g., trauma, drowning, overdose, asphyxia, electrocution, primary respiratory arrest, or other non-cardiac etiologies) are also excluded from enrollment in CARES.

Our study population included all OHCA events in patients ≥18 years enrolled in CARES with a recorded 9-1-1 call date and time between October 1, 2005 to December 31, 2010 (n=22,146). Events that occurred in nursing homes or other health care institutions were not included, given that these were thought to represent a population distinct from the majority of OHCA cases (n=3,558). The final sample for this analysis consisted of 18,588 OHCA events. The CARES study was approved by the Emory University institutional review board. Because the data is used primarily at the local sites for quality improvement, sites are granted a waiver of informed consent under the common rule. Analysis of aggregate de-identified data was performed at the Duke Clinical Research Institute.

Data Definitions

The time of the OHCA was defined as the time the 9-1-1 call was received. All events were stratified by timing of occurrence into: (1) daytime (0701-1500h), evening (1501-2300h), or overnight (2301-0700h); (2) weekday (Monday to Friday) or weekend (Saturday and Sunday); and (3) winter (December to February), spring (March to May), summer (June to August), or fall...
(September to November).

Outcomes

Temporal variability by time of day, day of week, and month of year in the incidence of OHCA, and rate of survival to hospital discharge was evaluated. Among patients who survived to hospital discharge, temporal variability in the rate of favorable neurologic function (defined as cerebral performance categories [CPC] 1 and 2)\textsuperscript{15} was also determined. A CPC score of 1 denotes mild or no neurologic disability and 2 denotes moderate neurologic disability.\textsuperscript{16}

Statistical Analysis

Descriptive statistics are summarized as medians with interquartile ranges (25\textsuperscript{th}, 75\textsuperscript{th} percentile) for continuous variables and counts (percentages) for categorical variables. The hourly, daily, and monthly frequency of OHCA incidence and rates of survival to hospital discharge are shown graphically and compared using Chi-square goodness of fit tests. Patient and event characteristics and outcomes were compared between time blocks using the Kruskal-Wallis test for continuous variables and the Chi-Square test for categorical variables. In order to equalize the assessed number of month and season time periods, the study period was limited to January 1, 2006 to December 31, 2010, for the analyses of month and season; as a result, 119 (0.6\%) OHCA events were excluded.

Logistic regression modeling was used to examine the association between the time of OHCA (evening and overnight as compared with daytime) and survival to hospital discharge after adjusting for patient age, sex, race (white versus others), first monitored cardiac rhythm (shockable versus non-shockable), witness status (witnessed versus unwitnessed arrest), layperson resuscitation (CPR or automated external defibrillator [AED] application), and EMS response time (time from 9-1-1 call received at dispatch to EMS arrival at scene). Shockable first
cardiac rhythm included ventricular fibrillation, ventricular tachycardia, and unknown shockable rhythm. Non-shockable first cardiac rhythm included asystole, pulseless electrical activity, and unknown non-shockable rhythm. Continuous covariates were tested for linearity, and non-linear adjustment covariates were transformed using spline functions or truncated, as appropriate. Rate of missingness was <1% for all covariates; patients with any missing covariate (n=179, 0.96%) were excluded, and imputation was not performed. Thus, the analysis population for logistic regression modeling was 18,409 OHCA events. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Logistic regression modeling was also used to examine the association between the occurrence of OHCA on weekends (compared with weekdays) and survival to hospital discharge, and between the occurrence of OHCA in the summer, in the fall, or in the winter (compared with spring) and survival to hospital discharge. The same list of adjustment covariates was used in the models.

Given that the 9-1-1 call time may variably be delayed from the actual time of OHCA occurrence (particularly among unwitnessed arrests), we repeated the analyses in the following two pre-specified subpopulations: (1) witnessed arrest with shockable first cardiac rhythm, because the 9-1-1 call time in this group most closely reflects the actual time of cardiac arrest, and because the probability of survival is highest with interventions most likely to improve outcomes; and (2) unwitnessed arrest with non-shockable first cardiac rhythm, because the 9-1-1 call time in this group least accurately reflects the actual time of cardiac arrest, and because the probability of survival is the lowest with interventions least likely to improve outcomes. All analyses were performed using SAS software version 9.2 (SAS Institute, Cary, North Carolina). All p-values <0.05 were interpreted as statistically significant.
Results

Characteristics of the Study Cohort

Of the 18,588 OHCA events that comprised our study cohort, the median (25th, 75th percentile) patient age was 63 (52, 76) years; 11,782 (63.4%) events occurred in male patients; 14,616 events (78.6%) occurred at home; 9,203 events (49.5%) were witnessed; 4,963 events (26.7%) had a shockable first cardiac rhythm; 3,386 events (18.2%) were witnessed arrests with a shockable first cardiac rhythm; 7,780 events (41.9%) were unwitnessed and had a non-shockable first cardiac rhythm; CPR was performed by a layperson in 4,888 events (26.3%), and an AED was applied by a layperson in 410 events (2.2%). The median (25th, 75th percentile) time from 9-1-1 call received to EMS arrival at the scene was 6.8 (5.0, 9.0) minutes. Survival to hospital discharge occurred in 1,885 (10.1%) events; survival to hospital discharge was 32.7% among events that were witnessed and had a shockable first cardiac rhythm, and 2.0% among unwitnessed events with a non-shockable first cardiac rhythm. Among survivors to hospital discharge, 1,507 (80.0%) had a favorable neurologic outcome.

Circadian Variability in OHCA Incidence and Outcomes

9-1-1 calls for OHCA occurred more frequently during the daytime [n=7503 (40.4%)] and evening [n=6883 (37.0%)] compared with night [n=4202 (22.6%)] (p<0.001), with a large peak in occurrence from 0800 to 1100 hours, and a smaller secondary peak from 1700 to 1900 hours (Figure 2). The morning and early evening peaks in 9-1-1 calls were observed only for unwitnessed arrests with a non-shockable first cardiac rhythm, but not for witnessed arrests with a shockable first cardiac rhythm (Figure 2). Overnight arrests were more likely to occur at home, to be unwitnessed, have a non-shockable first cardiac rhythm, and less likely to receive layperson CPR or AED application (Table). Time from 9-1-1 call to EMS arrival on scene was longest at
Rates of return of spontaneous circulation (ROSC) and survival to hospital admission were lowest for OHCA occurring at night (Table). Overall and among patients admitted to the hospital, survival to hospital discharge was also lowest for OHCA occurring overnight (Figure 3). Among the cohort of witnessed arrests with shockable first cardiac rhythm, survival to hospital discharge was 26.1% for arrests occurring overnight, compared with 34.4% for daytime arrests and 33.5% for evening arrests (p=0.001). There was no difference in survival to hospital discharge by time of day among unwitnessed arrests with non-shockable first cardiac rhythms (p=0.34). After multivariable adjustment, compared with daytime OHCAs, overnight (adjusted OR 0.81, 95% CI 0.70–0.95, p=0.008), but not evening OHCAs (adjusted OR 1.01, 95% CI 0.90–1.13, p=0.92), were associated with lower survival to hospital discharge. Rates of favorable neurologic outcomes among index hospitalization survivors were similar in the three time blocks (p=0.24; Table).

Circaseptan Variability in OHCA Incidence and Outcomes

There is circaseptan variability in the incidence of OHCA, with greatest occurrence on Saturday and lowest occurrence on Tuesday (p<0.001; Figure 4). This variability was observed for unwitnessed arrests with non-shockable first cardiac rhythm (p<0.001), but not for witnessed arrests with shockable first cardiac rhythm (p=0.18). Overall, 13015 (70.0%) of the OHCA events occurred on weekdays compared with 5573 (30.0%) on the weekend. Weighing for inverse of days (5 for weekdays and 2 for weekend), there was no difference in incidence of OHCA on weekdays versus weekends (p=0.27). Compared with OHCAs occurring on weekdays, cardiac arrest on weekends was more likely to occur at home (80.9% vs. 77.7%, p<0.001) and was less likely to be treated with layperson AED application (1.7% vs. 2.4%, p=0.002). Rates of
layperson CPR and time from 9-1-1 call to EMS arrival on scene were similar on weekends and weekdays.

Rates of ROSC (33.2% vs. 33.5%, p=0.74) and survival to hospital admission (21.5% vs. 21.2%, p=0.54) were similar on weekends and weekdays; however, among those admitted to the hospital, survival to hospital discharge was lower for OHCA on weekends compared with weekdays (44.9% vs. 47.1%, p=0.04). Overall, there was no difference in survival to discharge as a function of the day of the week (p=0.32; Figure 5), or when stratified by weekends versus weekdays (9.5% vs. 10.4%, p=0.06). Among witnessed arrests with shockable first cardiac rhythm, survival was lower for arrests occurring on weekends compared with weekdays (29.5% vs. 34.0%, p=0.01), but among unwitnessed arrests with non-shockable first cardiac rhythms, there was no difference in survival between arrests occurring on weekends or weekdays (2.2% vs. 2.0%, p=0.64). Among survivors to hospital discharge, there was no difference in favorable neurologic outcomes between OHCA episodes occurring on weekends or weekdays (p=0.57).

Circannual Variability in OHCA Incidence and Outcomes

The highest incidence of OHCA occurred in December (p<0.001; Figure 6) and results were similar for both witnessed arrests with shockable first cardiac rhythms (p<0.001) and for unwitnessed arrests with non-shockable first cardiac rhythms (p<0.001). Stratifying by season, incidence of OHCA was greatest during the fall (p<0.001). There were no significant differences in location of arrest, frequency of shockable first cardiac rhythm, and EMS response times between seasons, yet the proportion of witnessed arrests was greater during the summer (p=0.04).

Rates of ROSC and survival to hospital admission were lowest during winter (p=0.003 and 0.005, respectively); however, among those admitted to hospital, there was no difference in
survival to discharge by season (p=0.11). Overall survival to hospital discharge was highest in June (12.9%) and lowest survival in January (8.0%; p=0.002; Figure 7). When stratified by season, survival was greatest during the spring (11.1%) and lowest during the winter (8.8%). After multivariable adjustment, compared with spring, survival to hospital discharge remained lower for OHCA occurring during the winter (adjusted OR 0.81, 95% CI 0.70–0.94, p=0.006), with similar survival during the summer (p=0.81) or fall (p=0.28). No difference in rates of favorable neurologic outcomes was observed between seasons (p=0.31).

Discussion

In this large, population-based, multisite study of over 18,000 OHCA events, several important findings emerge. First, the morning and early evening peaks in OHCA occurrence, as defined by the time the 9-1-1 call was received, were absent among witnessed arrests with shockable first cardiac rhythm, and observed only among unwitnessed arrests with non-shockable first cardiac rhythm. Second, the highest incidence of OHCA was observed between Friday and Monday and in December. Third, OHCA survival to hospital discharge was lowest overnight and during the winter. Finally, temporal variability in the rates of favorable neurological outcomes was not observed.

Circadian Variability in OHCA Incidence and Outcomes

Over the last three decades, several4,5,7,8,10,17,18 but not all19,20 studies have demonstrated a circadian pattern in the incidence of OHCA with a typical peak in occurrence during the early morning hours and a smaller secondary peak in the early evening. Evidence for circadian patterns in the incidence of acute myocardial infarction19,20 with changes in potential physiologic triggers including blood pressure and heart rate, vascular tone, heart rate variability, blood viscosity, and
platelet aggregation\textsuperscript{5,21-23} have been proposed to explain the morning peak in OHCA occurrence, with no explanation provided for the early evening peak. The task of determining the true time of OHCA is difficult—especially during the night when there is an increased frequency of unwitnessed arrests. Early studies of temporal variability of OHCA used death certificates and hospital records\textsuperscript{4-6} to determine the time of OHCA, and were inaccurate given the delayed nature of the record keeping inherent in these circumstances. More recent studies have used the 9-1-1 call time as a surrogate for the time of cardiac arrest; although not as vulnerable to the problems of using death certificates, this is also an imperfect measure, given that the probability of a cardiac arrest being witnessed or discovered shortly after onset is most likely variable over the course of the day, due to human sleep/wake behavior.

Consistent with previous literature, using the time of 9-1-1 call as the surrogate for the time of cardiac arrest, we also observed a similar circadian pattern with a large increase in 9-1-1 calls from 0800 to 1100 hours and a smaller secondary increase from 1700 to 1900 hours. Nonetheless, our large sample size and knowledge of witness status and first cardiac rhythm allowed us to further stratify our study population according to events where the timing of the 9-1-1 call was the most and least likely to represent the actual time of cardiac arrest. The striking absence of both peaks among witnessed arrests with shockable first cardiac rhythm, with presence only among unwitnessed arrests with non-shockable first cardiac rhythm, is a novel finding. This finding suggests a strong possibility: that these peaks in 9-1-1 calls are due to finding patients in the morning who actually died during the night (thereby falsely classifying the deaths to have occurred in the morning), and family members returning from work in the evening to find patients who actually died in the afternoon (thereby falsely classifying the deaths to have occurred in the evening). This explanation is further supported by additional post-hoc analyses.
with the observation that these characteristic peaks occurred only among events happening at home, but not outside of the home (data not shown).

Consistent with previous studies,\textsuperscript{12,24} we found significant variability in survival to hospital discharge as a function of OHCA time, or more accurately, as a function of the 9-1-1 call time. Survival was lowest when the 9-1-1 call occurred between 2301 and 0700 hours. Patients who die overnight, but are found in the morning are categorized into the daytime group, which further underestimates the temporal differences in survival. Patients who experience events at night are disadvantaged for a number of reasons. First, these patients have a greater likelihood of having an unwitnessed arrest during sleep resulting in recognition and 9-1-1 call delays. Second, nighttime arrests are more likely to occur at home where AED use is uncommon and the frequency of bystander CPR is lower. Third, EMS response times were slightly longer at night, perhaps due to decreased staffing or performance; nevertheless, this delay requires further study. Finally, the odds of survival remained 19\% lower at night compared with during the day—even after adjustment for available patient and arrest characteristics, suggesting that temporal variability in other unmeasured factors may also be responsible for lower survival at night. Lower survival rate at night, both in admission to hospital and to discharge among those admitted to hospital, suggests that temporal variability both in pre- and post-hospital admission factors may contribute to differences in survival. Variability may include patient factors (e.g., etiology of cardiac arrest [primary arrhythmic or associated with myocardial infarction]), quality of resuscitation (e.g., chest compressions), EMS and emergency department staffing, and access to interventions such as urgent coronary angiography and therapeutic hypothermia; however, these postulates require further study and confirmation. It is possible that some hospitals offer less comprehensive treatment during the nighttime, potentially affecting patient outcomes.
Circaseptan Variability in Incidence and Outcomes

We found an increase in the incidence of OHCA from Friday to Monday, which is consistent with other studies that found the greatest incidence of OHCA on Saturdays\(^6,20\) and Mondays.\(^9,10,25,26\) Although the reasons remain speculative, changes in behavior around weekends, including alcohol intake, sleep-wake cycle, and physical activity may partly explain this observation.\(^27\) In contrast to previous studies,\(^8\) we did not observe significant variability in survival after OHCA by day of week. Similar EMS response times and rates of ROSC and survival to hospital admission suggest that pre-hospital processes of OHCA care are comparable on weekends and weekdays, yet lower rate of survival to discharge among those admitted to the hospital on weekends suggests that in-hospital care for OHCA may be different on weekends compared with weekdays.

Circannual Variability in Incidence and Outcomes

Seasonal variation in OHCA\(^9,26\) and sudden cardiac death\(^8\) have been described in several different populations, with exposure to cold considered to be one of the main factors influencing this variability. Nevertheless, it has been suggested that since seasonal variations of sudden death have also been found in areas with less extreme changes between summer and winter, such as Kuwait, the seasonal variation in sudden death may depend more on relative rather than absolute changes in the climate, and may also be influenced by behavioral changes associated with the seasons.\(^28\) Consistent with previous studies,\(^9,29\) we also found OHCA to occur with greatest frequency in December. This finding was observed despite including climatically varied sites. Stress during the winter holiday season, or migration out of the city during the summer months may be other potential explanations for these findings.

Rates of survival to hospital discharge were about 40% lower for OHCA occurring
during January compared with June. We observed a greater proportion of witnessed arrests during the summer months, possibly due to greater time spent outside of the house, which may partially account for increased survival during this time period. However, the odds of survival remained about 19% lower during winter—even after adjustment for known patient and event characteristics. Given that rates of ROSC and survival to hospital admission, but not rates of survival after hospital admission were lower during the winter, unmeasured patient and pre-hospital care factors are likely responsible for seasonal differences in survival rates. Despite the observations of temporal differences in incidence and survival with OHCA, we found no evidence for temporal variability in favorable neurologic outcomes among survivors.

Our findings have important implications from a public health and policy perspective both for pre-hospital and hospital-based OHCA care. Efforts are required to reduce diurnal variability and improve overall OHCA survival by increasing public knowledge of early cardiac arrest recognition, and enhancing public skills and readiness to perform CPR when necessary. Further reassessment of EMS and hospital resources and performance is recommended to evaluate for, and if present eliminate, temporal disparity in staffing, dispatch procedures, number of vehicles able to respond, quality of CPR, and hospital based interventions including implementation of neuroprotective therapy and access to early cardiac interventions. These postulates if confirmed support advocacy and implementation of regional cardiac resuscitation systems of care that provide 24/7 expert access to resuscitation-related services.\textsuperscript{30,31} The rationale for such regional centers includes widespread underutilization of proven but logistically complex interventions and selective availability of specialized resources and expertise at specific centers. Furthermore, ongoing translational and clinical research is necessary to study novel strategies to efficiently deliver consistent and timely care to such patients.
Limitations

Several issues merit consideration in the interpretation of our study. First, the data are observational, registry-based, and therefore, subject to unmeasured confounding and bias. We were unable to account for resuscitation specific variables (e.g., quality of chest compressions), the type of treating hospital (e.g. academic vs. community) or use of other treatments such as therapeutic hypothermia or urgent coronary angiography which may have contributed to the observed temporal variability in survival to hospital discharge. Second, voluntary participation in CARES may not generate representative samples of the OHCA patient population. Although the data were collected from numerous EMS sources that may have differences in record keeping of times, there should be no systematic differences in record keeping as a function of time. Third, it is unknown how the exclusion of OHCA events where resuscitation was not attempted would affect the temporal variation in the incidence. Fourth, as previously discussed, the use of 9-1-1 call time as a surrogate for actual time of cardiac arrest can be inaccurate, and thus, falsely classifying patients who died at night to have arrested (and died) in the morning, has the potential for misclassification bias. Although the assessment of the time of arrest from implantable cardiac defibrillator electrograms may be more accurate, they have limited generalizability because of selection bias in the type of patients that tend to have these devices implanted. Fifth, we were unable to relate timing of cardiac arrest to patient behaviors such as wake time, physical activities or medication compliance, or the type of cardiac arrest (e.g., myocardial infarction or primarily arrhythmic). Finally, we undertook multiple comparisons and findings should be interpreted with caution given the possibility of a type I error.
Conclusions

In this large, geographically diverse, population-based study, we observed temporal differences in the incidence of and survival after OHCA. The frequency of OHCA was increased around the weekends and during the winter, and survival was lowest when OHCA occurred overnight and during the winter. Reasons for these findings are likely multifactorial including variability in biologic processes in patients themselves and among all links in the “chain of survival.” Further study of immediate precipitants of cardiac arrest and temporal variability in pre- and post-hospitalization care is required to develop preventative strategies and optimize resource planning in an effort to improve OHCA outcomes.

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References:


Table 1. Patient Demographics, Arrest Characteristics, and Clinical Outcomes by Time of 9-1-1 Call Received

<table>
<thead>
<tr>
<th></th>
<th>Total N=18588</th>
<th>Daytime (0701-1500h) N=7503</th>
<th>Evening (1501-2300h) N=6883</th>
<th>Overnight (2301-0700h) N=4202</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>Patient demographics</strong></td>
<td></td>
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<tr>
<td>Age, years</td>
<td>63 (52, 76)</td>
<td>64 (53, 77)</td>
<td>63 (53, 76)</td>
<td>61 (50, 74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>11782 (63.4%)</td>
<td>4764 (63.5%)</td>
<td>4395 (63.9%)</td>
<td>2623 (62.4%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Race, White</td>
<td>7766 (41.8%)</td>
<td>3216 (42.9%)</td>
<td>2936 (42.7%)</td>
<td>1614 (38.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Arrest characteristics</strong></td>
<td></td>
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<tr>
<td>Location of arrest, home</td>
<td>14616 (78.6%)</td>
<td>5608 (74.7%)</td>
<td>5368 (78.0%)</td>
<td>3640 (86.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Witness status, witnessed arrest</td>
<td>9203 (49.5%)</td>
<td>3685 (49.1%)</td>
<td>3599 (52.3%)</td>
<td>1919 (45.7%)</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Bystander resuscitation</strong></td>
<td></td>
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<tr>
<td>Layperson CPR</td>
<td>4888 (26.3%)</td>
<td>2052 (27.4%)</td>
<td>1798 (26.1%)</td>
<td>1038 (24.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Layperson AED application</td>
<td>410 (2.2%)</td>
<td>199 (2.7%)</td>
<td>149 (2.2%)</td>
<td>62 (1.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shockable first cardiac rhythm*</td>
<td>4963 (26.7%)</td>
<td>2036 (27.1%)</td>
<td>2025 (29.4%)</td>
<td>902 (21.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time from 9-1-1 call received to EMS arrival at scene, mins</td>
<td>7.0 (5.3, 9.3)</td>
<td>6.7 (5.0, 9.0)</td>
<td>6.7 (5.0, 9.0)</td>
<td>7.0 (5.4, 9.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Clinical outcomes</strong></td>
<td></td>
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<tr>
<td>Overall survival to hospital discharge</td>
<td>1885 (10.1%)</td>
<td>808 (10.8%)</td>
<td>777 (11.3%)</td>
<td>300 (7.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ROSC</td>
<td>6207 (33.4%)</td>
<td>2540 (33.9%)</td>
<td>2428 (35.3%)</td>
<td>1239 (29.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Admission to hospital</td>
<td>4941 (26.6%)</td>
<td>1987 (26.5%)</td>
<td>1980 (28.8%)</td>
<td>974 (23.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Survival to hospital discharge among patients admitted to hospital†</td>
<td>1885/4941 (38.2%)</td>
<td>808/1987 (40.7%)</td>
<td>777/1980 (39.2%)</td>
<td>300/974 (30.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Favorable neurological outcomes‡</td>
<td>1507/1885 (80.0%)</td>
<td>644/808 (79.7%)</td>
<td>630/777 (81.1%)</td>
<td>233/300 (77.7%)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Data presented as counts (percentages) for categorical variables and medians (25th, 75th percentiles) for continuous variables.

*Shockable first cardiac rhythm includes ventricular fibrillation, ventricular tachycardia, and unknown shockable rhythm
†Among patients admitted to hospital
‡Among hospital survivors, cerebral performance categories 1 & 2
AED indicates automated external defibrillator; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ROSC, return of spontaneous circulation
Figure Legends:

**Figure 1.** Geographic Origin of Study Patients. The map represents regions participating in CARES. State sites depict states participating in statewide data collection. Current sites depicts regions participating in CARES.

**Figure 2.** Distribution of OHCA Occurrence by Hour of the Day. p<0.001 for Chi-squared goodness of fit across all hours of the day for the overall population, patients with unwitnessed arrest and non-shockable first cardiac rhythm, and patients with witnessed arrest and shockable first cardiac rhythm.

**Figure 3.** Distribution of Survival to Hospital Discharge by Hour of the Day. p<0.001 for Chi-squared goodness of fit across all hours of the day.

**Figure 4.** Distribution of OHCA by Day of the Week. p<0.001 for Chi-squared goodness of fit across all days of the week.

**Figure 5.** Distribution of Survival to Hospital Discharge by Day of the Week. p=0.32 for Chi-squared goodness of fit across all days of the week.

**Figure 6.** Distribution of OHCA by Month of the Year. p<0.001 for Chi-squared goodness of fit across all months of the year.

**Figure 7.** Distribution of Survival to Hospital Discharge by Month of the Year. p=0.002 for Chi-squared goodness of fit across all months of the year.
Figure 2

- **Overall population (N=18,588)**
- **Unwitnessed arrest with non-shockable first cardiac rhythm (N=7,780)**
- **Witnessed arrest with shockable first cardiac rhythm (N=3,386)**
Figure 3

Survival to hospital discharge (%) vs. Hour of Day

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Figure 4
Figure 5

Survival to hospital discharge (%) by day of the week.
Figure 7

Survival to hospital discharge (%) by month of year.
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